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Strokovni prispevek/Professional article

HEMOPTIZE PRI BOLNIKIH Z NORMALNIM RENTGENOGRAMOM PRSNEGA KOŠA

HEMOPTYSIS IN PATIENTS WITH NORMAL CHEST RADIOGRAPH

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Prispelo 1997-02-05, sprejeto 1997-04-23; ZDRAV VESTN 1997; 66: 465–7

Ključne besede: *bronhoskopija; bronhoalveolarni izpirek; krtačenje; bronhografija*

Izvleček – Izhodišča. *Pri bolnikih s krvavim izkašljevanjem in sumom, da krvavitev izhaja iz pljuč, v diagnostičnem postopku opravimo predvsem bronhoskopijo z upogljivim inštrumentom. Natančen vrstni red in izbira diagnostičnih postopkov med bronhoskopijo pri bolnikih s hemoptizami in normalno rentgensko sliko pljuč ni vsesplošno sprejet.*

Metode. *V retrospektivnem pregledu smo v obdobju 2 let zajeli bolnike s hemoptizami, normalno rentgensko sliko pljuč in lokalizirano bronhialno krvavitvijo. Med bronhoskopijo so odvzeli bronho-alveolarni izpirek prizadetega bronha na kislino odporne bakterije, krtačili krvaveči bronh za citološki pregled in na koncu opravili še selektivno bronhografijo.*

Rezultati. *Od 131 bolnikov s hemoptizami in normalno rentgensko sliko pljuč je imelo bronhoskopsko lokalizirano krvavitev 21 bolnikov (16%). Večina je bila moških s povprečno starostjo okoli 60 let. Pri 3 bolnikih smo dokazali bronhialni karcinom, pri 1 sum na malignom, pri nobenem pa nismo bakteriološko potrdili tuberkuloze oz. bronhografsko morebitnih bronhiektazij.*

Zaključki. *Kljub normalni rentgenski sliki pljuč in srca moramo pri bolnikih s hemoptizami, kadilcih ali bivših kadilcih, starejših od 40 let, obvezno opraviti še bronhoskopijo. Od specifičnih diagnoz je po incidenci na prvem mestu bronhialni karcinom. Tudi endobronhialna tuberkuloza ni izključena. Pri hemoptizah in normalni rentgenski sliki pljuč so bronhiektazije malo verjetne.*

Key words: *bronchoscopy; bronchoalveolar lavage; brushing; bronchography*

Abstract – Background. *The patients with hemoptysis and normal chest radiograph, must underwent fiberoptic bronchoscopy. The choice of diagnostic procedures during bronchoscopy is not generally accepted.*

Methods. *In the retrospective 2 years long survey, we evaluated patients with hemoptysis, normal chest radiograph and localized bronchial bleeding. All underwent fiberoptic bronchoscopy with broncho-alveolar lavage for acid-fast bacilli, bronchial brushing for cytological examination and finally bronchography of involved bronchus was done.*

Results. *There were 131 patients with hemoptysis and normal chest radiograph, and between them 21 (16%) patients accompanied with localized segmental bleeding. There were mostly men with average age about 60 years. We proved 3 bronchial carcinomas, 1 result was suspicious for carcinoma, none of the broncho-alveolar lavages was positive for Mycobacterium tuberculosis and none of bronchography revealed bronchiectasiae.*

Conclusions. *Normal chest radiograph in patients with hemoptysis, smokers and older than 40 years doesn't exclude the need for bronchoscopy. The incidence of bronchial carcinoma is most likely. Also endobronchial tuberculosis is possible. The bronchiectasiae rarely accompany normal chest radiograph.*

Uvod

Hemoptize imenujemo razne oblike izkašljevanja krvi. Ločimo hemoptize – izkašljevanje sledov ali malih količin krvi in hemoptoe – obilno krvavo izkašljevanje več kot 250 ml/24 ur (1).

Čeprav lahko bolnik krvavi iz katerega koli dela dihalnih poti, je krvavitev iz spodnjih dihal pogostejša kot iz zgornjih (2). Moramo pa upoštevati, da kri iz nosu oziroma žrela lahko v spanju zateka v spodnja dihala in se kasneje izkašlja.

Po navadi ni težko ločiti izkašljevanja krvi od hematemeze – bljuvanja krvi. O tem nam pove še sam bolnik. Kri iz dihal je svetlo rdeča in penasta, ima alkalen pH in vsebuje alveolarne makrofage, prežete s hemosiderinom. Kri, ki izhaja iz prebavil, pa je temna, kislega pH in pomešana z delci hrane (3).

Ko posumimo, da so organ izvora krvavitve pljuča, pričnemo iskati mesto krvavitve. Pri tem si pomagamo z rentgenogramom pljuč in srca ter z bronhoskopijo (1–6).

Splošno pravilo pravi, da so pri bolnikih srednjih let vodilni vzroki za hemoptize mitralna stenoza, tuberkuloza, pljučnica ali bronhiektazije, po 40. do 45. letu pa pljučni rak in tuberkuloza (2, 4, 7). Natančen vrstni red in izbira raznih diagnostičnih postopkov med samo bronhoskopijo pri bolnikih s hemoptizami, ki jih spremlja sicer normalen rentgenogram pljuč in srca, ni vsesplošno sprejet (8–11).

V študiji smo poglobljeno obdelali bolnike z normalnim rentgenogramom pljuč in srca, ki so bili zaradi hemoptiz bronhoskopirani in pri katerih je endoskopski izvid potrdil lokalizirane segmentne krvavitve.

Material in metode

V retrospektivnem pregledu smo zajeli bolnike, ki so se zaradi hemoptiz zdravili na pljučnem oddelku Bolnišnice Topolšica v obdobju od začetka januarja 1994 do konca decembra 1995. Vsem smo opravili bronhoskopijo z upogljivim inštrumentom (Olympus BF10 ali Olympus BF IT 10). Anestezija je bila lokalna s ksilokainom, premedikacija pa z atropinom. V skupini bolnikov, ki so imeli normalen rentgenogram pljuč, smo izbrali bolnike, pri katerih je endoskopski izvid pokazal lokalizirano segmentno (bronhialno) krvavitev. Že vrsto let se ravnamo po »hišni« doktrini. V takem primeru najprej opravimo bronhoalveolarni izpirek prizadetega bronha na kislino odporne bakterije (v prizadeti bronh vbrizgamo do 60 ml fiziološke raztopine ter jo nato posesamo v zbiralno posodo), nato krtačimo krvaveči bronh za citološki pregled, na koncu pa opravimo še selektivno bronhografijo.
Metodološko smo tako dobili enovito skupino bolnikov, ki smo jo obdelali po načelih biomedicinske statistike s pomočjo računalniškega programa Microsoft Excel.

Rezultati

V obdobju 24 mesecev smo bronhoskopirali 131 bolnikov s hemoptizami, vendar z normalnim rentgenogramom pljuč. Povečano srce smo ugotovili pri 21 bolnikih (16%).
Večina preiskovancev je bila moških (M=77 [59%], Ž=54 [41%]) s sorazmerno visoko povprečno starostjo (M=59 let oz. od 36 do 85 let, Ž=65 let oz. od 49 do 91 let).
Pri 39 bolnikih (30%) smo vso diagnostiko do potrditve končne diagnoze izpeljali ambulantno, ostale smo obravnavali hospitalno.
Za bronhoskopijo smo uporabljali upogljiva inštrumenta. Preiskava je večinoma potekala prek nosu (69%), v 30% prek ust in v 1% prek traheostome.
Po 6 tednih so bile vse kulture bronhoalveolarnih izpirkov na mikobakterijo tuberkuloze negativne.
Za malignost negativni citološki izvidi so nakazovali možnost na metaplazijo oz. na akutno ali kronično vnetje. Od treh na malignost pozitivnih izvidov smo v 2 primerih dokazali epidermoidni karcinom, v 1 primeru pa nemikrocelularni karcinom. 1 sumljiv izvid se je v nadaljnjem diagnostičnem postopku izkristaliziral v epidermoidni karcinom.
Vsi štirje bolniki so bili moški, kadilci in starejši od 60 let.

Tab. 1. *Bronhoskopski izvid pri bolnikih s hemoptizami in normalnim rentgenogramom pljuč (možnih več pojavov pri istem bolniku).*

Tab. 1. *Endoscopic appearance of bronchial mucosa in patients with hemopthysis and normal chest radiograph (in one patient was possible more findings).*

Bronhoskopski izvid Bronchoscopic finding	Bolniki Patients	Število No.	% %
Normalen izvid Normal finding		5	4
Akutni bronhitis Acute bronchitis		54	41
Kronični bronhitis Cronic bronchitis		38	29
Stanje po tuberkulozi Healed old tuberculosis		26	20
Posredni znaki srčnega popuščanja Indirect signs of cardiac failure		18	14
Omejena segmentna krvavitev Localised segmental bleeding		21	16
Segmentna zožitev Segmental narrowing		22	17
Difuzno ranljiva sluznica Diffuse vulnerable mucosa		5	4
Bronhomalacija osteohondroplastika Bronchomalathia osteochondroplastica		6	5

Tab. 2. *Rezultati bronhoalveolarnega izpiranja (BAL) na kislino odporne bakterije (ARB), citološkega izvida krčenja bronha in bronhografije pri bolnikih z lokalizirano segmentno krvavitvijo.*

Tab. 2. *Results of bronchoalveolar lavage (BAL) for acid-resistant bacteria (ARB), cytologic evaluation of bronchial brushing and bronchography in patients with localised segmental bleeding.*

Izvid Result	Pozitiven Positive	Negativen Negative	Sumljiv Suspicious	Skupno Total
ARB iz BAL-a ARB from BAL	0	21	0	21
Citologija Cytology	3	17	1	21
Bronhografija Bronchography	0	11	0	11

Razpravljanje

Bronhoskopija z upogljivim inštrumentom je uspešna metoda pri postavljanju dokončne diagnoze pri centralnih endobronhialnih boleznih. Občutljivost preiskave je krepko nad 95% (12). Kljub temu je diagnostična vrednost preiskave pri bolnikih s hemoptizami in normalnim rentgenogramom prsnega koša nizka. Večina poročil navaja občutljivost med 0 in 40% (7, 10, 13–15). Tudi pri naši skupini bolnikov smo določili mesto krvavitve le pri 21 bolnikih (16%), za ostalih 105 bolnikov (80%) pa smo na vzrok krvavitve posumili posredno. Le 5 bolnikov (4%) je imelo popolnoma normalen endoskopski izvid, pregledani so bili tudi pri specialistih ORL. Vzrok krvavega izkašljevanja je ostal pri njih popolnoma nepojasnjen.
Jackson s sod. je v skupini 47 bolnikov s hemoptizami odkril le 2 pljučna raka (13). Peters in sod. ni v skupini 26 bolnikov s hemoptizami in normalnim rentgenogramom prsnega koša odkril nobenega s specifično etiologijo (10). Nasprotno pa je Poe s sod. dokazal vzrok krvavitve v bronhialni sistem v 17% (8).
Incidenca bronhialnega karcinoma je pri bolnikih z normalnim rentgenogramom prsnega koša nizka (7, 8, 13–16). Santiago s sod. je odkril pljučnega raka pri komaj 4 bolnikih od 78 (5%), Poe s sod. pa le pri 12 bolnikih (6%) (7, 8). Tudi v naši študiji je odstotek bolnikov s pljučnim rakom nizek (3/21 oz. 14%). Če pa vzamemo v poštev vse bolnike, ki so imeli v anamnezi hemoptize, je pogostnost še nižja (3/131 oz. 2%). Seveda pa je uspešnost bronhoskopije pri odkrivanju pljučnega raka pri bolnikih s spremembami na rentgenogramu prsnega koša bistveno višja (13, 15–18).
Klinik, ki se sooča s klinično in radiološko sumljivo pljučno tuberkulozo, kulture bolnikovega izmečka na za kislino odporne bacile, pa so trikrat zapored negativne oz. jih ne more dati, mora preden prične ustrezno zdraviti, dokazati tuberkulozo bakteriološko in/ali histološko s pomočjo bronhoskopije (19–21). Le tako se bomo izognili lažno pozitivni podmeni oz. ne bomo spregledali pljučnega raka ali druge bolezni (1, 20).
Pri naših bolnikih z bronhialno krvavitvijo in normalno rentgensko sliko nismo pri nikomur dokazali na kislino odporne bakterije pozitivnega bronhialnega izpirka. Tudi vse kulture kužnin so bile po 6 tednih negativne. To pa ne pomeni, da pri normalni rentgenski sliki in hemoptizah tuberkuloza ni možna. Vsekakor je incidenca te kombinacije nizka, naša skupina bolnikov pa je bila premajhna, da bi take primere tudi zajela. Opisani so sporadični primeri endobronhialne tuberkuloze brez kliničnih in radioloških kazalcev bolezni, ki imajo edini simptom krvavkasto izkašljevanje (22, 23).
Pogostnost bronhiektazij pri bolnikih z normalno rentgensko sliko je tudi nizka (24, 25). V naši skupini, ki je sicer statistično

bistveno premajhna za zanesljivo sklepanje, so bile vse bronhiografije glede odkrivanja okultnih bronhiektazij negativne. Menimo, da bi v prihodnje lahko ta diagnostičen postopek pri bolnikih z normalno rentgensko sliko in omejeno bronhialno krvavitvijo izpustili.

Zadnje čase se v primeru hemoptiz in suma na bronhiektazije vedno pogosteje govori o CT diagnostiki prsnega koša (24, 25). Pri obeh študijah so med glavno karino in spodnjimi pljučnimi venami uporabljali reze v 5-milimetrskih razmikih in s prirejeno tehniko iskali razširjene bronhialne svetline. Opažali so visoko občutljivost omenjene tehnike.

Ker je CT diagnostika prsnega koša v primerjavi z bronhoskopijo in bronhografijo bistveno dražja, čeprav je za bolnike udobnejša, bi bilo morda potrebno izdelati slovenske smernice, kdaj uporabljati eno metodo oz. kdaj drugo.

V naši študiji še nismo uporabili te diagnostike, ker rentgenološko v nobenem primeru ni obstajal sum na bronhiektazije.

Literatura

1. Šorli J. Bolezni dihal. In: Kocijančič A, Mrevlje F. Interna medicina. Ljubljana: Državna založba Slovenije, 1993; 253–4.
2. Haeley P, Jacobson E. Common Medical Diagnoses: An Algoritmic Approach. Philadelphia: Saunders 1990; 14–5.
3. Fraser RG, Pare JAP. Diagnoses of diseases of the chest. Philadelphia: Saunders 1978; 38–9.
4. Babowitz ID, Ramakrishna S, Shim JS. Comparison of medical vs. surgical treatment of major hemopthysis. Arch Intern Med 1983; 143: 1343–6.
5. Zavala DC. Diagnostic fiberoptic bronchoscopy: techniques and results of bronchoscopy. Chest 1975; 68: 12–9.
6. Smiddy JF, Elliot RC. The evaluation of hemoptysis with fiberoptic bronchoscopy. Chest 1973; 64: 158–62.
7. Santiago S, Tobias J, Williams AJ. A reappraisal of the cause of hemopthysis. Arch Intern Med 1991; 151: 2449–51.
8. Poe RH, Israel RH, Marin MG et al. Utility of fiberoptic bronchoscopy in patients with hemoptysis and a nonlocalising chest roentgenogram. Chest 1988; 92: 70–5.
9. Heimer D, Bar-Ziv J, Scharf SM. Fiberoptic bronchoscopy in patients with hemopthysis and nonlocalising chest roentgenogram. Arch Intern Med 1985; 145: 1427–8.
10. Peters J, McClung HC, Teague RB. Evaluation of hemopthysis in patients with normal chest roentgenogram. West J Med 1984; 141: 624–6.
11. Aberle DA, Brown K, Joung DA, Batra P, Sleckel RJ. Imaging techniques in the evaluation of tracheobronchial neoplasms. Chest 1991; 99: 211–5.
12. Dierksman R. The diagnostic yield of bronchoscopy. Cardiovasc Intervent Radiol 1991; 14: 24–8.
13. Jackon CV, Savage PJ, Quinn DL. Role of fiberoptic bronchoscopy in patients with hemopthysis and normal chest roentgenograms. Chest 1985; 87: 142–4.
14. Sharma SK, Dey AB, Pande JN, Verma K. Fiberoptic bronchoscopy in patients with haemopthysis and normal chest roentgenograms. Indian J Chest Dis and Allied Sci 1991; 33: 15–8.
15. Rath GS, Shaff JT, Snider GL. Flexible fiberoptic bronchoscopy: techniques and review of 100 bronchoscopies. Chest 1973; 63: 689–93.
16. Lederle FA, Nichol KL, Parenti CM. Bronchoscopy to evaluate haemopthysis in older men with nonsuspicious chest roentgenograms. Chest 1989; 95: 1043–7.
17. Adelman M, Haponik EF, Bleeker ER, Britt EJ. Cryptogenic hemopthysis: clinical features, bronchoscopic findings, and natural history of 67 patients. Ann Intern Med 1985; 102: 829–34.
18. Suri JC, Singla R. Cryptogenic haemopthysis; role of fiberoptic bronchoscopy. Indian J Chest Dis and Allied Sci 1990; 32: 49–52.
19. Koren I. The value of fiberoptic bronchoscopic diagnostic methods in patients with negative sputum smear. Zdrav Vestn 1993; 62: 41–4.
20. Mehta J, Krish G, Berro E, Harvill L. Fiberoptic bronchoscopy in the diagnosis of pulmonary tuberculosis. Southern Med J 1990; 83: 753–5.
21. Chawla R, Pant K, Jaggi O, Chandrashekhar S, Thukral S. Fiberoptic bronchoscopy in smear negative pulmonary tuberculosis. Eur Respir J 1988; 1: 804–5.
22. Gadiolet J, Bayle J, Petrol M, Guerin J. La tuberculose bronchique. A propos de 4 cas. Rev Pneumol Clin 1990; 46: 109–13.
23. Breysem Y, Brande P, Bockaert J, Demedts M. Tracheobronchial tuberculosis ulceration. Report of 2 cases. Acta Clin Belg 1990; 45: 38–41.
24. Pak S, Flower S, Smith I, Cahn A, Twentyman O, Shneerson J. Hemoptysis: comparative study of the role of CT and fiberoptic bronchoscopy. Radiology 1993; 1801: 677–80.
25. McGuinness et al. Hemoptysis: prospective high-resolution CT/bronchoscopic correlation. Chest 1994; 105: 1155–62.

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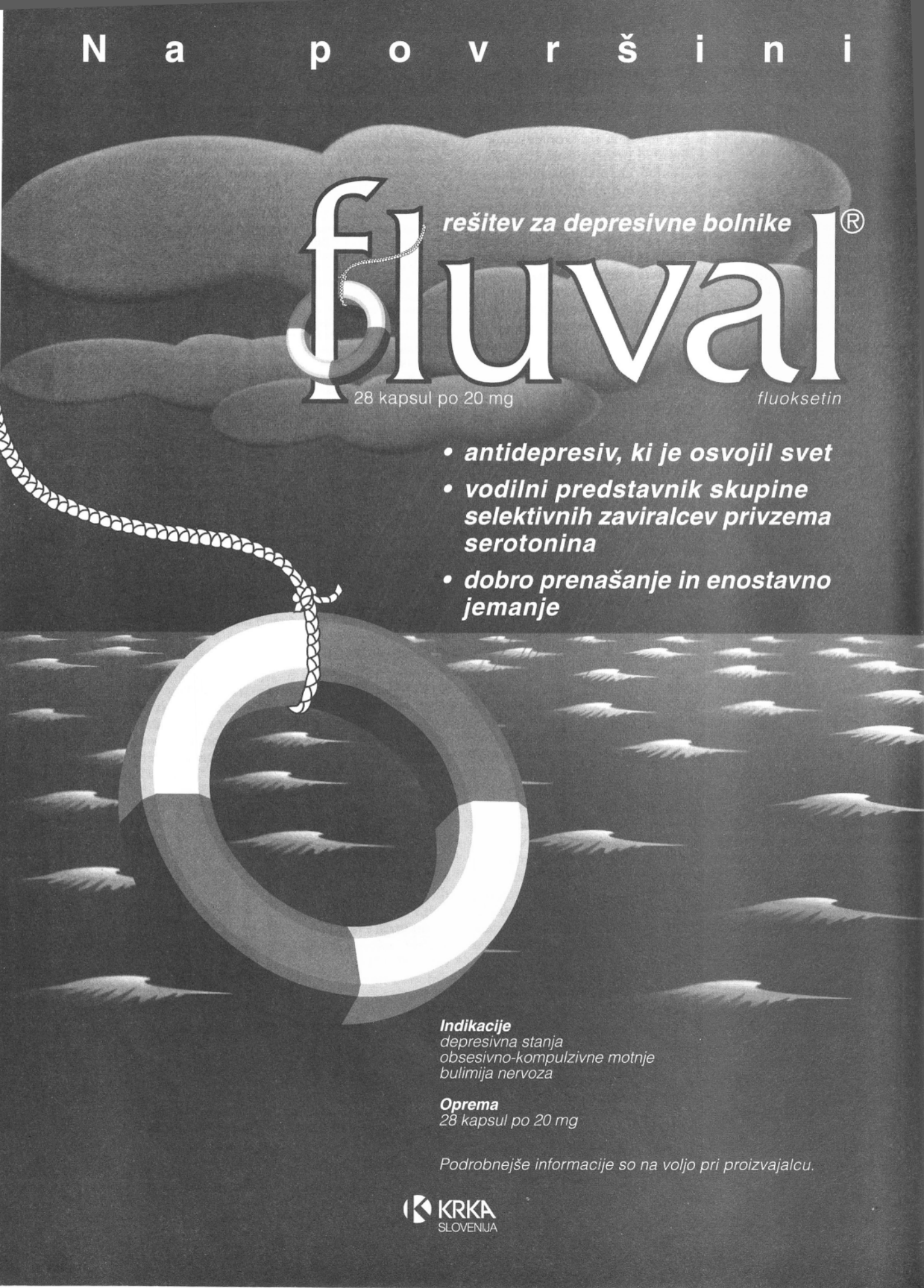

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EPIDEMIOLOGIJA INVAZIVNIH OKUŽB S HAEMOPHILUSOM INFLUENZAE TIP B PRI OTROCIH V SLOVENIJI, 1993–1995

EPIDEMIOLOGY OF INVASIVE HAEMOPHILUS INFLUENZAE TYPE B DISEASE IN CHILDREN IN SLOVENIA, 1993–1995

Milan Čižman[1], Metka Paragi[2], Marija Gubina[3], Nadja Jovan Kuhar[2], Marko Pokorn[1] in Slovenska skupina za proučevanje meningitisa (Alenka Kraigher, Jana Fišer, Jana Kolman, Dušan Novak, Bojan Drinovec, Tatjana Harlander, Davorin Sabotin, Alenka Štorman, Gorazd Lešničar, Dušan Kolarič, Marjan Strojan, Štefan Kopač, Lučka Kunstelj, Milan Špegel, Ana Meštrovič, Dana Košiček, Magda Lušič Drobnič, Rajko Kenda, Ludvik Hajdinjak, Stane Lovšin, Jože Bedernjak)

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Ključne besede: *Haemophilus influenzae tip b; invazivne okužbe; otroci; epidemiologija*

Izvleček – Izhodišča. *Haemophilus influenzae tip b pogosto povzroča sistemske okužbe pri otrocih, mlajših od 5 let. Pred uvedbo cepljenja proti tej bakteriji, ki je marsikje v svetu že rutinsko, je treba poznati osnovne epidemiološke podatke.*

Bolniki in metode. *V prospektivno triletno študijo, ki je zajela vso Slovenijo, smo vključili otroke, stare od 0 do vključno 14 let, v obdobju od januarja 1993 do decembra 1995. Pri njih smo izolirali H. influenzae tip b iz krvi, možganske tekočine ali druge, sicer sterilne telesne tekočine.*

Rezultati. *V triletnem obdobju smo dokazali 56 invazivnih okužb, ki jih je povzročil H. influenzae tip b, kar predstavlja 96,6% vseh izolatov H. influenzae. Od kliničnih sindromov smo najpogosteje ugotovili meningitis (68%), sledijo pljučnica (12%), bakteriemija/sepsa (7%) in v posameznih primerih še druge žariščne okužbe. Letna incidenca je bila pri otrocih pod 5 leti starosti 16,4 na 100.000 otrok, incidenca meningitisa pa 13,35 na 100.000 otrok v isti starostni skupini. Smrtnost je bila 3,6%.*

Zaključki. *S triletno študijo smo ugotovili nižjo incidenco invazivnih okužb s H. influenzae tip b v primerjavi s študijami v drugih razvitih državah. Rezultati nam bodo osnova za izračun ekonomske upravičenosti cepljenja v Sloveniji.*

Key words: *Haemophilus influenzae type b; invasive disease; children; epidemiology*

Abstract – Background. *Haemophilus influenzae type b is a frequent cause of systemic infections in children under 5 years of age. Active immunization against Haemophilus influenzae is routinely performed in many countries. A basic knowledge of epidemiology of these infections in Slovenia is necessary before introduction of vaccination.*

Patients and methods. *Children aged 0 to 14 years with Haemophilus influenzae type b isolated from blood, CSF or other normally sterile body site in a period from January 1993 to December 1995 were included in a nationwide prospective study.*

Results. *In a 3-year period, 56 invasive Hib infections were observed, representing 96.6% of all Haemophilus influenzae isolates. Meningitis was the most frequent clinical syndrome (68%), followed by pneumonia (12%), bacteremia/sepsis (7%) and other focal infections. The incidence of Hib disease in children under 5 years of age was 16.4/100,000, the incidence of Hib meningitis was 13.35/100,000 per year in the same age group. Mortality was 3.6%.*

Conclusions. *Compared to developed countries a lower incidence of invasive Hib disease was observed in our 3-year study. The results obtained will provide a basis for an cost-benefit evaluation of potential benefits of Hib vaccination in Slovenia.*

Uvod

Haemophilus influenzae tip b (Hib) pogosto povzroča težke okužbe (tab. 1) in smrt pri otrocih, mlajših od 5 let. Pred uvedbo cepljenja proti tej bakteriji v razvitih državah je bila incidenca okužb pri otrocih, mlajših od 5 let, med 20 in 65 primerov na 100.000 otrok. V manj razvitih predelih je bila incidenca do desetkrat višja (1–8). Leta 1988 so cepljenje proti Hib uvedli v ZDA, kasneje pa še v drugih razvitih državah. Po uvedbi cepljenja so v teh državah opažali več kot 90-odstotno znižanje incidence okužb s to bakte-

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rijo (9–13). V Sloveniji pa je bila incidenca meningitisa, povzročenega s Hib, v predhodnih študijah nižja kot v drugih razvitih državah (14, 15).

Tab. 1. *Bolezni in klinični sindromi, ki jih povzroča Haemophilus influenzae (28).*

Tab. 1. *Diseases and clinical syndromes caused by Haemophilus influenzae (28).*

Bolezen/sindrom Disease/syndrome	Tip Type	Komentar Comment
Invazivne	večinoma tip b	bakteriemija pogosto spremlja bolezen ali klinični sindrom
Meningitis Celulitis Septični artritis Bakteriemija Empiem Perikarditis Osteomielitis Tkivni absces Endoftalmitis Epiglotitis		
Neinvazivne	večinoma ne tip b ali netipizirajoči sevi	razširitev okužbe po kolonizaciji površine sluznic
Bronhitis Otitis media Sinusitis Okužba sečil		
Neopredeljen	tip b, drugi tipi ali	ima značilnosti invazivne in
Pljučnica	netipizirajoči sevi	neinvazivne bolezni

V članku prikazujemo rezultate triletne prospektivne nacionalne študije invazivnih okužb s Hib z namenom, da dobimo natančnejše epidemiološke podatke, ki nam bodo koristili pri uvedbi rutinskega cepljenja proti Hib.

Bolniki in metode

Definicija primera

Okužbo smo smatrali za invazivno, kadar smo izolirali Hib pri otrocih, starih 0–14 let, iz krvi, likvorja ali druge, sicer sterilne telesne tekočine. Invazivne bolezni smo razvrstili glede na lokalizacijo. Bolnike, pri katerih smo izolirali Hib iz krvi in klinično niso imeli znakov žariščne okužbe ali pa le blage znake vnetja zgornjih dihalnih poti, smo opredelili kot primere bakteriemije brez očitnega žarišča okužbe. Meningitis je bil opredeljen z izolacijo bakterij iz likvorja ali zvišanjem levkocitov v likvorju (več kot 10×10^6/L) in izolacijo bakterije iz krvi. Pljučnica je bila prisotna, če je imel bolnik značilne simptome in znake bolezni in so bile vidne značilne spremembe na rentgenski sliki pljuč. Celulitis smo opredelili kot lokalni vnetni proces v mehkem tkivu, sinusitis pa, če je imel bolnik ustrezne znake in simptome bolezni in značilne spremembe na rentgenski sliki. Diagnozo epiglotitisa je postavil otorinolaringolog z neposrednim pregledom grlnega poklopca. Artritis smo definirali klinično in ga potrdili z izolacijo bakterije iz sklepne tekočine ali krvi.

Populacija otrok

Število, starostno in geografsko porazdelitev otrok, starih do 15 let, smo dobili iz letnega statističnega letopisa Slovenije v letih 1993 do 1995. V Sloveniji je bilo v tem obdobju od 1,990.623 do 1,983.012 prebivalcev. Število otrok, mlajših od 15 let, se je znižalo s 379.419 v letu 1993 na 356.862 v letu 1995. Število rojstev se je prav tako znižalo v tem obdobju, in sicer z 19.793 na 18.980 otrok letno (16).

Otroci se zdravijo v Sloveniji na devetnajstih otroških oddelkih splošnih bolnišnic ali infekcijskih oddelkov in dveh klinikah. Izolacijo bakterij so izvršili v devetih mikrobioloških laboratorijih. Vsi laboratoriji in vsi otroški oddelki so sodelovali v študiji.

Zbiranje izolatov

Študija je trajala od 1. 1. 1993 do 31. 12. 1995. Mikrobiološki laboratoriji so izolirali H. influenzae po standardnem postopku (17). Vse izolate so poslali v transportnem gojišču na Inštitut za varovanje zdravja Republike Slovenije (IVZ) za potrditev in nadaljnjo analizo. Centralni laboratorij je poslal prijavo o izolaciji vodji projekta (M. Č.), ki je nato prosil za fotokopijo odpustnice iz bolnišnice, kjer se je bolnik zdravil. V protokol smo vnesli osnovne demografske podatke, kot so starost in spol bolnika, mesec pojava bolezni, trajanje hospitalizacije, klinično diagnozo in izhod bolezni. Vse klinične diagnoze smo preverili in uskladili z definicijo primera. Na IVZ so vse seve H. influenzae tipizirali s komercialnim setom (Difco laboratories, Detroit, Michigan). Za potrditev tipa b smo dodatno uporabljali še koaglutinacijski test (Phadebact Haemophilus test, Boule Diagnostics, Sweden) (18). Odpornost na antibiotike smo določali v vsakem mikrobiološkem laboratoriju z difuzijsko metodo in nato preiskavo ponovili v Mikrobiološkem laboratoriju IVZ. Prisotnost betalaktamaz smo določevali z nitrocefinskim testom.

Statistična analiza

Za statistično analizo smo uporabljali test hi kvadrat. Vrednost p, nižjo od 0,05, smo ocenjevali kot statistično značilno.

Rezultati

V triletnem obdobju smo izolirali Hib pri 56 otrocih. Tip b predstavlja 96,6% vseh izolatov H. influenzae. Pri enem osemmesečnem otroku z bakterijskim meningitisom smo izolirali H. influenzae tip f, pri drugem novorojencu s sepso pa je bil izoliran H. influenzae, ki ga ni bilo mogoče tipizirati. V prvem letu študije je zbolelo 16 otrok, v drugem 29 in v tretjem letu 11. Hib je bil izoliran iz krvi pri 27/56 (48,2%) otrok, iz likvorja pri 14/56 (24,9%) in iz obeh kužnin pri 15/56 (26,7%) otrok. Prevladovali so dečki v razmerju 30:26 (1,15/1, statistično ni značilno).

Porazdelitev po starosti

Petnajst (26,7%) otrok je bilo mlajših od enega leta, 43 (76,7%) od dveh let in 52 (92,8%) mlajših od 5 let. Povprečna starost je bila 22,2 meseca.

Incidenca

Letna incidenca Hib bolezni je bila 5,06 primera na 100.000 otrok, mlajših od 15 let, in 16,4 oz. 36,7 na 100.000, mlajših od 5 oziroma dveh let. Letna incidenca meningitisa kot najpogostejše klinične manifestacije okužbe s Hib je bila 13,35 na 100.000 otrok, mlajših od 5 let. Incidenca v posameznih geografskih regijah v Sloveniji je prikazana na tabeli 2.

Mesto okužbe

Meningitis je bil najpogostejši klinični sindrom. Ugotovili smo ga pri 38 otrocih. Sedem otrok je imelo pljučnico. Ti dve bolezni predstavljata 80% vseh invazivnih bolezni, povzročenih s Hib. Druga mesta okužbe so prikazana na tabeli 3.

Geografska porazdelitev

Incidenca je bila različna v posameznih regijah in je prikazana na tabeli 2.

Najvišja je bila v ljubljanski regiji. Sledi Celje in Novo mesto, kjer je incidenca skoraj za polovico nižja. Najnižja je v Kopru in Murski Soboti. Razlike so statistično značilne ($p<0,05$).

Tab. 2. *Število in incidenca invazivnih okužb pri otrocih <15 let s Haemophilus influenzae tipom b v Sloveniji v obdobju 1993–1995 po različnih geografskih regijah.*

Tab. 2. *Number and incidence of invasive Haemophilus type b disease in Slovenia in 1993–1995 in different regions of the country.*

Regija Region		Število Number	Incidenca Incidence	Število otrok <15 let v letih 1993–1995 Number of children <15 years, 1993–1995
Ljubljana		29	25,5	106.561
Infekc. kl.	24			
Pediatr. kl.	3			
Trbovlje	1			
MOB	1			
Maribor		9	9,8	71.605
Infekc. odd.	1			
Ptuj	5			
S. Gradec	3			
Celje		7	14,7	47.508
Infekc. odd.	5			
Otr. odd.	2			
Kranj		3	8,0	37.364
Otr. odd. SB Jesenice				
Novo mesto		4	14,3	27.847
Otr. odd.	4			
Nova Gorica		2	10,2	19.520
Koper		1	4,4	22.337
Murska Sobota		1	4,1	24.120

Tab. 3. *Diagnoze 56 otrok, starih <15 let, s sistemsko okužbo s H. influenzae tipom b po starosti v Sloveniji v obdobju 1993 do 1995.*

Tab. 3. *The diagnoses of 56 children under 15 years of age with invasive H. influenzae type b disease in Slovenia, 1993 to 1995.*

	Starost v mesecih Age in months					
	<12	13–24	25–60	>60	Število Number	%
Meningitis Meningitis	13	16	6	3	38	68
Pljučnica Pneumonia	2	4	1		7	12
Bakteriemija/sepsa Bacteremia/sepsis		1	3		4	7
Epiglotitis Epiglotitis		1	1		2	3,5
Artritis Arthritis			1	1	2	3,5
Celulitis Cellulitis	1	1			2	3,5
Sinusitis Sinusitis			1		1	1,7
Skupno Total	16	23	13	4	56	

Sezonska porazdelitev

Okužbe s Hib so se pojavljale skozi vse leto, najpogosteje jeseni in pozimi (od oktobra do marca). Drugi vrh je bil poleti, junija in julija.

Izid bolezni

Smrtnost okužb s Hib je bila 3,6%. Umrla sta dva otroka, oba zaradi meningitisa. Stara sta bila 7 in 13 mesecev. Izid bolezni pri ostalih bolnikih z meningitisom še ni povsem znan. Ob odhodu iz bolnišnice je bilo 24/38 (63%) otrok brez vidnih posledic, 5/38 (13,2%) je imelo posledice, pri ostalih sedmih (18,4%) pa se zaradi nizke starosti klinično ni dalo ugotoviti, ali so le-te prisotne ali ne. Otroci z drugimi kliničnimi diagnozami so bolezen preboleli brez posledic.

Trajanje hospitalizacije

Hospitalizacija je trajala v povprečju 18,3 (1–48) dneva pri otrocih, ki so imeli meningitis, 14,2 (5–20) dneva pri otrocih s pljučnico, 14,7 (13–17) z bakteriemijo in 11,4 (4–30) dneva pri otrocih z drugimi lokaliziranimi okužbami.

Občutljivost Hib

Osem od 52 Hib izolatov (15,3%) je tvorilo betalaktamaze. Občutljivost na kloramfenikol je bila 98% (53/54), prav takšna na cefotaksim (53/54). Na cefuroksim je bilo občutljivih 96% (52/54) sevov Hib, na ceftriakson 92% (49/53), ampicilin/sulbaktam 91% (50/55), amoksicilin/klavulansko kislino 89% (49/55), cefaklor 79% (42/53) in na TMP/SMX 60% (29/49).

Razpravljanje

Prospektivna nacionalna študija je v primerjavi z razvitimi državami pokazala nižjo incidenco okužb s Hib v vseh starostnih skupinah (2–4, 19). V Sloveniji je bila incidenca 16,4 na 100.000 otrok pri otrocih pod petimi leti starosti, v razvitih državah pa je bila pred uvedbo rutinskega cepljenja med 20 in 60 na 100.000 otrok pod petimi leti starosti. Izjema je edino študija v Italiji, kjer so našli še nižjo pogostnost (15,7 na 100.000 otrok) kot pri nas (20). Nižja je bila tudi incidenca meningitisa kot najpogostejšega kliničnega sindroma. Vprašanje je, ali je incidenca v resnici nižja ali pa niso bile dokazane vse okužbe.

Incidenca meningitisa v tokratni študiji je bila 13,35/100.000 otrok pod petimi leti starosti in je bila rahlo višja, kot smo jo ugotovili v retrospektivni študiji v obdobju 1979 do 1988, in je zajela približno polovico slovenske populacije (14). Če predpostavimo, da v Sloveniji postavimo diagnozo bakterijskega meningitisa z enako verjetnostjo kot v drugih razvitih državah, potem lahko zaključimo, da je v Sloveniji kot delu Južne Evrope incidenca invazivnih bolezni, ki jih povzroča Hib, nižja. V Sloveniji opažamo statistično značilne razlike v zbolevnosti med posameznimi regijami. To je lahko posledica različne naseljenosti populacije ali razlik in možnosti pri diagnosticiranju sistemskih okužb s Hib.

V prvem letu življenja je zbolelo 27% otrok in do petega leta 93%. Rezultati so podobni kot v Angliji in drugačni, kot so jih opazovali v Izraelu, kjer zboli do starosti dveh let že 93% otrok (4, 2).

Meningitis je bila najpogostejša klinična diagnoza invazivne bolezni, povzročene s Hib. V naši študiji je imelo meningitis 68% vseh otrok z izolacijo Hib. Delež je primerljiv s podatki drugih avtorjev, ki se gibljejo med 41% in 71% (3–5, 16, 21). Od drugih kliničnih sindromov odstopa predvsem epiglotitis, ki so ga v drugih študijah v Evropi ugotovili med 12 in 36% (3–5). Pogostnost pri nas je podobna kot v Izraelu in je tudi nižja kot v ZDA, kjer je epiglotitis predstavljal 4–17% vseh kliničnih sindromov (6, 22). Tudi rezultati ankete, ki smo jo izvedli v Sloveniji v obdobju 1993–1995, kažejo, da epiglotitis v Sloveniji pri otrocih ni pogosta bolezen (23). Razlogi za to niso jasni. Drugi klinični sindromi so zastopani v manj kot v 10% (3–5), le pri nas se pojavlja pljučnica v nekaj višjem odstotku. Dečki na splošno pogosteje zbolevajo za kužnimi boleznimi, kar velja tudi za invazivne bolezni, ki jih povzroča Hib. V naši študiji smo tudi opažali večji delež dečkov med zbolelimi, vendar razlika ni bila statistično značilna.

Med študijo smo opazovali zbolevanje z dvema vrhovoma od oktobra do marca in junija ter julija. Bimodalno zbolevanje so opazovali tudi v drugih študijah, prisoten pa je manjši zamik v mesecih (3, 5). Sezonsko zbolevanje je morda povezano z zbolevanjem za virusnimi okužbami, ki bi igrale vlogo v patogenezi invazivnih bolezni.

Smrtnost v naši študiji je 3,6% in je podobna kot v drugih razvitih državah, kjer je giblje med 1 in 5% (3, 4, 18, 19). Najpogostejši vzrok smrti je meningitis, redkeje epiglotitis ali druge okuže (19). Posledice po meningitisu so ugotavljali v razvitih državah med 9 in 19% (19), ponekod pa še pogosteje (24). Najpogostejše so nevrološke posledice in okvare sluha.

Povprečna hospitalizacija za meningitis je bila pri nas 18,3 dneva, kar je v povprečju za 50% več kot v razvitih državah Evrope, ZDA in Avstralije, kjer se je gibala med 9,5 in 14 dnevi. Daljša je tudi pri drugih kliničnih sindromih brez meningitisa in epiglotitisa (14 dni v primerjavi z 9,2 dneva). Priporočila za zdravljenje okužb se pogosto menjajo in po sedanjih priporočilih naj traja zdravljenje meningitisa, ki ga povzroča Hib, 7 do 10 dni, če meningitis poteka brez zapletov (25).

Občutljivost bakterij je pokazala, da v Sloveniji približno 15% Hib izloča betalaktamaze. Ta odstotek je podoben povprečnemu odstotku v Evropi (26). Antibiotik izbora v terapiji bakterijskega meningitisa je cefotaksim ali ceftriakson, pri preobčutljivosti na betalaktamske antibiotike pa kloramfenikol. Za zdravljenje drugih invazivnih okužb pridejo v poštev še drugi antibiotiki, kot na primer cefuroksim in amoksicilin/klavulanska kislina.

Slovenija je ena redkih držav v Evropi, kjer rutinsko cepljenje proti Hib še ni uvedeno. Vse študije v državah, kjer je incidenca višja, so pokazale, da je cepljenje ekonomsko upravičeno (19, 27). Študija v Italiji, kjer imajo podobne rezultate kot pri nas, je pokazala, da je cepljenje ekonomsko upravičeno, če je cena cepiva temu primerna (20). Ne glede na rezultate naše študije o ekonomski upravičenosti cepljenja je pomembneje upoštevati priporočilo drugih avtorjev, da se uvede cepljenje proti Hib, ne da bi prihranili denar, pač pa da zmanjšujemo zbolevnost, smrtnost ter invalidnost, ki jih te okužbe povzročajo.

Literatura

1. Bijlmer HA. World-wide epidemiology of Haemophilus influenzae meningitis industrialized versus non-industrialized countries. Vaccine 1991; 9: Suppl June: 55–9.
2. Reinert P, Liwartowski A, Dabernat H, Guyot C, Boucher J, Carrere C. Epidemiology of Haemophilus influenzae type b disease in France. Vaccine 1993; 11: Suppl 1: 38–42.
3. Gervaix A, Suter S. Epidemiology of invasive Haemophilus influenzae type b infections in Geneva, Switzerland, 1976 to 1989. Pediatr Infect Dis J 1991; 10: 370–4.
4. Tudor-Williams G, Frankland J, Isaacs D et al. Haemophilus influenzae type b disease in the Oxford region. Arch Dis Child 1989; 64: 517–9.
5. Takala AK, Eskola J, Peltola H, Mäkela H. Epidemiology of invasive Haemophilus influenzae type b disease among children in Finland before vaccination with Haemophilus influenzae type b conjugate vaccine. Pediatr Infect Dis J 1989; 8: 297–302.
6. Dajani AS, Asmar BI, Thirnmoorthi MC. Systemic Haemophilus influenzae disease: an overview. J Pediatr 1979; 94: 355–69.
7. Peltola H, Rod TO, Jonsdottir K, Böttige M, Coolidge SAJ. Life-threatening Haemophilus influenzae infections in Scandinavia: A five countries analyses of the incidence and the main clinical and bacteriologic characteristics. Rev Infect Dis 1990; 12: 708–15.
8. McIntyre PB, Leeder JR, Irwing LM. Invasive Haemophilus influenzae type b disease in Sydney children. 1985–1987: a population based study. Med J Austral 1991; 154: 832–7.
9. Peltola H, Kilpi T, Anttila M. Rapid disappearance of Haemophilus influenzae type b meningitis after routine childhood immunization with conjugate vaccines. Lancet 1992; 340: 592–4.
10. Hargreaves RM, Slack MPE, Howard AJ, Anderson E, Ramsay ME. Changing patterns of invasive Haemophilus influenzae disease in England and Wales after introduction of the Hib vaccination programme. BMJ 1996; 312: 160–1.
11. Garpenholt Ö, Silverdal SA, Hugosson S et al. The impact of Haemophilus type b vaccination in Sweden. Scand J Infect Dis 1996; 28: 165–9.
12. CDC. Progress toward elimination of Haemophilus influenzae type b disease among infants and children – United States, 1993–1994. MMWR 1995; 44: 545–50.
13. Canadian Paediatric Society and the laboratory centre for disease control. Recent trends in pediatric Haemophilus influenzae type b infections in Canada. Can Med Assoc J 1996; 154; 1041–7.
14. Čižman M, Gubina M, Lešničar G et al. Incidenca Haemophilus influenzae meningitisa pri otrocih v Sloveniji. In: Bobinac E ed. Znanstveni simpozij o gnojnim meningitisima Hrvatske. Dubrovnik: April 26–28, 1990: 28–31.
15. Čižman M, Paragi M, Jovan-Kuhar N, Gubina M, Kraigher A, Jazbec J and the Slovenian paediatric meningitis group. Incidence of Haemophilus influenzae meningitis among children in Slovenia. J Chemother 1995; 7: Suppl 4: 145–6.
16. Inštitut za varovanje zdravja Republike Slovenije. Zdravstveni statistični letopis Slovenije 1995. Zdrav Var 1996; 35: Suppl 5: 1–17.
17. Isenberg HD. Medical microbiology – Laboratory manuals. American Society for Microbiology 1992: 20–1.
18. Paragi M. Razširjenost serotipov pri invazivnih obolenjih, ki jih pri otrocih v Sloveniji povzročajo Haemophilus influenzae, Neisseria meningitidis in Streptococcus pneumoniae. Magistrsko delo. Univerza v Ljubljani, Medicinska fakulteta 1996.
19. Clements DA, Booy R, Dagan R et al. Comparison of the epidemiology and cost of Haemophilus influenzae type b disease in five Western countries. Pediatr Infect Dis J 1993; 12: 362–7.
20. Borgnolo G, Barbone F, Perino R, Gasparini V. Vaccinazione anti-Haemophilus influenzae tipo B in Italia. Medico e Bambino 1996; 3: 162–6.
21. Trollfors B, Claesson B, Strangert K, Tarangh J. Haemophilus meningitis in Sweden, 1981–83. Arch Dis Child 1987; 62: 1220–3.
22. Dagan R and Israeli Paediatric Bacteremia and Meningitis group. A two year prospective nationwide study to determine the epidemiology and impact of invasive childhood Haemophilus influenzae type b infection in Israel. Clin Infect Dis 1992; 15; 720–5.
23. Pokorn M, Čižman M, Žargi M et al. Acute epiglotitis in Slovenia – 1993 to 1995. In: Abstract Book. First International meeting on the therapy of infections. Florence 1996: abstract 94.
24. Baraff LJ, Sidney LI, Schriger DL. Outcomes of bacterial meningitis in children: a meta-analysis. Pediatr Infect Dis J 1993; 12: 389–94.
25. American Academy of Pediatrics. Haemophilus influenzae infections. In: Peter G ed. 1994 Red Book. Report of the Committee on Infectious Diseases. 23rd ed. Elk Grove Village, IL: American Academy of Pediatrics, 1994: 203–15.
26. Kayser FH, Montezoni G, Santanan P. The Second European Colaborative Study on the frequency of antimicrobial resistance in Haemophilus influenzae. Eur J Clin Microbiol Infect Dis 1990; 9: 810–7.
27. Trollfors B. Cost-benefit analyses of general vaccination against Haemophilus influenzae type b in Sweden. Scand J Infect Dis 1994; 26: 611–4.
28. Funkhouser A, Steinhoff MC, Ward J. Haemophilus influenzae disease and immunization in developing countries. Rev Infect Dis 1991; 13: Suppl 6: 542–54.

Strokovni prispevek/Professional article

POMEN PROSTATIČNEGA SPECIFIČNEGA ANTIGENA (PSA) PRI DIAGNOSTIKI RAKA PROSTATE

SIGNIFICANCE OF PROSTATE SPECIFIC ANTIGEN IN THE DIAGNOSIS OF PROSTATE CANCER

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Ključne besede: *rak prostate; gostota prostatičnega specifičnega antigena; ultrazvočno vodena transrektalna biopsija prostate; diagnoza*

Izvleček – Izhodišča. *Rak prostate je ena najpogostejših malignih bolezni pri moških. Incidenca raka prostate v Sloveniji narašča. Optimalni način zdravljenja raka prostate še ni znan, vendar le radikalna prostatektomija pri raku, omejenem na žlezo, daje možnost popolne ozdravitve. Zato sta zgodnja diagnoza in zdravljenje pomembna. Namen raziskave je bil ugotoviti pomen prostatičnega specifičnega antigena (PSA) in gostote prostatičnega specifičnega antigena (PSAD) pri zgodnji diagnostiki raka prostate. Ugotavljali in primerjali smo napovedno vrednost pozitivnega testa PSA in PSAD.*

Bolniki in metode. *V raziskavo smo vključili 171 bolnikov, ki so bili zaradi suma na rak prostate poslani za nadaljnjo diagnostiko. Vse bolnike smo pregledali digitorektalno in ultrazvočno transrektalno, izmerili smo volumen prostate, določili koncentracijo PSA v serumu in izračunali PSAD. Pri vseh bolnikih, ki so imeli sumljiv digitorektalni izvid ali koncentracijo PSA v serumu enako ali večjo od 4 ng/ml, smo naredili transrektalno ultrazvočno vodeno biopsijo prostate.*

Rezultati. *Ugotovili smo, da je test PSA pri nizkih mejnih vrednostih zelo občutljiv in razmeroma malo specifičen pri diagnostiki raka prostate. Z določanjem koncentracije PSA v serumu smo lahko ugotovili rake prostate v zgodnjem stadiju, ko še niso bili tipni pri digitorektalnem pregledu. Test PSAD je imel večjo napovedno vrednost kot test PSA.*

Zaključki. *PSA je visoko specifični označevalec žleznega tkiva prostate, rakavega in nerakavega. Test PSA je pri nizkih mejnih vrednostih zelo občutljiv, vendar je njegova specifičnost majhna. Z določanjem PSA v serumu lahko ugotovimo rake prostate, ki niso tipni pri digitorektalnem pregledu in so omejeni na prostato. Ugotavljanje PSAD zveča pozitivno napovedno vrednost testa. Z upoštevanjem mejne vrednosti PSAD 0,15 kot indikacije za punkcijo prostate pri netipnih rakih prostate bi lahko zmanjšali število negativnih punkcij prostate.*

Key words: *prostate cancer; prostate specific antigen density; ultrasound guided transrectal prostatic biopsy; diagnosis*

Abstract – Background. *Prostate cancer is among the most common cancers in men. The incidence of this malignancy in Slovenia is increasing. An optimal treatment has not been found yet and only organ-confined disease is potentially curable by radical prostatectomy. Therefore, early detection and treatment are important. The aim of this study was to assess the usefulness of prostate specific antigen (PSA) and prostate specific antigen density (PSAD) in early detection of prostate cancer. We determined and compared the predictive value of positive PSA and PSAD test.*

Patients and methods. *The study population consisted of 171 patients who were referred for further evaluation of suspected prostate cancer. Each patient underwent a digital rectal examination and transrectal ultrasonography, the volume of the prostate gland was determined, the serum PSA level was measured and PSAD calculated. Transrectal ultrasound-guided prostatic biopsy was performed in patients with the digital rectal examination suggestive of prostate cancer or a serum PSA level equal to or higher than 4 ng/ml.*

Results. *The PSA assay with low cutoff values proved to have a high sensitivity and comparatively low specificity in the detection of prostate cancer. By determining the serum PSA level, we were able to detect carcinomas at an early stage when they were not yet palpable on digital rectal examination. PSAD had a higher predictive value than PSA.*

Conclusions. *PSA is highly specific marker of prostate gland tissue, malignant and nonmalignant. The PSA assay with low cutoff values is highly sensitive but its specificity is low. By means of serum PSA measurement it is possible to detect organ-confined carcinomas that are not palpable on digital rectal examination. PSAD determination increases the positive predictive value of PSA. The number of negative prostatic biopsies could be reduced by observing a PSAD value of 0.15 as an indication for biopsy in the absence of palpable lesion.*

Uvod

Rak prostate je ena najpogostejših malignih bolezni pri moških. V Sloveniji je po pogostosti pri moških, starejših od 65 let, na drugem mestu. Zaradi daljšanja povprečne življenjske dobe incidenca raste in je bila v Sloveniji v obdobju med leti 1983–1987 22,7 bolnika na 100.000 moških (1). Optimalni način zdravljenja raka prostate še ni znan, vendar le radikalna prostatektomija pri raku, omejenem na žlezo, daje možnost popolne ozdravitve. Zato sta zgodnja diagnoza in zdravljenje pomembna (2).

Najpomembnejše metode za zgodnjo detekcijo raka prostate so digitorektalni pregled (3), določanje koncentracije prostatičnega

specifičnega antigena (PSA) v serumu (4–6) in transrektalna ultrazvočna preiskava prostate (4). Za dokončno diagnozo je vedno potrebna biopsija prostate (7, 8).
Prostatični specifični antigen (PSA) je v semenski tekočini odkril Hara s sodelavci leta 1970. Imenoval ga je gama seminoprotein (9). Leta 1979 je Wang s sodelavci izoliral antigen iz prostatičnega tkiva. Osamil ga je iz normalnega prostatičnega tkiva, tkiva benigne hiperplastične prostate in iz rakavega tkiva prostate. V drugem človeškem tkivu ga niso odkrili (10). Antigen je specifičen za prostato in različen od kisle fosfataze. Wang s sodelavci je odkril, da je PSA v serumu istoveten s PSA, osamljenim iz prostatičnega tkiva. PSA ni izdelek rakavega tkiva, temveč žleznih celic prostate, rakavih in nerakavih, zato je normalno vrednost težko določiti (11–13). Večina avtorjev in proizvajalcev monoklonskih PSA testov ima vrednost, manjšo od 4 ng/ml, za normalno. Poleg tega je bilo ugotovljeno, da enota rakavega tkiva prostate bolj zviša koncentracijo PSA v serumu kot enota nerakavega tkiva (11, 14). Zaradi precejšnjega prekrivanja vrednosti serumskega PSA pri moških z benigno hiperplazijo in rakom prostate, še posebej pri nizkih stadijih in posledično razmeroma majhno občutljivostjo in specifičnostjo PSA testa, so bile predlagane tri metode, ki bi te pomanjkljivosti zmanjšale. PSAD (PSA density ali gostota PSA), ki jo izračunamo tako, da vrednost PSA delimo z volumnom prostate (15, 16). PSA hitrost, kjer ugotavljamo časovne spremembe koncentracije PSA v serumu (17). PSA, prilagojen starosti bolniku, kjer s starostjo mejne vrednosti PSA večamo (18).
Namen raziskave je bil ugotoviti pomen prostatičnega specifičnega antigena (PSA) in gostote prostatičnega specifičnega antigena (PSAD) pri zgodnji diagnostiki raka prostate.

Bolniki in metode

V raziskavo so bili vključeni bolniki, ki so bili zaradi suma na rak prostate poslani za nadaljnjo diagnostiko. Vsi bolniki so bili seznanjeni z namenom, potekom in možnimi zapleti preiskave. Vse preiskave so bile opravljene kot del redne diagnostike raka prostate. Med junijem leta 1994 in decembrom 1995 je bilo pregledanih in punktiranih 238 bolnikov. Iz raziskave je bilo izključenih 67 bolnikov zaradi jemanja zdravil ali posegov, ki bi lahko vplivali na koncentracijo PSA in na volumen prostate;
1. ker so jemali zdravila, ki vplivajo na koncentracijo PSA v serumu – finasterid ali zdravila, ki se uporabljajo za hormonsko zdravljenje karcinoma prostate;
2. ker je bil čas med palpacijo in odvzemom krvi za določitev PSA manjši od tedna dni zaradi možnega vpliva na koncentracijo PSA v serumu;
3. ker jim je bil vstavljen stalni kateter zaradi retence urina in možnega vpliva na koncentracijo PSA v serumu;
4. ker so imeli prostatitis, ki zveča koncentracijo PSA v serumu;
5. ker so imeli poprejšnje posege, ki vplivajo na volumen prostate – transuretralna resekcija prostate ali klasična odprta prostatektomija.
V raziskavo je bilo vključenih 171 moških, starih od 48 do 92 let. Vključeni so bili bolniki, ki so imeli:
1. sumljiv palpatorni izvid, ne glede na vrednost PSA, ali
2. vrednost PSA v serumu, večjo od 4,0 ng/ml.
Bolnikom je bila kri odvzeta za PSA neposredno pred digitorektalnim pregledom ali vsaj en teden po njem. Za določevanje PSA je bil uporabljen monoklonski fluoroimunometrični test DELFIA PSA. Bolniki so preventivno zaradi preprečevanja okužbe pol ure pred punkcijo prostate in nato še pet dni po njej jemali peroralno kinolone. Kontraindikaciji za punkcijo sta bili jemanje antikoagulantnih sredstev in aktivni uroinfekt. Uporabljali smo ultrazvočni aparat Bruel & Kjaer 3535 in ultrazvočno multiplansko sektorsko sondo 8551. Punkcija je bila narejena s posebno Tru-Cut biopsijsko iglo premera 1,2 mm in s pomočjo avtomatskega biopsijskega aparata – Biopty System. Punkcija omogoča odvzem 17 mm dolgega stebrička tkiva za histološko preiskavo. Biopsije so bile sistematične. Prostata je bila punktirana na vrhu, sredini in bazi obojestransko lateralno, tako da je punkcijska pot zajela periferno cono. Kadar je bil palpatorni izvid močno sumljiv in se je skladal z ultrazvočnim izvidom, so bile biopsije usmerjene. Volumen prostate je bil izračunan ob predpostavki, da je prostata pravilen elipsoid iz treh parametrov po formuli – (širina × višina × dolžina prostate) × 0,523. Po izvidu punkcije so bili bolniki razvrščeni na skupino s pozitivnim histološkim izvidom (karcinom) in na skupino z negativnim izvidom.
Za statistično obdelavo podatkov smo uporabili Wilcoxonov test vsote rangov. Za statistično značilne smo označili vrednosti $p \leq 0.05$.

Rezultati

V raziskavo je bilo vključenih 171 bolnikov, ki so imeli pozitiven digitorektalni izvid ali koncentracijo PSA v serumu nad 4 ng/ml. Pri 97 bolnikih je bila punkcija pozitivna – 56,7%.
Med obema podskupinama bolnikov s pozitivnim histološkim izvidom – 97 bolnikov in negativnim izvidom punkcije – 74 bolnikov, je bila statistično značilna razlika v koncentraciji PSA v serumu $p<0,001$ (Wilcoxonov test vsote rangov). Statistično značilna razlika med obema podskupinama bolnikov je bila tudi pri PSAD $p<0,0001$ (Wilcoxonov test vsote rangov). Občutljivost testa PSA in PSAD je bila pri majhnih mejnih vrednostih velika, specifičnost pa majhna. PSAD test je bolje napovedal izid punkcije (tab. 1, 2).

Tab. 1. *Občutljivost, specifičnost in pozitivna napovedna vrednost PSA pri vseh 171 bolnikih.*

Tab. 1. *Sensitivity, specificity, positive predictive value of PSA for all 171 patients.*

Mejna vrednost PSA PSA cut-off level	Občutljivost Sensitivity %	Specifičnost Specificity %	Pozitivna napovedna vrednost Positive predictive value %
4	98	16	61
6	92	39	66
8	89	51	70
10	82	65	75
15	65	83	78
20	59	91	90
30	47	97	96

Tab. 2. *Občutljivost, specifičnost in pozitivna napovedna vrednost PSAD pri vseh 171 bolnikih.*

Tab. 2. *Sensitivity, specificity and positive predictive value of PSAD for all 171 patients.*

Mejna vrednost PSAD PSAD cut-off level	Občutljivost Sensitivity %	Specifičnost Specificity %	Pozitivna napovedna vrednost Positive predictive value %
0,10	100	22	63
0,15	96	49	71
0,20	93	64	77
0,30	81	83	87
0,40	70	87	88
0,50	66	94	94
0,60	59	94	93
0,80	48	98	97

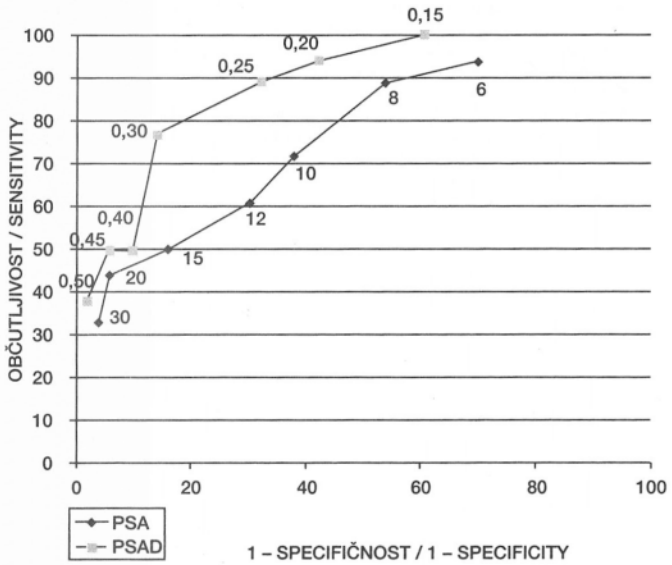
Negativni digitorektalni izvid in koncentracijo PSA več kot 4 ng/ml je imelo 65 od 171 bolnikov. Pri 18 bolnikih je bila punkcija pozitivna – 27,6%. V tej skupini je prav tako bila statistično značilna razlika med vrednostmi PSA $p<0,05$ (Wilcoxonov test vsote rangov) in vrednostmi PSAD $p<0,0001$ (Wilcoxonov test vsote rangov) glede na izvid punkcije (tab. 3). Občutljivost PSA in PSAD testa je bila tudi v tej skupini pri majhnih mejnih vrednostnih velika, specifičnost pa majhna. Prav tako je imel v tej skupini PSAD test večjo vrednost, bolje je napovedal izid punkcij (sl. 1).

Tab. 3. *Primerjava koncentracije PSA in vrednosti PSAD pri skupini bolnikov z negativnim digitorektalnim izvidom in vrednostjo PSA>4 ng/ml.*

Tab.3. *Comparison of PSA concentrations and PSAD values for patients with negative digital rectal examination and PSAD>4 ng/ml.*

		P	N	
	Število bolnikov No. of patients	18	47	Wilcoxonov test vsote rangov Wilcoxon's range sum test
PSA	Aritmetična sredina Mean	46,8	10,59	p=0,011
	Standardna deviacija St. dev.	113,7	7,0	
	Mediana Median	16,6	8,9	
	Razpon Range	5,1–500	4,3–38,7	
PSAD	Aritm. sredina Mean	1,04	0,22	p<0,0001
	Standardna deviacija St. dev.	2,06	0,13	
	Mediana Median	0,42	0,19	
	Razpon Range	0,21–9,17	0,05–0,76	

P – pozitivni histološki izvid (rak prostate); N – negativni histološki izvid
P – positive histology (prostate carcinoma); N – negative histology



Sl. 1. *Primerjava testov (ROC krivulja) PSA in PSAD pri skupini bolnikov, ki so imeli negativni digitorektalni izvid in PSA večji od 4 ng/ml.*

Fig. 1. *Receiver-operating-characteristic (ROC) curves for PSA and PSAD in our patient population with negative digital rectal examination and PSA > 4 ng/ml.*

Normalni digitorektalni izvid in koncentracijo PSA med 4 ng/ml in 10 ng/ml v serumu je imelo 33 od 171 bolnikov. Pri petih bolnikih je bila punkcija pozitivna – 15,2%.

V skupini bolnikov z negativnim digitorektalnim izvidom in vrednostjo PSA med 4 in 10 ng/ml ni bilo statistično pomembne razlike koncentracije PSA v serumu med podskupino s pozitivnim in podskupino z negativnim biopsijskim izvidom. Razlika v vrednosti PSAD med podskupino s pozitivnim in negativnim biopsijskim izvidom je bila statistično pomembna p<0,05 (Wilcoxonov test vsote rangov). Razpredelnica kaže dvakrat večje število lažno pozitivnih punkcij prostate pri PSA testu v primerjavi s PSAD testom (tab. 4).

Tab. 4. *Število resnično pozitivnih, število lažno pozitivnih punkcij prostate in pozitivna napovedna vrednost testa PSA in PSAD pri skupini bolnikov, ki so imeli vrednost PSA med 4 in 10 ng/ml in negativni digitorektalni izvid.*

Tab. 4. *Number of true positives, false positives and positive predictive value for patients with negative digital rectal examination and PSA value between 4 and 10 ng/ml.*

	Mejna vrednost Cut-off value	Resnično pozitivne True positives	Lažno pozitivne False positives	Pozitivna napovedna vrednost % Positive predictive value %
PSA	>4 µg/ml	5	28	16
PSAD	0,15	5	14	26

Večjih zapletov po transrektalnih biopsijah prostate ni bilo. En bolnik je imel vročino tri dni, ki je nato v nadaljevanju zdravljenja s kinoloni padla na normalo. Krvavitev iz rektuma je bilo malo in nobena ni terjala dodatnega posega, vse so se spontano ustavile.

Razpravljanje

Ugotovitve naše študije kažejo, da z določanjem PSA v serumu lahko ugotavljamo rake prostate v zgodnjem stadiju. Primerjava PSA in PSAD testa pri zgodnji diagnostiki raka prostate kaže, da ima PSAD test večjo specifičnost in pozitivno napovedno vrednost. Z uporabo PSAD testa zmanjšamo število negativnih punkcij prostate. Ugotovili smo statistično značilno razliko v koncentraciji PSA in vrednosti PSAD med bolniki s pozitivno punkcijo prostate in bolniki z negativno punkcijo. Prekrivanje vrednosti PSAD med bolniki z rakom prostate in bolniki, ki so imeli negativno biopsijo prostate, je bilo manjše kot pri koncentracijah PSA v serumu, kar se sklada z ugotovitvami drugih avtorjev (15, 19, 20). Zaradi precejšnjega prekrivanja vrednosti PSA pri benigni hipertrofiji prostate in pri začetnem raku prostate je to treba upoštevati pri odločitvah glede mejne koncentracije. Z nižanjem mejne vrednosti bomo zvečali občutljivost in zmanjšali specifičnost, posledično bomo zvečali odstotek negativnih biopsij, obratno pa lahko zaradi manjše občutljivosti in večje specifičnosti zgrešimo večji odstotek klinično pomembnih rakov. Občutljivost PSA je bila v naši študiji pri nizkih mejnih vrednostih velika, specifičnost majhna, prav tako je bila majhna pozitivna napovedna vrednost, kar se prav tako sklada z ugotovitvami drugih avtorjev (21, 22). Občutljivost PSAD je bila prav tako velika, test pa je imel večjo specifičnost in pozitivno napovedno vrednost.

Pri 65 bolnikih je bil digitorektalni izvid negativen in PSA >4 ng/ml. Pri 18 bolnikih je bila punkcija pozitivna, pri 47 bolnikih pa negativna. Pri vseh bolnikih, razen pri enem, ki je imel PSA 500 ng/ml, smo klinično ugotovili rak prostate, omejen na žlezo. Razlika med vrednostjo PSAD in koncentracijo PSA pri bolnikih s pozitivno in negativno punkcijo je bila statistično značilna, vendar je imel test PSAD ponovno boljše lastnosti, ker je bolje napovedal izid punkcije. Pri mejni vrednosti PSA 4 ng/ml je bila občutljivost 100% in pozitivna napovedna vrednost 28%. Pri mejni vrednosti PSAD 0,15 je bila občutljivost prav tako 100% in pozitivna napovedna vrednost 38%. Z uporabo testa PSAD bi v tej skupini prihranili punkcije 18 bolnikom. Krivulja, ki nam kaže razmerje med občutljivostjo in lažno pozitivno frakcijo, nam tudi v tej skupini bolnikov prikaže večjo vrednost testa PSAD.

33 bolnikov je imelo PSA med 4 in 10 ng/ml. Pet bolnikov je imelo pozitivno punkcijo, 28 negativno. Razlika PSAD med bolniki s pozitivno in med bolniki z negativno punkcijo je bila v tej skupini statistično značilna, razlika v koncentraciji PSA pa ne. Pozitivna napovedna vrednost PSA testa pri mejni vrednosti 4 ng/ml je bila 16% in 26% pri mejni vrednosti 0,15 testa PSAD. V tej skupini bi prihranili punkcije prostate 14 bolnikom, če bi uporabili test PSAD. Pozitivnih biopsij je bilo 56,7%, kar je nekoliko večji odstotek, kot ga navajajo nekateri drugi avtorji (4, 23). Vzrok je verjetno ta, ker

vzorec bolnikov v naši raziskavi ni bil pridobljen s presejanjem, temveč so bili to že selekcionirani bolniki, ki so bili pregledani v urološki ambulanti in zaradi suma na rak prostate napoteni k nam. Največja pogostost bolnikov z rakom prostate je bila med 70. in 74. letom, kar je v skladu z ugotovitvijo, da incidenca raka prostate s starostjo raste.

Zaključek

Študija potrjuje, da z določanjem PSA v serumu lahko ugotavljamo rake prostate v zgodnjem stadiju. Samo na podlagi zvečane vrednosti PSA smo v naši študiji ugotovili 18 rakov prostate od skupno 97 ugotovljenih. Ti raki niso bili tipni in so bili klinično v T1-T2 stadiju. Izsledki naše študije potrjujejo, da je uporaba PSAD koristna. PSAD bolje napove izid punkcije kot PSA in z uporabo PSAD bi lahko zmanjšali število negativnih punkcij. Glede na izsledke naše študije je mejna vrednost PSAD 0,15 primerno merilo za biopsijo pri bolnikih z negativnim digitorektalnim izvidom.

Literatura

1. Pompe-Kirn V. Epidemiološke značilnosti raka prostate v Sloveniji. In: Zbornik referatov slovenskega urološkega simpozija o raku na prostati. Ljubljana: Urološka sekcija SZD Slovenije, 1995.
2. Dillioglugil Ö, Miles BJ, Scardino PT. Current controversies in the management of localized prostate cancer. Eur Urol 1995; 28: 85–101.
3. Kojima M, Babaian RJ. Algoritms for early detection of prostate cancer. Cancer 1995; 75: Suppl: 1860–8.
4. Brawer MK. The diagnosis of prostatic carcinoma. Cancer 1993; 71: Suppl: 899–905.
5. Scardino PT. Early detection of prostate cancer. Urol Clin North Am 1989; 16: 635–54.
6. Ellis WJ, Chetner MP, Preston SD, Brawer MK. Diagnosis of prostatic carcinoma: the yield of serum prostate specific antigen, digital rectal examination and transrectal ultrasonography. J Urol 1994; 152: 1520–5.
7. Mašera A, Ovčak Z. Patohistološka diagnostika karcinoma prostate. In: Zbornik referatov slovenskega urološkega simpozija o raku na prostati. Ljubljana: Urološka sekcija SZD Slovenije, 1995.
8. Pedersen-Torp ST, Lee F. Transrectal biopsy of the prostate guided by transrectal ultrasound. Urol Clin North Am 1989; 16; 703–12.
9. Hara M, Koyanagi Y, Inoue T, Fukuyama T. Some physico-chemical characteristics of gamma-seminoprotein, an antigenic component specific for human seminal plasma. Jpn J Leg Med 1971; 25: 322–4.
10. Wang MC, Valenzuela LA, Murphy GP, Chu TM. Purification of a human prostate specific antigen. Invest Urol 1979; 17: 159–63.
11. Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E. Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. N Engl J Med 1987; 317: 909–16.
12. Gillat D, Reynard JM. What is the »normal range« for prostate-specific antigen? Use of a receiver operating characteristic curve to evaluate s serum marker. Br J Urol 1995; 75: 341–6.
13. Dalkin BL, Ahmann FR, Kopp JB et al. Derivation and application of upper limits for prostate specific antigen in men aged 50–74 years with no clinical evidence of prostatic carcinoma. Br J Urol 1995; 76: 346–50.
14. Babaian RJ, Miyashita H, Evans RB, Ramirez EI. The distribution of prostate specific antigen in men without clinical or patological evidence of prostate cancer: relationship to gland volume and age. J Urol 1992; 147: 837–40.
15. Benson MC, Whang IS, Olsson CA, McMahon DJ, Cooner WH. The use of prostate specific antigen density to enhance the predictive value of intermediate levels of serum prostate specific antigen. J Urol 1992; 147: 817–21.
16. Bazinet M, Meshref AW, Trudel C et al. Prospective evaluation of prostate-specific antigen density and systematic biopsies for early detection of prostatic carcinoma. Urology 1994; 43: 44–52.
17. Partin AW, Oesterlung JE. The clinical usefulness of prostate specific antigen. Update 1994. J Urol 1994; 152: 1358–68.
18. Oesterling JE, Cooner WH, Jacobsen SJ, Guess HA, Lieber MM. Influence of patient age on the serum PSA concentration. Urol Clin North Am 1993; 20: 671–80.
19. Semjonov S, Hamm M, Rathert P, Hertle L. Prostate-specific antigen corrected for prostate volume improves differentiation of benign prostatic hyperplasia and organ-confined prostatic cancer. Br J Urol 1994; 73: 538–43.
20. Wolff JM, Scholz A, Boeckman W, Jakse G. Differentiation of benign prostatic hyperplasia and prostate cancer employing prostatic-specific antigen density. Eur Urol 1994; 25: 295–8.
21. Oesterling JE. Prostate specific antigen: a critical assessment of the most useful tumor marker for adenocarcinoma of the prostate. J Urol 1991; 145: 907–32.
22. Catalona WJ, Richie JP, Ahmann FR et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. J Urol 1994; 151: 1283–90.

Pregledni prispevek/Review article

CREUTZFELDT-JAKOBOVA BOLEZEN (CJB) IN BOVINA SPONGIFORMNA ENCEFALOPATIJA

CREUTZFELDT-JAKOB DISEASE AND BOVINE SPONGIFORM ENCEPHALOPATHY

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Ključne besede: *okužbe s počasnimi virusi; prionski protein; spongiformne encefalopatije*

Izvleček – *Prenosljive spongiformne encefalopatije (SE) so degenerativne bolezni osrednjega živčevja ljudi in živali. Njihova značilnost so spongiformne degenerativne spremembe osrednjega živčevja (vakuolizacija celic in status spongiozus), astrocitna glioza in propadanje nevronov. V prizadetih možganih se nabira nenormalna amiloidna beljakovina. Bolezni se prenašajo na poskusne živali z inokulacijo ali z uživanjem okužene hrane. Inkubacijska doba za živali in pri ljudeh je zelo dolga in traja do nekaj let; bolezen se vedno fatalno konča. Povzročitelji so odporni na postopke, ki običajne mikroorganizme inaktivirajo. Vsaj za nekatere od teh bolezni je pomembna tudi genetska dovzetnost gostitelja.*

Med SE pri človeku poznamo bolezen Creutzfeldt-Jakob (CJB) (hereditarno-familiarna oblika, z avtosomno-dominantnim dedovanjem in točkastimi mutacijami ali insercijami na odgovornem genu). Poznani sta še iatrogena oblika in sporadična – neznanega izvora. Nova oblika CJB je bila opisana leta 1996.

Poznamo tudi sindrom Gerstmann-Strausler-Scheinker, fatalno familiarno insomnijo, kuru in nekatere druge, še ne dovolj pojasnjene bolezni.

Bovina spongiformna encefalopatija (BSE) in scrapie (praskavica) sta med živalmi najpogostejši SE.

Molekularna narava povzročiteljev ni povsem jasna. Najbolj znana hipoteza opisuje konformacijske spremembe v gostiteljevi beljakovini, poznani kot »prionski beljakovini«, ne da bi pri tem bil prizadet genetski material. Ta opazovanja temeljijo na nesposobnosti, da bi uničili infektivnost prečiščenih pripravkov z metodami, za katere vemo, da inaktivirajo nukleinske kisline. Tudi napori, da bi našli za agens specifično nukleinsko kislino, so bili zaman.

Nekateri avtorji menijo, da obstaja agensov genom z zaščitenimi nukleinskimi kislinami.

Zadnji rezultati o prenosu agensa BSE na miši so pokazali, da več kot 55% inokuliranih živali ni imelo patološkega prionskega proteina, so pa dobile nevrološko bolezen in propadanje nevronov. Zdi se možno, da še neidentificiran agens lahko prenaša BSE..

Epidemiološke študije BSE kažejo, da bolezen izvira iz dodatne hrane, ki vsebuje meso in kosti in ki je kontaminirana z agensom, sličnim onemu, ki povzroča praskavico. Taka hrana je prišla v rabo v Veliki Britaniji leta 1988. Epidemija je že dosegla svoj vrh in zdi se, da je že v upadanju.

O možnosti prenosa BSE iz goveda na človeka, ki je užival okuženo meso, so razpravljali več let, vendar so bila mnenja o tem različna. Leta 1996 so opisali novo obliko CJB, ki se klinično in epidemiološko v marsičem razlikuje od klasične bolezni. Posumili so na povezavo te oblike bolezni z BSE. Razlaga se je zdela za to skupino bolnikov

Key words: *slow-virus infections; prion protein; spongiform encephalopathies*

Abstract – *Transmissible spongiform encephalopathies (TSE) are neurodegenerative diseases, that affect human and animals. They are characterized by a spongiform degeneration in the central nervous system (cellular vacuolization and status spongiosus), astrocytic gliosis and neuronal loss; all are associated with the accumulation in affected brains of an abnormal isoform of the normal cellular protein. These diseases are transmissible to experimental animals by inoculation or by ingestion in food. The incubation period in both human and animal disorders is prolonged for years and the outcome is always fatal. Causative agents are resistant to standard decontamination procedures, that inactivate conventional microorganisms. Genetic susceptibility of the host is also relevant in at least some of these diseases.*

Human TSE include Creutzfeldt-Jakob disease (hereditary-familial form, associated with punctual mutations or insertions in the responsible protein gene; iatrogenic and sporadic form of unknown origin). A new variant of the disease (vCJD) was described in 1996. Known are also Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia, kuru and some others, not yet satisfactorily classified diseases. Bovine spongiform encephalopathy (BSE) and scrapie are the most common animal TSE.

The molecular nature of these agents is unclear. Mostly discussed hypothesis describes a conformational change in the host protein known as 'prion protein', without involvement of any genetic material. These observations base on the inability to destroy infectivity in purified preparations by methods known to inactivate nucleic acids; the efforts to detect agent-specific nucleic acid were also unsuccesful.

However, several authors have indicated the existence of an agent genome with protected nucleic acids. The latest results on the transmission of the BSE agent to mice have shown that more than 55 percent of inoculated animals had no pathologic prion protein, but exhibited neurologic disease and neuronal death. It apperas, that a further unidentified agent may actually transmit BSE.

The BSE epidemic has been extensively studied. Current evidence suggests, that the disease originated from supplementary feed containing meat and bone meal (MBM), contaminated by a scrapie-like agent from sheep or cattle. The use of MBM was banned in Great Britain in 1988. The epidemic is well past its peak and seems to be in a phase of decline.

The transmissibility of BSE from cattle to humans, who have eaten contaminated beef, has been discussed over years with controversial statements. In 1996, The National CJD Surveillance Group has reported cases of a new variant CJD (vCJD), which differ clinically and epidemiologically from classical CJD cases. The possibility was raised, that these cases are casually linked to BSE; this appeared to

zelo verjetna. Zadnje študije, ki temeljijo na molekularni analizi prionskih proteinov, so prinesle nove dokaze za to možnost.
Diagnoza bolezni CJB je bila do nedavnega lahko potrjena le z biopsijo ali nekropsijo možganov. V zadnjem času so bile razvite metode, ki so z biopsijo tonzil omogočale imuno-cito-bistokemične preiskave bolnikov z različico bolezni (CJB). Pri živalih je praskavica lahko dokazana že preden se bolezen klinično pojavi. Preiskava likvorskih beljakovin (skupina 14-3-3) kot tudi za nevrone specifične enolaze so tudi možnosti za diagnozo, ki je lahko postavljena pred smrtjo.

be the most plausible explanation for this cluster of cases. In the meantime, recent studies have brought further evidence for this transmissibility basing on molecular analysis of prion strain variation and the aetiology of new variant CJD.
The diagnosis of CJD could, until recently, only be confirmed by brain biopsy or necropsy. Methods have been now developed for immuno-cyto (histochemistry using the tonsil biopsy in vCJD and in animals (scrapie could be diagnosed long before the onset of clinical disease).
The study of cerebrospinal fluid proteins (14-3-3 group) as well as neuron-specific enolase may be tried for a premortem diagnosis.

Splošni pregled prenosljivih spongiformnih encefalopatij (PSE)

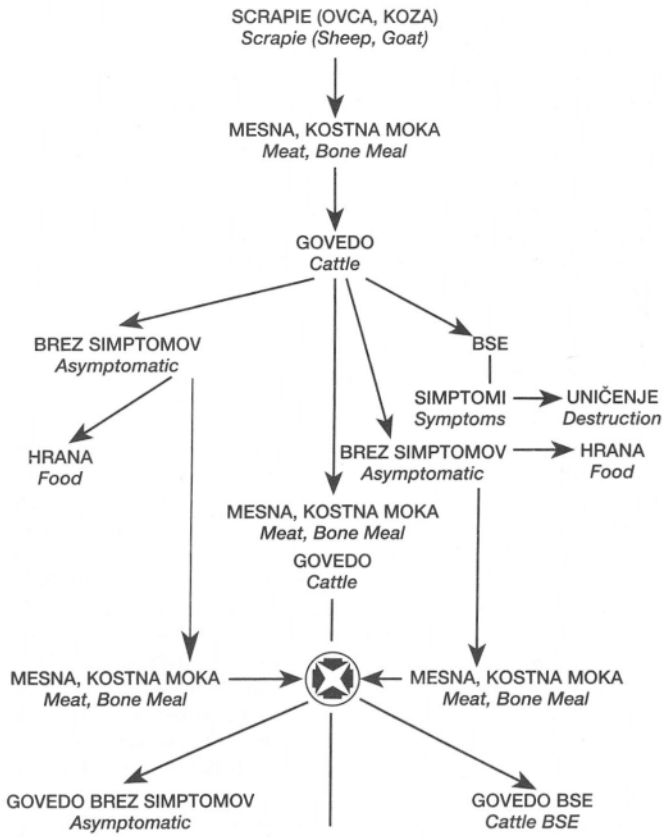
PSE so bolezni, ki prizadenejo ljudi in živali. Osnovne spremembe so v osrednjem živčevju (OŽ) in se kažejo kot spongiformne spremembe (vakuolizacija celic in status spongiosus), astroglioza (pomnožitev reaktivnih astrocitov) in propadanje nevronov z vsemi posledicami. V poznem stadiju bolezni prihaja do odlaganja amiloidne beljakovine in tvorbe t. i. plakov (ploščic). Intenziteta, število in lokalizacija plakov niha od bolezni do bolezni oz. bolnika. Inkubacija bolezni je nenavadno dolga, deset ali celo dvajset let po okužbi pride do izbruha bolezni. Bolezen se vedno konča s smrtjo. Za povzročitelje teh bolezni je značilna visoka odpornost nasproti kemikalijam, ki služijo v medicini za razkuževanje (formaldehid, alkohol, jodovi preparati, kalijev permanganat). Tudi avtoklaviranje pri 134–138°C, čeprav na splošno priporočano, povzročitelja ne uniči vedno. Učinkoviti so klorovi preparati (natrijev hipoklorit) ali kombinacija avtoklaviranja in NaOH (1, 2).
Človeške in živalske PSE je mogoče prenesti na živali iste ali druge vrste z intracerebralno, intravensko ali intramuskularno okužbo, pa tudi oralno s hrano; temu načinu prenosa pripisujejo velik pomen. Eksperimentalne okužbe povzročajo značilne klinične slike, ki se tudi po večkratnem zaporednem prenašanju ne spreminjajo.
Od človeških bolezni je dobro znana bolezen kuru, ki je endemična med pripadniki plemena Fore v Vzhodni Papui – Novi Gvineji in se prenaša s t. i. ritualnim kanibalizmom, uživanjem možganov umrlih sorodnikov (3). S prenehanjem kanibalizma v 1950. letih se je značilno zmanjšalo število novih bolnikov, vendar se posamezni primeri zaradi dolge inkubacije pojavljajo še danes. Najdaljša znana inkubacija pri kuru je znašala 34 let (!).
Gerstmann-Sträussler-Scheinkerjeva bolezen je zelo redka, hereditarna, živčno-degenerativna bolezen (4). V zadnjih letih so opisane fatalna familiarna insomnija (5), Alpersova bolezen (6) ter familiarna progresivna subkortikalna glioza (7); zadnji dve še nista dobili dokončnega mesta v razvrstitvi PSE, posebno poslednja ne, ker je genetski lokus za patološke beljakovine na kromosomu 17, za razliko od ostalih PSE, pri katerih je gen na kromosomu 20. Omenjajo še neke druge bolezni, kot so Alzheimerjeva demenca, in še nekatere druge (8), ter Parkinsonovo bolezen (9). Vendar ni jasnega mnenja o razvrstitvi teh bolezni.
Creutzfeldt-Jakobova bolezen, Creutzfeldt-Jakob Disease, CJB (10, 11) je znana po vsem svetu s pogostostjo 0,5 do enega primera na milijon prebivalcev. Povprečna starost bolnikov je 65 let. Za klinično sliko je značilna hitro napredujoča demenca in mioklonus ter značilne spremembe v EEG. Bolezen traja približno štiri mesece, prognoza pa je fatalna. Patološke spremembe v možganih so značilne za PSE; plake so našli v približno 5% primerov. V zadnjih desetih letih je za to boleznijo umrlo tudi nekaj mlajših oseb.
CJB se pojavlja v več oblikah, kot so (A) hereditarno-familiarna oblika z avtosomno-dominantnim dedovanjem ter točkastimi mutacijami ali insercijami na odgovornem genu na kromosomu 20. Največja akumulacija teh primerov je bila med Židi v Libiji (12) in na Slovaškem (13). (B) Iatrogena oblika je opisana pri otrocih, ki so zaostali v rasti in so dobivali rastni hormon, ali pri neplodnih ženskah, zdravljenih z gonadotropinom. Oba hormona sta bila ekstrahirana iz hipofiz mrličev, s klinično ali asimptomatično CJB. Bolezen je prenehala z uvedbo rekombinantnih hormonov hipofize. Iatrogena bolezen se je razvila tudi po transplantaciji roženice (v ZDA opravijo letno do dvesto tisoč teh posegov), transplantaciji trde možganske opne (najbolj pogosto po odstranitvi možganskega tumorja), po rabi neustrezno steriliziranih instrumentov (v smislu CJB) pri možganskih operacijah. Ne izključujejo tudi možnosti prenosa CJB s transfuzijo krvi; štiri osebe s CJB v Avstraliji so dobile kri oseb, ki so bile zdravljene s hipofiznimi hormoni (14). Zboleli so tudi nevrokirurgi, patologi, zobozdravniki, histopatološki tehniki in medicinske sestre. O iatrogenih okužbah so objavili obsežno literaturo, na podlagi katere so izdelali pravila za delo z morebitno kužnim materialom (15, 16). (C) Sporadični primeri CJB zavzemajo okrog 80% vseh opisanih primerov bolezni. V teh primerih je kužna narava bolezni najbolj očitna, ker ni hereditarno-familiarne anamneze in ni dokaza mutacije na odgovornem genu. (D) Varianta CJB (vCJB), opisana 1996 (17), se klinično razlikuje od do sedaj znanih oblik CJB. V letih 1995–1996 je opisanih 10 primerov v Veliki Britaniji, sedaj pa je znanih 16 primerov, eden od teh v Franciji. Povprečna starost je bila 29 let (zmanjšana dovzetnost pri starejših osebah? imunost?). Primeri CJB pri mlajših osebah, opisani v prejšnjih letih, so ustrezali klasični obliki CJB. V prvi fazi vCJB so v ospredju psihiatrični simptomi (agresivnost), ugotovljeni pri vseh desetih opisanih primerih. Prav tako je pri vseh ugotovljena ataksija, pri 7 do 10 pa tudi mioklonus. EEG, značilen za klasično CJB, ni bil prisoten. Pri vseh umrlih so našli plake, pri klasični obliki bolezni pa so plaki prisotni le v 5% primerov. Po tem vCJB spominja na kuru. Bolezen lahko traja tudi do dve leti, klasična CJB pa le kakšne štiri mesece.
Od bolezni pri živalih je najbolj znana scrapie, praskavica (18), ki je znana že 200 let in je razširjena po vsem svetu. Zelo veliko zbolelih ovac je v Veliki Britaniji še danes. Klinična slika bolezni in nevropatološke spremembe ustrezajo drugim PSE. Čeprav igra genetski faktor pri praskavici zelo veliko vlogo, je bilo možno bolezen prenesti na druge živalske vrste, celo s hrano. Praskavica je najdalj in najbolje znana PSE; o bolezni menijo, da je genetska in kužna hkrati, kar velja – vsaj deloma – tudi za druge PSE. Aprila 1985 so opazili v Angliji primer nove bolezni pri kravah mlekaricah frizijsko-holsteinske pasme. Skoraj istočasno je bila odkrita nova in čudna bolezen še pri desetih kravah v različnih geografskih področjih. Živali so bile stare 3–6 let. Poprej zdrava goveda so postala preobčutljiva, razdražljiva, prestrašena, njihovo gibanje je bilo nekoordinirano. Bolezen so imenovali »bovina spongiformna encefalopatija«, BSE (19), v laičnem tisku pa jo pogosto imenujejo »bolezen norih krav«. Zanimivo je, da so podobno bolezen pri neki kravi opisali že leta 1883 (20). Epidemija se je bliskovito širila in je do srede 1996 klinično zbolelo in bilo uničeno okrog 160.000 govedi. Koliko jih je ostalo klinično brez simptomov, vendar okuženih, se ne vé. Britanska vlada je izredno skopa s podatki; pa tudi kmetje so k temu prispevali, ker so živali – pri prvem najmanjšem znaku bolezni – oddali v klavnico kot zdravo, ker je bila premija za zdravo žival enkrat višja kot za bolno. Danes menijo, da je število okuženih krav vsaj petkrat višje (!).

Epidemiološke raziskave so hitro pokazale, da je glavni dejavnik epidemije v Veliki Britaniji način prehrane živali; prehrana je bila edini skupni imenovalec pri vseh zbolelih živalih na širokem področju Velike Britanije (21, 22). Porast cene soje in ribje moke, ki so ju do takrat redno pokladali živini, je privedla do tega, da so iz klavniških odpadkov, v glavnem od ovc in govedi, pričeli delati t. i. mesno/kostno moko (MKM), sterilizirano pri temperaturi 121°C in ekstrahirano z organskimi topili. Od sredine 1970. let so znižali temperaturo sterilizacije na 80–90°C in opustili ekstrakcijo s topili; na ta način so zvišali prisotnost maščob od 5 na 12 odstotkov, kar je zvišalo število kalorij in seveda prodajno ceno. Važni dejavniki pri tem so bili (A) znatno zvišanje števila ovac s praskavico v Veliki Britaniji in (B) povečana raba ovčjih glav oz. možganov za pridelavo MKM in seveda (C) raba klavniških odpadkov govedi – bolnih ali asimptomatskih – za pridelavo MKM. Zato je bila l. 1988 prepovedana raba MKM z beljakovino prežvekovalcev v prehrani goveda (t. i. Feed ban), vendar tega odloka niso strogo spoštovali. MKM so kljub prepovedi rabe doma v Angliji še naprej izvažali v številne dežele še nekaj let. Julija 1989 je komisija Evropske skupnosti predlagala prepoved izvoza MKM iz Velike Britanije, vendar je britanska vlada to odklonila (23, 24). Tako se je bolezen z izvozom MKM in okuženih, vendar na videz zdravih živali, razširila in se je do sedaj pojavila v Severni Irski, Republiki Irski, Švici (ena najbolj okuženih dežel za Veliko Britanijo), Franciji, Sultanatu Oman, Danski, Nemčiji, Falklandskih otokih, Portugalski, Kanadi, Italiji, Norveški ter na Nizozemskem. Sedaj je izvoz govedine in govejih izdelkov iz Velike Britanije na splošno prepovedan, pa tudi uvoz iz Švice je prepovedalo 21 držav. Škode za gospodarstvo ni treba omenjati. Nemška vlada celo predlaga prepoved uvoza iz Velike Britanije in Francije določenih delov ovac (možgani, hrbtenjača, oči), ker je možno, da se je BSE vrnila nazaj k ovcam (25). Razlikovati BSE od praskavice pri zbolelih ovcah pa rutinsko ni mogoče. Omeniti je treba, da zakonodaja v državah ni enotna. Prepoved rabe MKM tudi v prehrani svinj in perutnine je v Veliki Britaniji v veljavi od marca 1996, druge države pa so prepovedale rabo MKM le v prehrani goveda, da bi tako preprečili t. i. tehnološki kanibalizem, v prehrani drugih živali pa jo še naprej rabijo.

Epidemija BSE je dosegla višek l. 1993 in od takrat je število na novo zbolelih govedi v upadanju. Temu je razlog prepoved rabe MKM v prehrani prežvekovalcev l. 1988, čeprav nekaj let ni bila strogo izvajana. Z doslednimi ukrepi bo epidemija prenehala (26); nekaj novih primerov vedno lahko pričakujemo zaradi vertikalno prenesene BSE govedo→tele, ki se zdi kljub nekaterim pomislekom (27) dokazana (28). Ta prenos pa ne more vzdrževati epidemije, ker je ta način prenosa v naravi pričakovati v manj kot enem odstotku. Drugi pa trdijo, da ta optimizem ni upravičen. Vprašanje je tudi, kaj je z vsemi okuženimi, asimptomatskimi govedmi. Različna so tudi mnenja o tem, koliko in katera goveda je treba uničiti. Prihodnost BSE epidemije v drugih, predvsem evropskih deželah, je težko predvideti, vendar epidemije, kot je bila v Veliki Britaniji, verjetno ne bo.

Pri pridelavi MKM, ki je ostala kužna, je znižanje temperature na 80–90°C samo eden od dejavnikov, ki so dovolili preživetje agensa. Odločilen dejavnik je bila tudi opustitev ekstrakcije z maščobnimi topili. Že l. 1965 so opisali (29), da topila zmanjšajo oz. odstranijo možnost okužbe s povzročiteljem praskavice. Nekaj podobnega se je zgodilo pri pripravi hormonov iz hipofize mrličev (rastni hormon in gonadotropin) z asimptomatično ali klinično CJB. Iatrogena CJB se je po dajanju teh hormonov pojavila v državah, v katerih so opustili ekstrakcijo z acetonom in jo nadomestili z bolj sodobnim zmrzovanjem (30). Proizvajalci MKM so ta podatek prezrli, ker z zvišanjem temperature na 136–138°C sterilizacija ni bila popolna (2).

Opisane so še: encefalopatija kun (31), kronična bolezen hiranja kopitarjev (32), praskavici podobna spongiformna encefalopatija mačk, ki so jedle okuženo meso (konzerve?) (33), ter podobne encefalopatije pri nekaterih antilopah, pumah in gepardih, živečih v zooloških vrtovih.



Sl. 1. *Bovina spongiformna encefalopatija (BSE). Rpidemiologija.*

Fig. 1. *Bovine spongiform encephalopathy (BSE). Epidemiology.*

Etiologija PSE

O etiologiji bolezni je več med seboj nasprotnih teorij. Nenavadne značilnosti povzročitelja praskavice so razlog, da so mislili, da ne vsebuje nukleinske kisline, torej genetskega materiala, ker ga ni bilo mogoče inaktivirati z metodami, ki uničijo nukleinske kisline, kot so UV-žarki (34), nukleaze, psoralen in dvovalentni cink (35); uničiti ga je bilo mogoče le s kemičnimi snovmi, ki inaktivirajo beljakovine, kot so npr. fenol in urea (36).

Kužnost beljakovin v odsotnosti genomske nukleinske kisline je nekaj povsem novega in v biologiji doslej neznanega. Na to teorijo so opozorili že l. 1967 Griffith (37) in Pattison (38).

Pri čiščenju materiala (možganov zdravih in zbolelih živali ali človeka) so odkrili beljakovino, molekulske teže 33.000–35.000 D (Dalton), ki so jo imenovali prionski protein (PrP) in ki se pojavlja v dveh izoformah, in sicer kot PrP^{C} (celularni) v normalnih možganih in PrP^{Sc} v zbolelih; za obe obliki je odgovoren isti kromosomski gen (43). PrP^{C} se nahaja tudi v nekaterih drugih tkivih, bodisi embrionalnih bodisi odraslih. V normalnih možganih se nahaja na površini nevronov, pritrjen z eno gliko-inozitol-fosfolipidno vezo (44, 45). Delovanje proteaz (Proteinase K) razgradi PrP^{C} v celoti, PrP^{Sc} pa je deloma odporen proti proteolizi in ostane molekula z molekulsko težo 27.000–30.000 D (51); včasih je ta beljakovina označena tudi kot PrP 27–30 in je kužna, dobila pa je ime prion (PrP) »Proteinaceous Infectious Particle« (35). Po nekaterih pa prion označuje zvezo med proteinom in virionom, ime pa naj bi ločilo agens od konvencionalnih virusov ter poudarjalo njegovo dvojno naravo protein-virion (39). Ime prion je bilo sicer že znano od l. 1848, vendar je bilo dano morskim pticam južne hemisfere (40). To teorijo imenujejo danes »Protein Only« (41).

Za razliko od normalnega prionskega proteina (PrP^{C}) se patološki (PrP^{Sc}) akumulira intracelularno, v citoplazmatskih vezikulah (46). Zaporedje aminokislin PrP^{C} in PrP^{Sc} je pri isti živalski vrsti enako,

zato jih na ta način niso mogli razlikovati. To je tudi verjetno razlog, da pri bolnikih v poteku bolezni niso opazili tvorbe protiteles, uperjenih proti PrP^{Sc} (47–49). Tudi imunološko, z mono- ali poliklonskimi protitelesi (najpogosteje z zajčjimi) ali celò s protitelesi za sintetične prionske polipeptide (50), ni bilo mogoče razlikovati PrP^{C} od PrP^{Sc}. Zapis za prionski protein ima prionski gen, PRNP (51), ki je pri človeku lokaliziran na kromosomu 20. Ekspresija prionskega gena poteka po znani poti: Genska DNA → Transkripcija (prepis genetske informacije DNA → RNA) → cDNA → translacija (sinteza proteina) → PrP^{C}. Ko prion (PrP) pride v organizem, npr. po oralni poti, se širi po limfnih poteh do končnega cilja, osrednjega živčevja.

Neposredna reakcija patološkega PrP^{Sc} z normalnim PrP^{C} povzroča nadaljnjo konverzijo PrP^{C} → PrP^{Sc} z avtokatalitičnim procesom. Tvorba kompleksa PrP^{C} ↔ PrP^{Sc} lažje uspe, če je zaporedje aminokislin dveh izoformov PrP enako ali zelo podobno (homologija); pri razlikah v zaporedju prihaja (pri eksperimentalni okužbi transgenskih miši) do značilnega podaljšanja inkubacije (52, 53). PrP^{C} reagira s PrP^{Sc} ob posredovanju posebne makromolekule, verjetno tudi beljakovinske narave, imenovane »Protein X« (54). Poudariti je treba, da beljakovina X ni identična s PrP^{Sc}. Po reakciji med PrP^{C} in PrP^{Sc} pride do konformacijske spremembe beljakovine. Sprememba je posttranslacijska, ker je bila sinteza beljakovine že končana. PrP^{C} je sestavljen iz 42% oblike alfa-vijačnice ter 3% oblike beta-nagubanega lista (45, 55), medtem ima PrP^{Sc} le 30% oblike alfa-vijačnice in 43% beta-nagubanega lista. Vse reakcije naj bi potekale brez nukleinskih kislin. Weissmann (41) omenja še reakcijo PrP^{Sc} z nukleinsko kislino jedra okužene celice, ki naj bi nadomestila nikoli jasno dokazano patološko nukleinsko kislino.

Razumljivo je, da v tem primeru ni mogoče razlikovati nukleinske kisline normalne in okužene celice. V nadaljnjem poteku pride do tvorbe in odlaganja iz PrP^{Sc}, sestavljenega amiloida v obliki t. i. plakov, vendar ne vedno. Pri odlaganju amiloida sodeluje tudi t. i. protein Y, ki prav tako kot protein X še ni natančneje raziskan. Odkritje dveh reakcijskih mest pri PrP^{C}, od katerih eno reagira s PrP^{Sc}, drugo pa s proteinom X, je verjetno vzrok za visoko specifičnost razmnoževanja PrP^{Sc} (53).

Posebno zanimivost predstavljajo poskusi s transgenskimi mišmi, ki so jim z zapletenim postopkom odstranili prionski gen; to so t. i. knock-out miši, $PrP^{0/0}$ (56). Če je PrP zares ključna sestavina povzročitelja (PrP^{Sc}), potem bi žival brez PrP^{C} morala biti odporna proti praskavici. Vendar se je pokazalo, da te miši ohranijo sposobnost replicirati agens v nizkem titru; zato je narava agensa scrapie še nepojasnjena (57). Zanimivo je, da so miši brez PrP^{C} živele normalno vsaj 18 mesecev. Odsotnost PrP^{C} beljakovin v možganih in drugih tkivih ni imela škodljivega učinka za zdravje živali. Eno tolmačenje je, da ima odsotnost tega genskega produkta učinek šele v starosti ali pa šele v naslednjih generacijah. Mogoče pa je bila izguba te beljakovine nadomeščena z drugimi, sorodnimi ali različnimi. Nekateri raziskovalci menijo, da je PrP^{C} potreben le v zgodnji fazi razvoja in da se nadalje tvori zaradi nekakšne genetske inercije (58). Podoben pojav so opazili tudi pri nekaterih drugih poskusih; tako npr. večina genetskega zaporedja glivic ni bistvenega pomena za rast in razmnoževanje celic (59). Kljub temu funkcija prionske beljakovine v normalnem organizmu še ni znana. Eni menijo, da PrP^{C} sodeluje v aktivaciji limfocitov (60); drugi mislijo, da deluje, vsaj deloma, kot rastni dejavnik glia-celic (61). Opisana je tudi sekretorna oblika PrP^{C} (62).

Poskusi so pokazali, da so miši brez gena za PrP^{C} (PRNP) odporne proti okužbi s praskavico (63). Pri miših, ki so imele še približno polovico PrP^{C}, sta bili inkubacija in potek bolezni podaljšani, smrt pa je nastopila pozneje. Nadaljnji poskusi so dali »himerske« miši, ki so imele človeški in mišji PRNP gen (64). V takih miših inkubacija po okužbi z agensom BSE ni bila skrajšana zaradi humanega PrP^{C} in produciran je bil samo mišji PrP (65). Tako naj bi bil humani PrP^{C} za bovini prion manj občutljiv kot mišji; to so imeli za dober znak, ki naj bi govoril o majhni možnosti prenosa BSE na človeka.

Vendar avtorji svojih rezultatov nimajo za dokončne in predlagajo ponovitev poskusov.

Teorije o virusih in viroidih – to so kužni agensi, manjši od virusov (66) – še niso zavržene. Študije sicer kažejo na osnovno vlogo gostiteljevega PrP^{C} pri pojavu bolezni, vendar menijo, da prion ni identičen s kužnim agensom (67). Ni verjetno, da bi bil sam PrP^{Sc} razmnoževalna sestavina. Agens naj bi vseboval t. i. beljakovino sredice (core-protein) in nukleinsko kislino, zaščiteno s celično membrano. Novejša raziskovanja kažejo na prisotnost specifične nukleinske kisline ter ene ali dveh vezanih beljakovin kot sestavino virusa. Ti dve sestavini nista kužni, preden se združita v nukleaza-rezistentne, sedimentirajoče delce. Značilno je tudi, da SDS (Sodium Dodecyl Sulphate) odstrani skoraj vse sledove PrP, brez značilnega padca kužnega titra. Celo večji, sedimentirajoči delci priona (PrP) niso več kužni. Avtorji uporabljajo izraz »virus« za opis agensa zaradi njegove biologije (prenosa kužnosti v biološkem poskusu), zaradi virusom podobne velikosti in gostote ter zaradi njegove inaktivacije s kemikalijami, ki uničujejo kompleks nukleinska kislina–beljakovina (68). Sakaguchi in sodelavci (68) so uspeli razločiti PrP^{Sc} od kužnosti v žlezah slinavkah mišk, okuženih z agensom CJB; titer agensa je padal, ko se je PrP^{Sc} akumuliral v tkivu. Rezultati so pokazali, da je akumulacija PrP^{Sc} sicer povezana z razmnoževanjem agensa, vendar ni verjetno, da bi PrP^{Sc} predstavljal sam agens. PrP^{Sc} je morda samo ena sestavina kužnega agensa (70, 71). Tudi visoko kužne frakcije, dobljene z ultracentrifugiranjem (120S), niso vsebovale PrP^{Sc} (72). Tudi rekombinantni (v laboratoriju sintetizirani) prion ni bil kužen.

Poglavje o nukleinskih kislinah še ni zaključeno. Poborniki proteinske teorije trdijo, da nukleinska kislina, večja od 100 nukleotidov, ne more biti odločilnega pomena za kužnost prionskih preparatov praskavice, in sicer zaradi (1) zelo majhne ciljne velikosti kužnosti agensa praskavice (73–75), (2) majhnega odnosa nukleinske kisline proti enoti kužnosti v visoko purificiranih prionskih preparatih (76, 77) ter (3) pomanjkanja dokazov o za praskavico specifični nukleinski kislini v prionskih preparatih ali možganih, okuženih s praskavico (78), in (4) odpornosti kužnosti po obdelavi s preparati, ki modificirajo ali poškodujejo nukleinsko kislino (35). Na podlagi teh rezultatov menijo, da nukleinska kislina, ki vsebuje več 50 do 100 nukleotidov, ni pomembna za kužnost. Novejše študije sicer govorijo v tem smislu (79), vendar so objavljena tudi nasprotna mnenja (80, 81). Možno je, da imajo nukleinske kisline nenavadno strukturo ali da so zelo majhne (manj kot 50 baznih parov purin-pirimidin) ter jih zato ni bilo mogoče dokazati; mogoče pa so genetska zaporedja baznih parov podobna zaporedjem genoma gostitelja (82). Tudi drugi so ugotovili, da je homologna ssDNA prisotna pri praskavici, CJB in BSE (83–86). Omenja se tudi očitek, da so zagovorniki beljakovinske teorije storili vse, da ne bi dokazali prisotnosti nukleinskih kislin.

O elektronsko-mikroskopskih preiskavah obstaja obsežna, deloma kontradiktorna literatura, objavljena v zadnjih 25 letih. V možganih hrčkov, okuženih s praskavico, so našli značilne strukture, tanjše od virusov, vendar s strukturalnimi značilnostmi virusa (87). Podobno so našli male, virusom podobne delce v možganih bolnikov s CJB (88, 89) ali pri ovcah s praskavico. Vendar jasnih dokazov za virusno etiologijo še ni.

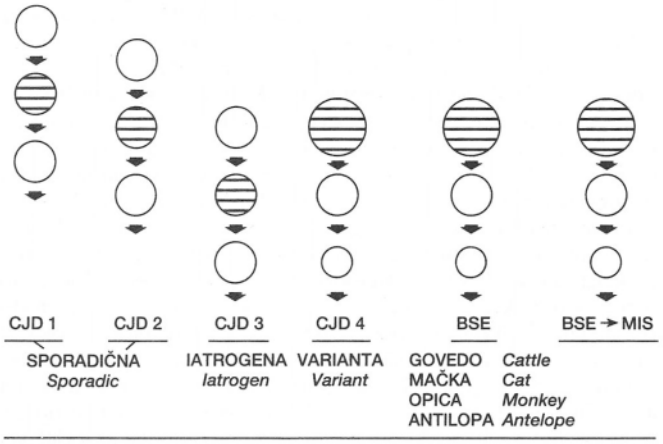
Na prisotnost genetskega materiala v povzročitelju kaže tudi obstoj več sevov agensa, ki so jih najprej opazili pri praskavici, pozneje pri kuni (dva seva) in CJB (91–93). Pri miših, eksperimentalno okuženih s praskavico, so opazili dva seva, ki povzročata bolezen po kratki ali po dolgi inkubaciji in sta v zvezi s t. i. Sinc-genom (Scrapie incubation time gene). Pri agensu praskavice so že našli več kot 20 različnih sevov; v eni živali jih je istočasno prisotnih lahko več. Pri pasažah manj virulentni sevi izginejo in končno ostane le virulenten (94). Značilnosti sevov, ki ostanejo nespremenjeni tudi po zaporednem presajevanju v živalih, se kažejo (1) z dolžino inkubacije in (2) s tipom in razširitvijo nevropatoloških sprememb v različnih predelih možganov. Obstoj številnih sevov agensa in celo možnost mutacije nakazujeta, da naj bi agens praskavice (in ostali odgovorni za PSE) imel svoj genom za

Skupina 1 *Group 1*	Skupina 2 *Group 2*
>300 telet od krav z dokazano BSE *>300 calves born to cows with confirmed BSE*	>300 telet od klinično zdravih krav, starejših od 6 let *>300 calves born to cows (>6 y. old) with no clinical disease*
Opazovalna doba 7 let (do pojava BSE) *Observation time 7 years until BSE developed*	
BSE pri 42/273 *42/273 with BSE*	BSE pri 13/273 *13/273 developed BSE*

Višek 29 primerov v prvi skupini govori za 10-odstotno vertikalno prenosljivost.
Excess of 29 cases in group 1 predicts a 10% transmission rate.

Sl. 2. *Vertikalni prenos BSE krava→tele.*

Fig. 2. *Vertical transmission Cow→Calf.*



WB VARIANTA CJD USTREZA WB BSE PRI GOVEDU IN Z BSE AGENSOM OKUŽENIMI ŽIVALMI (COLLINGE J, 1996)
WB variant CJD corresponds to WB of BSE in cattle and in animals inoculated with BSE

Sl. 3. *Western blot proteaze rezistentnega prion proteina (PrP^{Sc}).*

Fig. 3. *Western blot of protease-resistent prion protein (PrP^{Sc}).*

replikacijo (95). Debla praskavice imajo (genetsko) informacijo, ki ni odvisna od gostitelja, vendar PrP^{C} gostitelja reagira s to informacijo in tako regulira razvoj bolezni (96). Tudi pri agensu BSE-ja so našli za agens specifično kužno molekulo (97). Beljakovinska teorija zavrača take možnosti in poskuša naravo sevov pojasniti na drug način s specifično (fizikalno?) strukturo priona, vendar to še ni dokazano. Pri sevih so opazili celo fenomen t. i. interference; npr. miške, okužene s sevom dolge inkubacije, niso več reagirale na okužbo s sevom kratke inkubacije, ki je bil cepljen nekaj tednov pozneje. Ta pojav je dobro znan iz humane virologije.

Proti teoriji o prionu kot edinem odgovornem za nastanek in prenos bolezni govorijo tudi poskusi z Amphotericinom B. Pri hrčkih, okuženih s praskavico in zdravljenim s tem antibiotikom, se klinična bolezen pojavi pozneje kot pri nezdravljenih kontrolah, vendar titer kužnosti ni moten (disociacija razmnoževanja agensa in vivo). PrP^{Sc} je sicer nujen za razvoj bolezni, vendar ni verjetno, da bi bil bistvenega pomena za replikacijo agensa (98). Tudi rezultati drugih študij kažejo na to, da nabiranje PrP^{Sc} in razmnoževanje agensa nista edina dejavnika, ki sta potrebna za začetek klinične bolezni (99). Pri najnovejših poskusih prenosa BSE na laboratorijske miši so ugotovili (100), da so vse inokulirane miši kazale nevrološke simptome in propad nevronov, vendar pri več kot 55% niso mogli dokazati PrP^{Sc}. Po serijskih pasažah, potem ko se je povzročitelj prilagodil na gostitelja, se je PrP^{Sc} spet pojavil. Avtorji menijo, da je PrP^{Sc} zagotovo udeležen v patološkem procesu in prilagajanju na določeno živalsko vrsto, vendar naj bi bil povzročitelj neki drug, še neidentificiran agens.

Genetika CJB

Familiarno CJB so ugotovili pri približno 10% vseh primerov bolezni (101, 102). Dednost je povezana z avtosomno-dominantnim načinom prenosa, značilno izraženem pri heterozigotih, ki imajo eno normalno in eno okvarjeno alelo na ustreznem lokusu PRNP gena (t. i. Mendelove ali single gen bolezni, Mendel, 1866). Dominantnost se nanaša na fenotip in ne na genotip. Najbolj pogosta mutacija pri familiarni CJB je v PRNP regiji pri kodonu 200; $200^{Gly-Lys}$ (103). To mutacijo so nekateri opisali v 82% raziskovanih primerov (104) na Slovaškem, Poljskem, v Nemčiji, Tunisu, Grčiji, Libiji in Čilu. Pri nekaterih primerih so odkrili mutacijo na kodonu 178 istega gena; $178^{Asp-Asn}$ (105). Bolezen je verjetno asociirana z mutacijami tudi pri kodonih 180 in 232. Pri vseh mutacijah na kodonih gre za t. i. točkaste mutacije, našli pa so tudi druge spremembe. Owen (106) je pri CJB dokazal insercijo v eni aleli PRNP gena; pozneje so dokazali, da je ta insercija rezultat ene šeste, ponavljajoče se sekvence 24-nukleotidov (oktapeptid), poleg petih, že normalno prisotnih ponovitev v N-terminalni regiji beljakovine (107). V nekaj primerih so našli CJB povezano s 5, 7, 8 (108) ali celo 11 in 14 (109) ponovitvami v regijah, ki kodirajo oktapeptide. Opisane ponovitve igrajo določeno vlogo v predispoziciji za familiarno CJB.

Polimorfizem pri kodonu 129 je velikega pomena za humane PSE. Tukaj ne gre za mutacijo, ampak za v naravi nastopajoči polimorfizem. Alele na kodonu so metionin (met) in valin (val), možnosti pa so kombinacije met/met in val/val (homozigoti) in met/val (heterozigoti). V normalni populaciji je približno 40% heterozigotov in 60% homozigotov (bolj pogosti met/met). Pri sporadični CJB so našli 78% homozigotov met/met, pri novi varianti vCJB pa 100% istih (110). Tudi pri iatrogeni CJB prevladujejo homozigoti, najbolj pogosto met/met. Pri živalih s PSE ne igra polimorfizem na tem kodonu nobene vloge. Ta polimorfizem je omejen na človeka, živali s PSE so bile vse homozigoti met/met.

Vprašanje prenosa BSE – človek

Prvi pomisleki o možnosti prenosa BSE na človeka so bili objavljeni že l. 1988 (111). Pri ljudeh naj bi bil oralni prenos najbolj verjeten (23). Glavna nevarnost je prisotnost perifernih živčnih in limfatičnih tkiv v govejem mesu, ki so lahko kužna; meso je lahko kontaminirano tudi v klavnicah s hrbtnim mozgom ali drugimi, zelo kužnimi tkivi (posebej nevarne so motorne žage za razcepitev hrbtenice). V zadnjih letih so o tem problemu objavili obsežno literaturo za in proti.

Poborniki teorije, da se bolezen ne prenaša, omenjajo praskavico, eno od podobnih PSE. Čeprav je znana že 200 let, razširjena po vsem svetu in eden pomembnih virov človeške prehrane (uživali so tudi rizične organe, kot so možgani in oči), ni bilo epidemioloških podatkov, ki bi kazali na kužnost praskavice za človeka. Danes menijo, da je temu vzrok dejstvo, da ne obstaja zadostna homologija PrP ovca–človek. Homologija ovca–govedo (98%) pa podpira trditev za kužnost ovca–govedo (112).

Situacija se je v trenutku spremenila, ko je britanska vlada marca 1996 objavila, da je uživanje govedine pri desetih mladih bolnikih s CJB, zbolelih 1995–1996, najbolj verjeten vzrok bolezni, ker drugega skupnega imenovalca niso mogli dokazati; osnova vladne izjave je bilo poročilo Willa in sodelavcev (17). Seveda tudi to ni dokončni dokaz; absolutni dokaz bi dala eksperimentalna oralna okužba človeka z BSE. Iz etičnih razlogov tega dokaza ne bo možno dobiti nikoli. V komisiji Evropske unije je Weissmann l. 1996 predlagal eksperimentalno okužbo opic, vendar so ga zelo napadli (114), češ da je bilo opice že mogoče eksperimentalno (intracerebralno) okužiti in da bariera vrste človek–opica pravzaprav ne obstaja. Pa tudi na rezultate bi zaradi dolge inkubacije morali čakati dolga leta. Bolj pomembno da bi bilo izkoreniniti BSE nasploh; ljudem (milijonom oseb), ki so jedli

okuženo meso, pa ni več mogoče pomagati. Velik korak naprej v študiju epidemiologije prenosa prionskih bolezni so prinesle molekularno-biološke raziskave PrP^{Sc}. S purifikacijo možganov dobljeni PrP^{Sc} so tretirali s Proteinazo K in tako dobljeni PrP-res (proteinaze-rezistenten) so podvrgli elektroforezi na 16% trisglycin gelu in nato prenesli na Milliporjevo membrano (electroblot). Tako dobljeni imunoblot so tretirali z antiprionskimi serumi (primarna protitelesa), mono- ali poliklonskimi ter nato s sekundarnimi protitelesi za primarna protitelesa, ki so bila markirana npr. s hrenovo peroksidazo; končno je z ustreznim substratom reakcija postala vidljiva. Metodo imenujejo Western blot in so rezultati tudi kvantitativni. Parchi in sod. (92) so s to metodo pregledali 19 primerov sporadične CJB. Western blot je pokazal tri glavne izoforme v obliki trakov ali zon. Ti trije izoformi se razlikujejo po stopnji glikozilacije (imajo enega ali dva sladkorja ali so brez njega). Študij je odkril dva tipa PrP^{Sc} (tip 1 in tip 2). Enega najpomembnejših študijev so opravili Collinge in sodelavci (93). Klinična skupina je obsegala 26 primerov sporadične CJB, 7 primerov iatrogene CJB in deset primerov nove variante vCJB. Rezultati so tudi pokazali tri izoforme brez sladkorja, z enim ali dvema sladkorjema. Tipe je bilo možno kvantitativno in po stopnji glikozilacije zelo natančno razlikovati. Pri sporadični CJB so potrjeni tipi 1 in 2. Pri iatrogeni CJB, pri kateri je prišlo do periferne okužbe s prioni, je bil najden tip 3. Pri iatrogeni CJB, nastali po neposredni okužbi s presadkom trde možganske opne, je bil rezultat podoben sporadični CJB; to je bilo potrjeno tudi klinično (115). Najbolj pomembne rezultate so dobili z materiali pacientov z novo varianto vCJB. Čeprav so velikosti trakov podobne tipu 3, je ta tip možno jasno razlikovati od ostalih treh tipov po značilnem tipu in intenziteti trakov; zato je označen kot tip 4. Ta molekularni marker podpira trditev, nastalo na podlagi klinično-patoloških in epidemioloških raziskav (17), da je nova varianta, vCJB, jasen in novi podtip prionskih bolezni. Spontani pojav tega novega seva pri vseh desetih primerih vCJB v Western blotu ni verjeten. Primeri izvirajo iz nekega novega, verjetno živalskega vira. Prion vCJB so našli pri govedu, v miših, eksperimentalno okuženih z BSE, v naravno okuženih mačkah in antilopah ter pri opicah, okuženih v laboratoriju. Ti rezultati potrjujejo v dobri meri omenjeno hipotezo prenosa BSE z goveda na človeka. Obenem je potrjen tudi obstoj različnih sevov PrP^{Sc} pri CJB, kot je bilo že dolgo znano pri agensu praskavice ovc. Preiskali bodo tudi, če je BSE morda ponovno prenesena tudi na ovce in če lahko še naprej persistira v populaciji ovac (116). Nekateri avtorji omenjajo le dva tipa CJB (143), vendar so tudi oni potrdili, da je vCJB možno razlikovati v Western blotu od sporadičnih in iatrogenih primerov CJB (144).

Krakauer in sodelavci (117) so raziskovali filogenezo PrP^{C} pri raznih vrstah sesalcev. Avtorji so mnenja, da sta dve substituciji aminokislin edinstveni le pri hominoidih in govedu: tirozin-histidin pri kodonu 155 PRNP in asparagin-serin pri kodonu 143 PRNP. Ni verjetno, da bi bil to slučaj. To je morda razlog za predispozicijo oz. občutljivost na okužbo z BSE pri človeku. Drugi avtorji (118) se ne strinjajo s temi zaključki in predlagajo študij tridimenzionalne strukture prionskega proteina in njegovih interakcij in boljše razumevanje molekularne osnove pri sevih povzročitelja prionskih bolezni.

Epidemiologi londonske šole za higieno in tropsko medicino ter Nacionalne enote za spremljanje CJB v Edinburghu (119) so na podlagi izkušenj z vCJB poskusili predvideti število primerov te bolezni v prihodnjih letih. Pojavljanje novih primerov vCJB je odvisno od dolžine inkubacije bolezni in učinkovitosti prepovedi rabe specifičnih govejih delov v prehrani človeka. Statistične analize so dale zelo različne rezultate, ki so lahko le predvidevanja in se pričakovani rezultati lahko spremenijo. V najslabšem primeru, pri 25-letni inkubaciji in 90-odstotni učinkovitosti predvidenih epidemioloških ukrepov, je pričakovati med 700 in 80.000 (!) primerov vCJB. Če se BSE zares lahko prenaša na človeka s hrano, je odločilnega pomena vrsta in količina kužnega govejega materiala v človekovi prehrani.

Diagnostika PSE intra vitam

Metode za diagnostiko bolezni za časa življenja, še posebej pred nastopom kliničnih znakov, so ogromnega pomena; na tem področju je bilo do nedavnega tudi iz politično-ekonomskih razlogov narejeno zelo malo. Z rabo antiseruma za sintetične peptide ovčjega PrP (pri PRNP kodonih 94–105, 100–111, 145–177, 126–143 in 223–224), ki ga je opisal Goldmann (120), je uspelo imuno-histokemično dokazati PrP^{Sc} v možganih ovac z naravno praskavico (121). Klasični poskusi v patogenezi praskavice na laboratorijskih miših (122) so pokazali, da je prvo razmnoževanje povzročitelja, sicer apliciranega intrakutano, mogoče dokazati v limfatičnih tkivih. Tudi pozneje so dokazali zgodnji pojav povzročitelja v tonzilah ter retrofaringealnih in mezenterialnih bezgavkah (123); to tudi govori za možno naravno okužbo prek prebavnega trakta. Prione so našli tudi v humanih limforetikularnih tkivih. Na osnovi teh klasičnih dognanj so našli PrP^{Sc} v tonzilah ovac v predkliničnem stadiju, daleč pred nastopom bolezni (124), in sicer v starosti 9 1/2 do 10 mesecev. Upoštevajoč dolžino inkubacije pri ovcah, je bila diagnoza na ta način postavljena približno eno leto pred izbruhom bolezni. Tako je na voljo predklinična diagnoza bolezni (125). Ta test so preverili tudi v Indiji (126). Priporočajo rabo tenke igle za aspiracijo materiala iz tonzil; igla naj bi bila podobna tistim, ki jih uporabljajo v citologiji za aspiracijo tumorskih celic. Opisana tehnika je manj invazivna od klasične biopsije, punkcija pa je lahko tudi hitro narejena. Najdba makrofagov z granularnimi depoziti PrP^{Sc} bo velikega diagnostičnega pomena v humani in veterinarski medicini, pa tudi za poskuse na živalih. Na ta način naj bi kontrolirali tudi ovce, katerih možgane rabijo za pripravo cepiv, saj je praskavica endemična v mnogih področjih, kjer pripravljajo taka cepiva, pa tudi primeri CJB so opisani v takih krajih (127). Omeniti je treba okužbo številnih ovac, cepljenih s cepivom zoper Louping-ill, ki so ga pripravili iz možganov ovac, cepljenih s tem virusom, vendar okuženih s praskavico, ampak brez kliničnih znakov bolezni (128).

Tudi najnovejša dela so potrdila korist biopsije tonzil v diagnostične namene. Proučevali so tonzile, dobljene pri nekropsiji, z imuno-histokemično metodo na tkivu, fiksiranem s formalinom ali formaldehid-periodatom, ali pa z metodo Western blot, na zmrznjenem tkivu (129). Pacientka je bila stara 35 let in je umrla za vCJB. PrP^{Sc} so dokazali v tonzilarnih germinativnih centrih. Tudi Western blot je odkril proteaza-rezistenten PrP^{Sc} (PrP-res); velikost in intenziteta treh con (trakov) PrP^{Sc}-ja (z dvema, enim ali brez sladkorja) sta ustrezali tipu, dokazanem v možganih pacientke, označili pa so ga kot tip 4 (93), ki je značilen za vCJB. Opisano diagnostično metodo bodo lahko uporabili tudi pri iatrogeni CJB po periferni okužbi s prioni. Tudi pri tonzilektomiranih osebah je diagnoza možna, ker ostane vedno nekaj limforetikularnega tkiva na mestu operacije. Da bi se izognili iatrogeni kontaminaciji s povzročiteljem CJB, bo treba izdelati kit za biopsijo za enkratno uporabo. Biopsijo bo lahko izvesti v lokalni anesteziji. Tonzilarni test so v Veliki Britaniji zelo pozdravili.

Diagnoza PSE je mogoča tudi z možgansko biopsijo, vendar je to zelo invaziven poseg zaradi možnega ekstraduralnega hematoma ali možganskega abscesa, pa tudi vse instrumente je treba uničiti. Pomembno je tudi s punkcijo zadeti patološko tkivo. Pa tudi bolniku ni več mogoče pomagati. Pri asimptomatskih bolnikih nima metoda seveda nobenega pomena. L. 1996 je omenjen pregled sedimenta urina okuženega goveda (Narag H, Neue Revue 9, 22.2–1996), vendar metoda še ni opisana v strokovni literaturi, pa tudi britanska vlada ni podprla avtorja; ta je prišel v Švico po pomoč.

Posebno poglavje diagnostike PSE za časa življenja predstavlja biokemična analiza beljakovin v cerebrospinalnem likvorju. Moore (130) je opisal beljakovine, ki jih je imenoval 14-3-3 na osnovi sistematske analize možganskih beljakovin. To so kisle beljakovine molekulske mase od približno 30.000 D in izoelektrične točke 5. Mnogo jih je v možganih, posebno v nevronih. Družina teh beljakovin ima zelo dobro konservirano zaporedje aminokislin.

Menijo, da igrajo vlogo v prenosu signalov v mehanizmu fosforilacije (131). Družino 14-3-3 beljakovin so našli tudi v muhah, glivicah in rastlinah. Zdi se, da je ta beljakovina humani ekvivalent bovine 14-3-3 beljakovine; hitro potujočo sestavino so imenovali 14-3-3-2, počasnejšo pa 14-3-3-1 (132). Z zajčjim antiserumom za 14-3-3 in metodo RIA (Radio Immuno Assay) so to beljakovino dokazali v možganih, v manjši količini tudi v jetrih, ledvicah, skeletni muskulaturi in eritrocitih, pa tudi v serumu in cerebrospinalnem likvorju. Vendar testi pri 84 nevroloških pacientih niso dali značilnih rezultatov (132). Šele nekaj let pozneje so jih klinično-laboratorijsko preučili bolj natančno (133). Počasna beljakovina, imenovana 131, je imela molekulsko maso 29.000 D, bolj hitra, 130, pa 26.000 D. Izrednega pomena je, da antiserum za PrP v Western blotu ni reagiral s temi beljakovinami. Za dokaz beljakovin rabijo 2-dimenzionalno elektroforezo (izoelektrično fokusiranje ter PAG [poliakrilamidno] elektroforezo v prisotnosti SDS). Beljakovine so našli tudi v 5 od 10 primerov herpes encefalitisa, vendar ne pri drugih nevroloških boleznih, razen pri PSE. Avtorji menijo, da so te beljakovine po poreklu iz možganov, od koder pridejo v cerebrospinalni likvor. Treba je omeniti, da je bila metoda za dokazovanje zelo zapletena in zato ni prišla v rutinsko rabo v medicinski biokemiji nevroloških bolnikov.

Hsich in sodelavci (134) so našli beljakovine 130 in 131 v normalnih možganih, deloma sekvencirali njihove aminokisline ter našli, da ustrezajo beljakovinam, znanim kot 14-3-3. Opisali so zelo enostavno in hitro imunoencimsko metodo, ki je bila tudi nekoliko bolj občutljiva kot 2-dimenzionalna elektroforeza. S to metodo so pregledali 71 bolnikov in 30 živali s PSE ter 186 humanih in 94 živalskih kontrol. Pri 71 pacientih s CJB je bil test pozitiven v 68 primerih. Pri živalih je bila občutljivost 87%, specifičnost pa 99%. Test je bil pozitiven tudi pri 12 od 24 bolnikov s herpetičnim encefalitisom. Prisotnost beljakovin 14-3-3 v cerebrospinalnem likvorju je verjetno povzročena z masivno destrukcijo nevronov ter difuzijo njihovih proteinov v likvor; zato tudi pozitivni rezultati pri herpetičnem encefalitisu (12 od 24) in možganski kapi (7 od 7).

Test naj bi bil le marker za nevronsko poškodbo in ga ni treba uporabljati pri pacientih brez klinično jasne demence. Test je bil pozitiven tudi pri dveh pacientih z novo varianto vCJB (135). Testi za proteine 14-3-3 se zdijo velikega pomena (136), vendar jih je treba uporabljati kritično. Ni še znano, kako hitro v toku bolezni postane test pozitiven. Upoštevati je treba tudi stabilnost beljakovin 14-3-3, ker bo treba vzorce verjetno pošiljati v biokemične centralne laboratorije. Slabo hranjeni vzorci beljakovin lahko zaradi razgradnje dajo lažno negativne rezultate (135). Takojšnje zamrzovanje je idealno, tudi hranjenje pri < 4°C.

Konserviranje pri > 4°C ni dobro. En pozitivni rezultat so našli tudi pri primeru pljučnega raka (137).

Wakayama in sodelavci (138) so prvi raziskovali raven nevronsko-specifične enolaze (NSE) v serumu in cerebrospinalnem likvorju. NSE je dimerični, citoplazmatski encim, ki ga je mnogo v perikarionu živčnih celic in aksonih. NSE so kvantitativno analizirali z dvojnim testom RIA, pri tem so uporabljali en komercialni kit (Eiken, Tokyo, Japonska). Avtorji so ugotovili, da je raven NSE znatno zvišana v zgodnjem stadiju CJB, ko računalniška tomografija kaže le minimalne ali pa nobenih abnormalnosti. Zvišano NSE so našli tudi pri akutnem ishemičnem infarktu, ko encim prodre iz možganov v cerebrospinalni likvor (139). Tudi na Japonskem so našli pri bolnikih s CJB zvišane vrednosti NSE v zgodnjem stadiju bolezni, pred pojavom kliničnih simptomov (140). Raven naj bi služila kot biokemični marker za prisotnost aktivnega procesa v možganih in kot taka bila indikator za zgodnjo diagnozo CJB. Rezultati so potrjeni tudi v najnovejšem času (141, 142). Koncentracije NSE v cerebrospinalnem likvorju, višje od 35 ng/ml, naj bi kazale na diagnozo CJB (Kit Hoffmann-La Roche, Basel, Švica). Pozitivne rezultate so opazili tudi pri hipoksični okvari možganov, ishemičnem infarktu (kap), subduralnem hematomu in tumorjih.

Literatura

1. Taylor DM. Inactivation of SE agents. Br Med Bull 1993; 49: 810–21.
2. Taylor DM, Fraser H, McConnell I et al. Decontamination studies with the agents of BSE and scrapie. Arch Virol 1994; 139: 313–26.
3. Gajdusek DC, Zigas V. Degenerative system of the central nervous system in New Guinea: epidemic occurrence of »kuru« in native populations. N Engl J Med 1957; 257: 974–8.
4. Gerstmann J. Ueber ein noch nicht beschriebenes Reflexphänomen bei einer Erkrankung des zerebellaren Systems. Wien Med Wochenschr 1928; 78: 906–8.
5. Lugaresi E, Medori R, Montagna P et al. Fatal familial insomnia and dysautonomia with selective degeneration of thalamic nuclei. N Engl J Med 1986; 315: 997–1003.
6. Alpers BJ. Diffuse progressive degeneration of the gray matter of the cerebrum. Arch Neurol Psychiat 1931; 25: 469–505.
7. Petersen RB, Tabaton M, Chen SG et al. Familial progressive subcortical gliosis: presence of prions and linkage to chromosome 17. Neurology 1995; 45: 1062–7.
8. Gajdusek DC. Unconventional viruses and the origin and disappearance of kuru. Science 1977; 197: 943–60.
9. Sommer SS, Rocca WA. Prion analogues and twin studies in Parkinson's disease. Neurology 1996; 46: 273–5.
10. Creutzfeldt G. Ueber eine eigenartige herdförmige Erkrankung des Zentralnervensystems. Z Ges Neurol Psychiat 1920; 57: 1–18.
11. Jakob A. Ueber eigenartige Erkrankungen des Zentralnervensystems mit bemerkenswertem anatomischen Befunde. Z Ges Neurol Psychiat 1921; 64: 147–228.
12. Goldfarb LG, Korczyn AD, Brown P, Chapman J, Gajdusek DC. Mutation in codon 200 of scrapie amyloid precursor gene linked to CJD in Sepharic Jews of Lybian and non-Lybian origin. Lancet 1990; 336: 637–8.
13. Goldfarb LG, Mitrova E, Brown P, Toh BH, Gajdusek DC. Mutation in codon 200 of scrapie amyloid protein gene in two clusters of CJD in Slovakia. Lancet 1990; 336: 514–5.
14. Dumble LJ, Klein RD. CJD legacy for Australian women treated with human pituitary gonadotropins. Lancet 1992; 340: 847–8.
15. Committee on Health Care Issues, American Neurological Association. Precautions in handling tissues, and other contaminated materials from patients with documented or suspected Creutzfeldt-Jakob disease. Ann Neurol 1986; 19: 75–7.
16. Budka H, Aguzzi A, Brown P et al. Tissue handling in suspected CJD and other human spongiform encephalopathies (Prion diseases). Brain Path 1995; 5: 319–22.
17. Will RG, Ironside JW, Zeidler M et al. A new variant of Creutzfeldt–Jakob disease in the United Kingdom. Lancet 1996; 347: 921–5.
18. Comber T. Real improvements in agriculture (on the principles of A. Young, Esq.). Letters to Reade Peacock, Esq. and to Dr. Hunter, Physician in York, concerning the Rickets in sheep. Nicoll, London, 1772 (Institute of agricultural history).
19. Wells GAH, Scott AC, Johnson CT et al. A novel progressive spongiform encephalopathy in cattle. Vet Rec 1987; 121: 419–20.
20. Sarradet M. Un cas de tremblant sur un boeuf. Rev Vet 1883; 7: 310–2.
21. Wilesmith JW, Wells GAH, Cranwell MP, Ryan JBM. Bovine spongiform encephalopathy: epidemiological studies. Vet Rec 1988; 123: 638–44.
22. Morgan KL. Bovine spongiform encephalopathy: time to take scrapie seriously. Vet Rec 1988; 122: 445–6.
23. Dealler SF, Lacey RW. Transmissible spongiform encephalopathies: The threat of BSE to man. Food Microbiol 1990; 7: 253–79.
24. Butler D. Brussles inquiry criticizes BSE secrecy. Nature 1996; 384: 8–9.
25. Anon. BSE link prompts German to vote on sheep. Nature 1996; 383: 753–3.
26. Anderson RM, Donnelly CA, Ferguson NM. Transmission dynamics and epidemiology of BSE in British cattle. Nature 1996; 382: 779–88.
27. Ridley RM, Baker HF. No maternal transmission. Nature 1996; 384: 17–7.
28. Bradbury J. Maternal transmission of BSE demonstrated in cattle. Lancet 1996; 348: 393–3.
29. Mould DL, Dawson AM, Smith W. Scrapie infectivity reduced by lypophilic solvents and by CsCl. Res Vet Sci 1965; 6: 151–4.
30. Josefsberg Z, Aran O, Laron Z. Safety of pituitary growth hormone extracted with acetone/acetic acid. Lancet 1994; 344: 130–30.
31. Hartsough GR, Burger D. Encephalopathy of mink. I. Epizootiologic and clinical observations. J Infect Dis 1965; 115: 387–92.
32. Williams ES, Young S. Chronic wasting disease of captive mule deer: a spongiform encephalopathy. J Wild Dis 1980; 16: 89–98.
33. Wyatt JM, Pearson GR, Smerdon T, Gruffyd-Jones TJ, Wells GAH. Spongiform encephalopathy in a cat. Vet Rec 1990; 126: 513–3.
34. Alper T, Cramp WA, Haig DA, Clarke MC. Does agent of scrapie replicate without nucleic acid? Nature 1967; 214: 764–6.
35. Prusiner SB. Novel proteinaceous infectious particles cause scrapie. Science 1982; 216: 136–44.
36. Hunter GD, Gibbons RA, Kimberlin RH, Millson GS. Further studies of the infectivity and stability of extracts and homogenates derived from scrapie affected mouse brains. J Comp Path 1969; 79: 101–8.
37. Griffith JS. Self-replication and scrapie. Nature 1967; 215: 1043–4.
38. Pattison IH, Jones KM. The possible nature of the transmissible agent of scrapie. Vet Rec 1967; 80: 2–9.

39. Lee KH, Harrington MG. Premortem diagnosis of CJD by cerebrospinal fluid analysis. Lancet 1996; 348: 887–7.
40. Brown P. The brave new world of transmissible spongiform encephalopathy. Mol Neurobiol 1994; 8: 79–87.
41. Weissmann C. Unified theory of prion propagation. Nature 1991; 352: 679–83.
42. Bolton DC, Meyer RK, Prusiner SB. Scrapie PrP 27–30 is a sialoglycoprotein. J Virol 1985; 53: 596–606.
43. Basler K, Oesch B, Scott M, Westaway D et al. Scrapie and cellular isoforms are encoded by the same chromosomal gene. Cell 1986; 46: 417–28.
44. Stahl N, Borchelt DR, Hsiao K, Prusiner SB. Scrapie prion protein contains a phosphatidylinositol glycolipid. Cell 1987; 51: 229–40.
45. Stahl N, Baldwin MA, Teplow DB, Hood L et al. Structural studies of the scrapie prion protein using mass spectrometry and amino acid sequencing. Biochemistry 1993; 32: 1991–2002.
46. Taraboulos A, Jendroska K, Serban D, Yang S-L, DeArmond SJ, Prusiner SB. Regional mapping of prion protein in brain. Proc Natl Acad Sci USA 1992; 89: 7620–4.
47. Chandler RL. Attempts to demonstrate antibodies in scrapie disease. Vet Rec 1959; 71: 58–9.
48. Haig DA, Clarke MC. Observations on the agent of scrapie. NINDB Monograph No.2, Slow, Latent, and Temperate Virus Infections 1965; 215–9.
49. Marsh RF, Pan IC, Hanson RP. Failure to demonstrate specific antibody in transmissible mink encephalopathy. Infect Immun 1970; 2: 727–30.
50. Groschup MH, Pfaff E. Studies on a species-specific epitope in murine, ovine and bovine prion protein. J Gen Virol 1993; 74: 1451–6.
51. Oesch B, Westaway D, Wälchli M, McKinley MP et al. A cellular gene encodes scrapie PrP 27–30 protein. Cell 1985; 40: 735–46.
52. Scott M, Foster D, Mirenda C, Serban D et al. Transgenic mice expressing hamster prion protein produce species-specific scrapie infectivity and amyloid plaques. Cell 1989; 59: 847–57.
53. Prusiner SB, Telling GC, Cohen PE, DeArmond SJ. Prion diseases of human and animals. Sem Virol 1996; 7: 159–53.
54. Telling GC, Scott M, Mastrianni G, Gabizon R et al. Prion propagation in mice expressing human and chimeric PrP transgenes implicates the interaction of cellular PrP with another protein. Cell 1995; 83: 79–90.
55. Pan KM, Baldwin M, Nguyen J, Gasset M et al. Conversion of alfa-helices into beta-sheets features in the formation of the scrapie prion proteins. Proc Natl Acad Sci USA 1993; 90: 10962–6.
56. Büehler H, Fischer M, Lang Y, Bluethmann H et al. Normal development and behaviour of mice lacking the neuronal cell-surface PrP protein. Nature 1992; 356: 577–82.
57. Chesebro B, Caughey B. Scrapie agent replication without the prion protein. Current Biol 1993; 3: 696–8.
58. Weissmann C, Büehler H, Fischer M, Aguet M. Role of the PrP gene in transmissible spongiform encephalopathies. Intervirology 1993; 35: 164–75.
59. Goebl MG, Petes TD. Most of the yeast genomic sequences are not essential for cell growth and division. Cell 1986; 46: 983–92.
60. Cashman NR, Loertscher R, Nalbatonglu J, Shaw I et al. Cellular isoform of the scrapie agent protein participates in lymphocyte activation. Cell 1990; 50: 185–92.
61. Oleszak EL, Murdoch G, Manuelidis L, Manuelidis EE. Growth factor production by CJD cell lines. J Virol 1988; 62: 3103–8.
62. Hay B, Prusiner SB, Lingappa VR. Evidence for a secretory form of the cellular prion protein. Biochemistry 1987; 26: 8110–5.
63. Büehler H, Aguzzi A, Sailer A, Greiner R-A et al. Mice devoid of PrP are resistant to scrapie. Cell 1993; 73: 1339–47.
64. Telling GC, Scott M, Hsiao KH, Foster D et al. Transmission of CJD from humans to transgenic mice expressing chimeric human-mouse protein. Proc Natl Acad Sci USA 1994; 91: 9936–40.
65. Collinge J, Palmer MS, Sidle KCL, Hill AF et al. Unaltered susceptibility to BSE in transgenic mice expressing human prion protein. Nature 1995; 378: 779–83.
66. Diener TO. Is the scrapie agent a viroid? Nature 1972; 235: 218–9.
67. Manuelidis L, Sklaviadis T, Manuelidis EE. Evidence suggesting that PrP is not the infectious agent in CJD. EMBO Journal 1987; 6: 341–7.
68. Manuelidis L, Fritchm W. Infectivity and host responses in CJD. Virology 1996; 216: 46–59.
69. Sakaguchi S, Katamine S, Shigematsu K, Nakatani A. Accumulation of proteinase K-resistant prion protein (PrP) is restricted by the expression level of normal PrP in mice inoculated with a mouse-adapted strain of the CJD agent. J Virol 1995; 69: 7586–92.
70. Somerville RA. The transmissible agent causing scrapie must contain more than protein. Med Virol 1991; 1: 131–44.
71. Somerville RA, Dunn AJ. The association between PrP and infectivity in scrapie and BSE infected mouse brain. Arch Virol 1996; 141: 275–89.
72. Sklaviadis T, Manuelidis L, Manuelidis EE. Characterization of major peptides in CJD and scrapie. Proc Natl Acad Sci USA 1986; 83: 6146–50.
73. Alper T, Haig DA, Clarke MC. The exceptionally small size of the scrapie agent. Biochem Biophys Res Comm 1966; 22: 278–84.
74. Latarjet R, Muel B, Haig DA, Clarke MD, Alper T. Inactivation of the scrapie agent by near monochromatic ultraviolet light. Nature 1970; 227: 1341–3.
75. Bellinger-Kawahara C, Cleaver JE, Diener TO, Prusiner SB. Purified scrapie prion resists inactivation by UV radiation. J Virol 1987; 61: 159–66.
76. Meyer N, Rosenbaum V, Schmidt B, Gilles K et al. Search for a putative scrapie genome in purified prion fractions reveals a paucity of nucleic acids. J Gen Virol 1991; 72: 37–49.
77. Kellings K, Meyer N, Mirenda C, Prusiner SB, Riesner D. Further analysis of nucleid acids in purified scrapie prion preparations by improved return refocussing gel electrophoresis. J Gen Virol 1992; 73: 1025–9.
78. Oesch B, Groth DF, Prusiner SB, Weissmann C. Search for a scrapie-specific nucleic acid: a progress report. Novel infectious agents and the central nervous system. Wiley, Chichester: Ciba Foundation Symposium, 1988: 209–23.
79. Riesner D, Kellings K, Wiese U, Wulfert M, Mirenda C, Prusiner SB. Prions and nucleic acids: Search for 'residual' nucleic acids and screening for mutations in the PrP-gene. Dev Biol Stand 1993; 80: 173–81.
80. Akowitz A, Sklaviadis T, Manuelidis L. Endogenous viral complexes with long RNA cosediment with the agent of CJD. Nucleic Acid Res 1994; 22: 1101–7.
81. Carp RI, Ye X, Kascsak RJ, Rubenstein R. The nature of the scrapie agent. Biological characteristics of scrapie in different scrapie strain-host combination. Ann NY Acad Sci 1994; 724: 221–31.
82. Aiken JM, Marsh RF. The search for scrapie agent nucleic acid. Microbiol Rev 1990; 54: 242–6.
83. Narang HK, Asher DM, Gajdusek DC. Evidence that DNA is present in abnormal tubulophilamentous structures found in scrapie. Proc Natl Acad Sci USA 1988; 85: 3575–9.
84. Narang HK. Detection of single-stranded RNA in scrapie-infected brain by electron microscopy. J Mol Biol 1990; 216: 469–73.
85. Narang HK. Evidence that scrapie-associated tubulophilamentous particles contain a single-stranded DNA. Intervirology 1993; 36: 1–10.
86. Narang HK. Evidence that homologous ssDNA is present in scrapie, Creutzfeldt-Jakob disease, and bovine spongiform encephalopathy. Ann NY Acad Sci 1994; 724: 314–26.
87. Oezel M, Diringer H. Small virus-like structures in fractions from scrapie hamster brain. Lancet 1994; 343: 894–5.
88. Narang HK. Virus-like particles in Creutzfeldt-Jakob biopsy material. Acta Neuropath 1975; 32: 163–8.
89. Oezel M, Xi Y-G, Baldauf E, Diringer H, Pocchiari M. Small virus-like structures in brains from cases of sporadic and familial Creutzfeldt-Jakob disease. Lancet 1994; 344: 923–4.
90. Narang HK. Virus-like particles in natural scrapie of the sheep. Res Vet Sci 1973; 14: 108–10.
91. Deslys J-P, Lasmezas C, Dormont D. Selection of specific strains in iatrogenic Creutzfeldt-Jakob disease. Lancet 1994; 343: 848–9.
92. Parchi P, Castellani R, Capellari S, Ghetti B et al. Molecular basis of phenotypic variability in sporadic Creutzfeldt-Jakob disease. Ann Neurol 1996; 39: 767–78.
93. Collinge J, Sidle KCL, Meads J, Ironside J, Hill AF. Molecular analysis of prion strain variation and the aetiology of 'new variant' CJD. Nature 1996; 383: 685–90.
94. Kimberlin RH, Walker CA. Evidence that the transmission of one source of scrapie agent to hamsters involves separation of agent strains from a mixture. J Gen Virol 1978; 39: 487–96.
95. Bruce ME, Dickinson AG. Biological evidence that scrapie agent has an independent genome. J Gen Virol 1987; 68: 79–89.
96. Bruce ME, McConnell, Fraser, Dickinson AG. The disease characteristics of different strains of scrapie in Sinc congenic mouse lines: implications for the nature of the agent and host control of pathogenesis. J Gen Virol 1991; 72: 595–603.
97. Bruce M, Chree A, McConnell I, Foster J, Pearson G, Fraser H. Transmission of bovine spongiform encephalopathy and scrapie to mice: strain variation and the species barrier. Phil Trans R Soc London B 1994; 343: 405–11.
98. Xi YG, Ingrosso L, Ladogana A, Masullo C, Pocchiari M. Amphotericin B treatment dissociates in vivo replication of the scrapie agent from PrP accumulation. Nature 1992; 356: 598–601.
99. McKenzie D, Kaszowski J, Marsh R, Aiken J. Amphotericin B delays both scrapie agent replication and PrP-res accumulation early in infection. J Virol 1994; 68: 7534–6.
100. Lasmezas CI, Deslys J-P, Robain O, Jaegly A et al. Transmission of the BSE agent to mice in the absence of detectable abnormal prion protein. Science 1997; 275: 402–4.
101. Masters CL, Harris JO, Gajdusek DC, Gibbs CJ Jr, Bernoulli C, Asher DM. Creutzfeldt-Jakob disease: Patterns of worldwide occurrence and the significance of familial and sporadic clustering. Ann Neurol 1979; 5: 177–88.
102. Brown P, Cathala F, Raubertas RF, Gajdusek DC, Castaigne P. The epidemiology of Creutzfeldt-Jakob disease: Conclusion of a 15-year investigation in France and review of the world literature. Neurology 1987; 37: 895–904.
103. Goldgaber D, Goldfarb LG, Brown P, Asher DM et al. Mutations in familial Creutzfeldt-Jakob disease and Gerstmann-Sträussler-Scheinker syndrome. Exp Neurol 1989; 106: 204–6.
104. Goldfarb LG, Brown P, Mitrova, Cervenakova L et al. Creutzfeldt-Jakob disease associated with the PRNP codon 200^{Lys} mutation: An analysis of 45 families. Eur J Epidemiol 1991; 7: 477–86.
105. Goldfarb LG, Brown P, Haltia M, Cathala F et al. Creutzfeldt-Jakob disease cosegregates with the codon 178^{Asn} PRNP mutation in families of European origin. Ann Neurol 1992; 31: 274–81.
106. Owen F, Poulter M, Lofthouse R, Collinge J et al. Insertion in prion protein gene in familial Creutzfeldt-Jakob disease. Lancet 1989; i: 51–2.
107. Owen F, Poulter M, Shah T, Collinge J et al. An in-frame insertion in the prion protein gene in familial Creutzfeldt-Jakob disease. Molec Brain Res 1990; 7: 273–6.
108. Goldfarb LG, Brown P, Cervenakova L, Gajdusek DC. Genetic analysis of Creutzfeldt-Jakob disease and related disorders. Phil Trans R Soc London B 1994; 343: 379–84.

109. Owen F, Poulter M, Collinge J. A dementing illness associated with a novel insertion in the prion protein gene. Molec Brain Res 1992; 13: 155–5.
110. Diringer H. Creutzfeldt-Jakob disease. Lancet 1996; 347: 1332–3.
111. Holt TA, Phillips J. Bovine spongiform encephalopathy. Br Med J 1988; 296: 1581–3.
112. Prusiner SB, Füzi M, Scott M, Serban D et al. Immunologic and molecular biologic studies of prion proteins in bovine spongiform encephalopathy. J Infect Dis 1993; 167: 602–13.
113. Butler D. Funding row delays Brussels BSE research. Nature 1996; 383: 565–5.
114. Ridley RM, Baker HF. Oral transmission of BSE to primates. Lancet 1996; 348: 1174–4.
115. Brown P, Preece MA, Will RG. 'Friendly fire' in medicine: hormones, homografts and Creutzfeldt-Jakob disease. Lancet 1992; ii: 24–7.
116. Page G. BSE transmission data cause confusion. Nature 1996; 382: 381–1.
117. Krakauer DC, Pagel M, Southwood TRE, Zanotto de PM. Phylogenesis of prion protein. Nature 1996; 380: 675–5.
118. Goldmann W, Hunter N, Somerville R, Hope J. Prion philogeny revisited. Nature 1996; 382: 32–3.
119. Cousens SN, Vynnycky E, Zeidler M, Will RG, Smith PG. Predicting the CJD epidemic in humans. Nature 1997; 385: 197–8.
120. Goldmann W, Hunter N, Foster JD, Salbaum JM, Beyreuther K, Hope J. Two alleles of a neural protein gene linked to scrapie in sheep. Proc Natl Acad Sci USA 1981; 87: 2476–80.
121. Keulen van LJM, Schreuder BEC, Meloen RH, Poelen-Van den Berg M et al. Immunohistochemical detection and localization of prion protein in brain tissue of sheep with natural scrapie. Vet Path 1995; 32: 299–308.
122. Eklund CM, Kennedy RC, Hadlow, WJ. Pathogenesis of scrapie virus infection in mice. J Infect Dis 1967; 117: 15–22.
123. Hadlow WJ, Kennedy RC, Race RE. Natural infection of Suffolk sheep with scrapie-virus. J Infect Dis 1982; 146: 657–64.
124. Keulen van LJM, Schreuder BEC, Meloen RH, Mooij-Harkes G, Vromans MEW, Langeveld JPM. Immunohistochemical detection of prion protein in lymphoid tissues of sheep with natural scrapie. J Clin Microbiol 1996; 34: 1228–31.
125. Schreuder BEC, Keulen van LJM, Vromans MEW, Langeveld JPM, Smits MA. Preclinical test for prion disease. Nature 1996; 381: 563–3.
126. Arya SC. Immunohistochemical detection of prion protein in lymphoid tissues of sheep, cattle, and humans. J Clin Microbiol 1996; 34: 2639–9.
127. Arya SC. Transmissible spongiform encephalopathies in sheep-brain derived rabies vaccine. Biologicals 1994; 22: 73–3.
128. Gordon WS, Brownlee A, Wilson DR. Studies in louping-ill, tickborne fever and scrapie. Proc.3rd Int. Congress for Microbiology, Baltimore: Waverlay, 1940: 362–3.
129. Hill AF, Zeidler M, Ironside J, Collinge J. Diagnosis of a new variant Creutzfeldt-Jakob disease by tonsil biopsy. Lancet 1997; 349: 99–100.
130. Moore BE, Perez VJ. In: Carlson FD ed. Physiological and biochemical aspects of nervous integration. New York: Prentice-Hall, 1967.
131. Aitken A, Collinge DB, Heusden van BPH, Isobe T. 14-3-3 proteins: a highly conserved, widespread family of eukaryotic proteins. Trends Biochem Sci 1992; 17: 498–501.
132. Boston PF, Jackson P, Thompson RJ. Human 14-3-3 protein: Radioimmunoassay, tissue distribution and cerebrospinal fluid levels in patients with neurological disorders. J Neurochem 1982; 38: 1475–82.
133. Hsich G, Kennedy K, Gibbs CJ Jr, Lee KH, Harrington MG. The 14-3-3 brain protein in cerebrospinal fluid as a marker for transmissible spongiform encephalopathies. N Engl J Med 1996; 335: 924–30.
134. Harrington MG, Merril CR, Asher DM, Gajdusek DC. Abnormal proteins in the cerebrospinal fluid of patients with Creutzfeldt-Jakob disease. N Engl J Med 1986; 315: 279–83.
135. Will RG, Zeidler M, Brown P, Harrington M, Lee KH, Kennedy KL. Cerebrospinal-fluid test for new variant Creutzfeldt-Jakob disease. Lancet 1996; 348: 955–5.
136. Collinge J. New diagnostic test for prion diseases. N Engl J Med 1996; 335: 963–5.
137. Shoji M, Kawamoto S, Setoguchi Y et al. The 14-3-3-protein as the antigen for lung cancer-associated human monoclonal antibody AE6F4. Hum Antib Hybrid 1994; 5: 123–30.
138. Wakayama Y, Shibuya S, Kawase J, Sagawa F, Hashizume Y. High neuron-specific enolase level of cerebrospinal fluid in the early stage of Creutzfeldt-Jakob disease. Klin Wochenschr 1987; 65: 798–801.
139. Hay E, Royds RA, Davies-Jones GAB, Lewtas NA, Timperley WR, Taylor CB. Cerebrospinal fluid enolase in stroke. J Neurol Neurosurg Psychiatry 1984; 47: 724–9.
140. Jimi T, Wakayama A, Shibuya S, Nakata H. High levels of nervous system-specific proteins in cerebrospinal fluid in patients with early stage Creutzfeldt-Jakob disease. Clinica Chim Acta 1992; 211: 37–46.
141. Zerr I, Bodemer M, Räcker S, Grosche S et al. Cerebrospinal fluid concentration of neuron-specific enolase in diagnosis of Creutzfeldt-Jakob disease. Lancet 1995; 345: 1609–10.
142. Zerr I, Bodemer M, Otto M, Poser S et al. Diagnosis of Creutzfeldt-Jakob disease by two dimensional gel electrophoresis of cerebrospinal fluid. Lancet 1996; 348: 846–9.
143. Parchi P, Capellari S, Chen SG, Petersen RB, Gambetti P et al. Typing of prion isoforms. Nature 1997; 386: 232–3.
144. Collinge J, Hill AF, Sidle KCL, Ironside J. Typing of prion isoforms. Answer. Nature 1997; 386: 233–4.

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Pismo uredništvu/Letter to the editor

NADOMESTNO HORMONSKO ZDRAVLJENJE IN RAK DOJKE

Miha Debevec

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Rak dojke je najpogostejša vrsta raka pri ženskah v razvitem svetu in od leta 1965 tudi pri nas. V ZDA ugotovijo tega raka pri 12% žensk in 3,5% jih zaradi njega tudi umre (1). Register raka za Slovenijo navaja za leto 1994 733 novih bolnic z rakom dojke, kar predstavlja incidenco 71,5 na 100.000 žensk (2).

Pri ugotavljanju ogrožene populacije za tega raka je poleg družinske obremenjenosti najpomembnejši dejavnik hormonsko stanje žensk. Ugotovili so, da vplivajo na pogostost zbolevanja zgodnja menarha, nosečnost, starost ob prvem porodu, dojenje in pozna menopavza. Zgodnja menarha pred 12. letom in pozna menopavza po 55. letu povečujeta, zgodnji prvi porod in dojenje pa zmanjšujeta tveganje za raka dojke.

Postmenopavzalno obdobje je stanje endokrinega pomanjkanja, vendar pa z dodajanjem ovarijskih hormonov ne moremo povsem doseči hormonskega stanja pred menopavzo (3). Zato ugotovitve glede raka dojke pri premenopavzalnih ženskah ne držijo tudi za postmenopavzalne ženske, čeprav te dobivajo nadomestno hormonsko terapijo (HT). To dajejo za ublažitev klimakteričnih težav, preprečevanje in zdravljenje osteoporoze in ishemične bolezni srca. Številne epidemiološke študije, nikakor pa ne vse, dokazujejo, da so ženske, ki so dobivale HT po menopavzi, pogosteje dobile raka dojke kot tiste, ki HT niso dobivale (4). Nivo estrogenov v plazmi in urinu naj bi bil v pozitivni korelaciji z rakom dojke (5). Z estrogeni lahko izzovejo in pospešijo raka dojke pri poskusnih živalih (6).

V praksi so za onkologa pri obravnavi žensk po menopavzi, ki pridejo na pregled zaradi dojk in po nasvet glede jemanja HT, ki jo je ordiniral ginekolog ali internist (endokrinolog ali kardiolog), pomembni naslednji dejavniki:

Sestava in način aplikacije HT

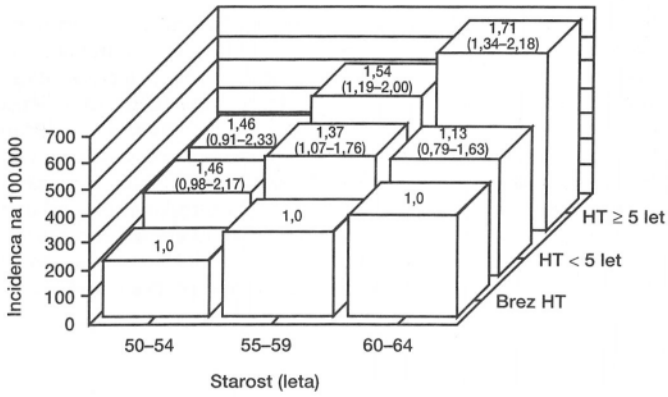
V ZDA so večinoma uporabljali konjugirane konjske estrogene, v Evropi pa več sintetiziranih t. i. »naravnih« estrogenov, kar morda vpliva na ugotovitve dolgoletnih epidemioloških študij (3). HT se daje oralno, sublingvalno, transdermalno, subkutano, rektalno in vaginalno. Pri parenteralni uporabi se zmanjša vpliv estrogenov na koagulacijske dejavnike v jetrih. Dodajanje progestinov poleg estrogenov ne zmanjšuje nevarnosti za raka dojke (4). Odmerki pod 0,625 mg estrogenov dnevno ne povečajo nevarnosti za raka dojke (7).

Starost

Povprečna starost ob menopavzi je v razvitih deželah okoli 51 let (8). Dobre tri četrtine raka dojke se pri nas odkrije po 50. letu starosti (2). Incidenca raka dojke s starostjo narašča (2), nevarnost zaradi jemanja HT pa prav tako (4). Zgodnja naravna in iatrogena menopavza naj bi celo zmanjšala nevarnost za raka dojke (6).

Trajanje HT

Čas jemanja HT je odločilni dejavnik pri nastanku raka dojke. Nekajmesečno do nekajletno jemanje HT za ublažitev klimakteričnih težav je skoraj nepomembno. Šele večletna redna HT, kot se daje zaradi osteoporoze in koronarne bolezni, očitno povečata nevarnost za raka dojke, pri čemer je treba upoštevati sočasno tudi povečano ogroženost zaradi starosti same. Na sliki 1 je nazorno prikazana ta ogroženost, kot so jo ugotovili v študiji 121.700 medicinskih sester v starosti 30 do 55 let v obdobju 1978 do 1992. Med njimi so ugotovili 1935 primerov invazivnega raka dojke (4). Tudi druge študije in metaanaliza le-teh so pokazale podobno ogroženost (5, 7–10).



Sl. 1. *Incidenca in nevarnost za raka dojke glede na starost in hormonsko terapijo po Colditzu in sod., 1995 (4).*

Benigne spremembe v dojkah

Pri ženskah, ki so imele ali pa še imajo benigne spremembe v dojkah, HT po menopavzi ne poveča nevarnosti za raka (5, 7). Lahko pa HT vpliva na povečanje teh sprememb, kar otežuje klinično kontrolo. Sicer pa je ugotovljeno, da HT zmanjšuje občutljivost in zanesljivost mamografije (11–13).

Drugi dejavniki ogroženosti

Od vseh dejavnikov ogroženosti za raka dojke je najpomembnejša družinska obremenitev po materini strani pri mlajših, premenopavzalnih ženskah (6). Metaanaliza 10 študij je pokazala, da se pri postmenopavzalnih ženskah z družinsko obremenitvijo nevarnost zaradi HT ne poveča (5). Za druge dejavnike ogroženosti, kot so: rasa, reprodukcijske značilnosti, kontracepcijske tablete, alkohol, kajenje, mastna hrana, telesna teža, poklic in različni vplivi okolja, so izračunali nevarnost za raka dojke (14, 15), ni pa dovolj podatkov, koliko se pri vsakem posameznem dejavniku ali pri kombinacijah teh dejavnikov ogroženost poveča zaradi HT po menopavzi.

Možnosti za zgodnje odkrivanje

Poglavitni metodi za odkrivanje raka dojke sta klinični pregled in mamografija. Ultrazvok je koristen pri razlikovanju solidnih spre-

memb od cističnih, ki jih sicer lahko razločimo tudi s punkcijo, in pri lokalizaciji netipljivih mamografskih sprememb za punkcijo pod ultrazvočno kontrolo. Za samo odkrivanje rakastih sprememb ultrazvok ni uporaben.

Dojke so različne velikosti, oblike in konzistence, zaradi tega klinični izvid ni pri vseh ženskah enako zanesljiv. Tudi mamografija je zaradi tega različno občutljiva in zanesljiva, pri majhnih in ploskih dojkah včasih sploh ni uporabna. Vedno moramo računati tudi z lažno negativnimi, teh je do 15% (15), in lažno pozitivnimi ugotovitvami. Prve lahko zavedejo k manjši pozornosti bolnice in zdravnika, druge pa je možno z biopsijo korigirati.

Vse to vpliva tudi na zanesljivost nadaljnjih kontrolnih pregledov. Onkolog mora pri določanju pogostosti kontrolnih pregledov in mamografij žensk, ki dobivajo HT, upoštevati pomanjkljivosti detekcijskih možnosti, obenem pa vse dejavnike, ki nevarnost za raka dojke povečujejo, in tudi obremenitev z rentgenskimi žarki pri pogostih mamografijah. Večinoma zadostuje po 50. letu mamografija vsakih 12 do 24 mesecev in le izjemoma pogosteje. Klinični pregled je lahko mnogo pogostejši, vendar je treba upoštevati tudi morebitno psihično obremenitev zaradi stalnih pregledov, pa tudi konkretne možnosti za izvedbo pregleda. Pri nas je čakalna doba za pregled včasih daljša, kot je interval do potrebnega kontrolnega pregleda.

Sklep

Vsako zdravljenje s hormoni je dvorezno. Na eni strani koristi, na drugi strani pa povzroči nezaželene učinke, če že naravnost ne škoduje. Vsak zdravnik, ki odredi HT ženski po menopavzi, mora skrbno pretehtati vse morebitne posledice tovrstnega zdravljenja in izkoristiti tudi možnosti nehormonskega zdravljenja, ki jih ni tako malo (16). Za onkologa je nedvomno bolj enostavno in varno, če ženski po menopavzi HT odsvetuje, kot da v primeru kasnejšega raka tvega očitke, da je ravnal nestrokovno. Vendar je dolžan upoštevati tudi težave preiskovanke in utemeljenost odrejene HT. Večja nevarnost za raka dojke zaradi HT po menopavzi se pojavi šele po dovolj velikem odmerku in po dolgi uporabi. V primerjavi z nevarnostjo za pljučnega raka pri hudih kadilcih je nevarnost za raka dojke zaradi HT po menopavzi kar nekajkrat manjša. Vendar je HT vedno iatrogena, kajenje pa nikoli.

Literatura

1. Utian WH. Hormone replacement therapy and breast cancer: is there a relation? Advances in the treatment of the menopause and osteoporosis. Br J Obstet Gynecol 1994; 101: 170–4.
2. Onkološki inštitut v Ljubljani, Register raka za Slovenijo. Incidenca raka v Sloveniji. Ljubljana: Poročilo RR št. 36, 1997.
3. Belchetz PE. Hormonal treatment of postmenopausal women. N Engl J Med 1994; 330: 1062–71.
4. Colditz GA, Hankinson SE, Hunter DJ, Willet WC, Manson JE, Stampfer MJ et al. The use of estrogens and progestins and the risk of breast cancer in postmenopausal women. N Engl J Med 1995; 332: 1589–93.
5. Colditz GA, Egan KM, Stampfer MJ. Hormone replacement therapy and risk of breast cancer: Results from epidemiologic studies. Am J Obstet Gynecol 1993; 168: 1473–80.
6. Sands R, Boshoff C, Jones A, Studd J. Current opinion: Hormone replacement therapy after a diagnosis of breast cancer. Menopause 1995; 2: 73–80.
7. Dupont WD, Page DL. Menopausal estrogen replacement therapy and breast cancer. Arch Intern Med 1991; 151: 67–72.
8. Hammond CB. Menopause and hormone replacement therapy: an overview. Obstet Gynecol 1996; 87: 2S–15S.
9. Schairer C, Byrne C, Keyl PM, Brinton LA, Sturgeon SR, Hoover RN. Menopausal estrogen and estrogen-progestin replacement therapy and risk of breast cancer (United States). Cancer Causes Control 1994; 5: 491–500.
10. Donegan WL, Soratt JS. Cancer of the breast. Philadelphia: Saunders, 1995: 130.
11. Laya MB, Larson EB, Taplin SH, White E. Effect of estrogen replacement therapy on the specifity and sensitivity of screening mammography. J Natl Cancer Inst 1996; 88: 643–9.
12. Blume E. Mammography affected by hormone replacement therapy. J Natl Cancer Inst 1996; 88: 638–8.
13. Black WC, Fletcher SW. Effects of estrogen on screening mammography: another complexity. J Natl Cancer Inst 1996; 88: 627–8.
14. Velentgas P, Daling JR. Risk factors for breast cancer in younger women. J Natl Cancer Inst 1994; 16: 15–22.
15. Vogel VG. Screening younger women at risk for breast cancer. J Natl Cancer Inst 1994; 16: 55–60.
16. Bachmann GA. Nonhormonal alternatives for the management of early menopause in younger women with breast cancer. J Natl Cancer Inst 1994; 16: 161–7.

134. REDNA LETNA SKUPŠČINA SLOVENSKEGA ZDRAVNIŠKEGA DRUŠTVA

Otočec, 17.–18. 10. 1997

Petek, 17. 10. 1997

13.30–16.30	**Seja Glavnega odbora**
17.00–19.00	**134. skupščina Slovenskega zdravniškega društva**
20.00	**Slavnostna večerja s podelitvijo diplom častnim članom Slovenskega zdravniškega društva**

Sobota, 18. 10. 1997

9.00–13.40	**Biotehnologija, bioinženiring, kloniranje – upi in strahovi**	
	Moderator in organizator:	*doc. dr.* ***Alojz Ihan***
9.00–11.00	Doc dr. ***Alojz Ihan***	Gen in njegova enkratna zgodba
	Prof. dr. ***Miklavž Grabnar***	Smeri razvoja biotehnologije in njihova aplikacija v medicini
	Prof. dr. ***Rado Komelj***	Tehnološki domet genetske zlorabe
	Prof. dr. ***Jože Drinovec***	Biotehnologija in farmacevtska industrija
11.00–11.30		Odmor
11.30–13.30	Doc. dr. ***Borut Peterlin***	Kakšne možnosti zdravljenja in diagnostike nam lahko nudijo nova odkritja na področju biotehnologije in genskega inženiringa
	Doc. dr. ***Gregor Tomc***	Implikacije genskega inženiringa
	Dr. ***Ivan Štuhec***	Moralni vidiki biotehnologije
	Akad. prof. dr. ***Jože Trontelj***	Stališča Odbora za smernice v biotehnologijo Sveta Evrope
	Akad. prof. dr. ***Tine Hribar***	O človekovi nenadomestljivosti
13.30–13.40		Zaključki in ev. sklepi (deklaracija) o biotehnologiji in genskem inženiringu

Udeležbo na strokovnem sestanku priznava Zdravniška zbornica Slovenije kot strokovno izpopolnjevanje zdravnikov in jo upošteva pri podaljševanju licence.

Kotizacijo 15.000,00 SIT plačate lahko na žiro račun: Slovensko zdravniško društvo, Ljubljana 50101-678-48620 ali pred pričetkom srečanja.

SLOVENSKO ZDRAVNIŠKO DRUŠTVO –
SEKCIJA ZA SPLOŠNO MEDICINO IN FIZIATRIČNA SEKCIJA

v sodelovanju s

KRKO ZDRAVILIŠČI, d.o.o.

organizira

3. KRKINE REHABILITACIJSKE DNEVE

Šport hotel Otočec, 26. in 27. september 1997

Petek, 26. septembra 1997

Zunajsklepni revmatizem

15.00		Pozdrav gostitelja
15.30	***Mojca Kos-Golja***	Zunajsklepni revmatizem: dagnostika, diferencialna diagnoza
16.10	***Martin Štefančič***	Miofascialni bolečinski sindrom
16.45	***Zmago Turk, Marija Gažić***	Najpogostejši bolečinski sindrom mehkih tkiv
17.20		Odmor
17.35	***Nada Mijoč, Matjaž Roženberger, Danica Simonič***	Problematika zunajsklepnega revmatizma v ambulanti splošnega zdravnika
17.55	***Simona Pregelj***	Farmakoterapija zunajsklepnega revmatizma
18.15		Diskusija

Sobota, 27. septembra 1997

Kontinuirana skrb za srčno-žilnega bolnika

8.30	***Pavel Poredoš***	Kardiovaskularne bolezni in telesna aktivnost
8.50	***Josip Turk***	Epidemiologija bolezni srca in ožilja (Podatki študije Euro Aspire)
9.05	***Miran Kenda***	Sodobni pogled na preventivo bolezni srca in ožilja
9.25	***Dražigost Pokorn***	Vloga prehrane pri preventivi bolezni srca in ožilja
9.45		Odmor
10.00	***Daroslav Ivašković***	Celovita rehabilitacija srčno-žilnega bolnika v Zdravilišču Šmarješke Toplice
10.15	***Tomislav Majič***	Mesto, vloga in programi zdravilišča v sekundarni preventivi bolezni srca in ožilja
10.30	***Andrej Kožar***	Čustvene spremembe pri koronarnem bolniku v času zdravljenja v zdravilišču Šmarješke Toplice
10.45	***Metod Prašnikar***	Ocena telesne okvare pri bolnikih z boleznimi srca
11.00	***Breda Žagar, Duša Oblak***	Preventiva bolezni srca in ožilja z zdravili
11.15		Diskusija
11.35		Odmor

Kronična obstruktivna pljučna bolezen

11.50	***Stanislav Šuškovič***	Etiopatogeneza, diagnostika, zdravljenje KOPB
12.20	***Andrej Dernikovič***	Pacient s KOPB v ambulanti splošnega zdravnika
12.40	***Radiša Radulovič***	Rehabilitacija bolnika s KOPB v Zdravilišču Strunjan
13.00		Odmor
13.05	***Marija Potočnik***	Dihalne vaje in metode relaksacije pri KOPB
13.25	***Alenka Jerman***	Zdravljenje bakterijskih infekcij pri bolnikih s KOPB
13.45		Diskusija

Dodatne informacije: ***Natalija Novak*** in ***Stane Barbo,*** telefon 068 / 75 700, 75 419 (Šport hotel Otočec)
Prijave: do 15. 9. 1997, Natalija Novak, telefon: 068 / 75 700 ali telefax: 068 / 75 420
Bivanje: Šport hotel Otočec, telefon 068 / 75 700, 75 701
Kotizacija: 12.000,00 SIT, plača se na ŽR 52100-603-30970 ali pred pričetkom seminarja.

Zdravniška zbornica Slovenije bo priznala udeležbo na 3. Krkinih rehabilitacijskih dnevih pri podaljšanju licence za zdravnike v splošni medicini in zdravnike fiziatre.

INŠTITUT ZA VAROVANJE ZDRAVJA REPUBLIKE SLOVENIJE

vabi

zdravnike, zdravstvene delavce z visoko in višjo izobrazbo ter zdravstvene inšpektorje

na seminar

ZAGOTAVLJANJE KVALITETE IN KONTROLA KVALITETE HLADNE VERIGE PRI TRANSPORTU IN SHRANJEVANJU CEPIVA

Seminar bo 24. in 25. oktobra 1997 v predavalnici Inštituta za varovanje zdravja R Slovenije, Trubarjeva 2 (vhod z Obrežne steze 2)

PROGRAM

Petek, 24. 10. 1997

14.00–14.45	***A. Radšel, A.Kraigher***	Nalezljive bolezni in pomen cepljenja Cepilni program R. Slovenije in rezultati programa
14.50–15.35	***M. Matjašič, A. Kraigher***	Cepiva in njihove lastnosti
15.35–15.50		Odmor
15.50–18.10	***A. Kraigher***	Pomen hladne verige, shranjevanje, razdeljevanje in transport cepiva Predstavitev standardov, principi zagotavljanja in kontrola kvalitete

Sobota, 25. 10. 1997

8.00–12.20	***A. Kraigher, A. Hočevar, A. Petrič***	Pomen hladne verige, shranjevanje in transport cepiva. Predstavitev standardov, principi zagotavljanja in kontrola kvalitete
12.20–14.00		Odmor za kosilo
14.00–17.20	***L. Šmon, A. Urbanc***	Učna delavnica: Izdelava protokola za zagotavljanje kvalitete in kontrola hladne verige za lastno skladišče in transport Izdelek – priprava dokumentacije za lastno skladiščenje

Seminar je priznan s strani Zdravniške zbornice Slovenije za podaljšanje licence.

Kotizacija za seminar znaša 11.600,00 SIT. Nakažite jo na ŽR Inštituta za varovanje zdravja, št.: 50100-603-41773, sklicna številka 610, do 1. 10. 1997

Prosimo, da se za seminar prijavite pisno do 12. 10. 1997 na naslov:

Inštitut za varovanje zdravja R Slovenije
Enota za izobraževanje,
Trubarjeva 2, 1000 Ljubljana
tel.: 061 / 1327-295, fax.: 061 / 323-955

Predvideno število udeležencev je 30.

PRIJAVNICA

Prijavljam se na seminar

ZAGOTAVLJANJE KVALITETE IN KONTROLA KVALITETE HLADNE VERIGE PRI TRANSPORTU IN SHRANJEVANJU CEPIVA

Ime in priimek: _____

Naslov: _____

Zaposlen: _____

Telefon, telefaks: _____

Datum: _____ Podpis: _____

INŠTITUT ZA VAROVANJE ZDRAVJA REPUBLIKE SLOVENIJE

vabi

zdravnike, zobozdravnike, zdravstvene delavce in sodelavce z visoko in višjo izobrazbo na vseh ravneh zdravstvene dejavnosti in druge na seminar

HIGIENA PREHRANE – DIETETIKA

Seminar bo od 20. do 22. novembra 1997 v predavalnici Inštituta za varovanje zdravja R Slovenije, Trubarjeva 2 (vhod z Obrežne steze 2)

PROGRAM

Četrtek, 20. 11. 1997

08.00–08.45	***D. Pokorn***	Uvod: Prehrana in zdravje
08.50–09.35	***V. Koch***	Prehrambene navade Slovencev
09.40–11.10	***J. Pokorn***	Varna hrana
11.30–13.00	***M. Adamič***	Zakonodaja s področja higiene prehrane
14.30–16.50	***D. Pokorn***	Ocena stanja hranjenosti
17.00–18.30	***M. Adamič***	Prehrana v zdravju posebej ogroženih skupin prebivalstva

Petek, 21. 11. 1997

08.00–10.20	***D. Pokorn***	Prehrana bolnika Prehrana onkološkega bolnika
10.35–12.05	***B. Kremžar***	Prehrana kirurškega bolnika
13.30–15.00	***B. Kremžar***	Enteralna in parenterealna prehrana
15.10–16.40	***M. Kuhar***	Intoleranca na hrano
17.00–17.45	***J. Lainščak***	Prehrana pri celiakiji

Sobota, 22. 11. 1997

08.00–09.30	***M. Medveščck***	Prehrana pri sladkorni bolezni
09.40–12.00	***T. Pohler***	Uporaba računalnika pri načrtovanju prehrane
13.30–15.00	***V. Koch***	Sestavljanje jedilnikov
15.20–18.40	***V. Koch***	Sestavljanje jedilnikov: Uporaba računalnika (učna delavnica)

Zdravniška zbornica seminar priznava za podaljšanje licenc zdravnikom in zobozdravnikom.

Kotizacija za seminar znaša 24.900,00 SIT. Nakažete jo na Ž.R. Inštituta za varovanje zdravja RS, št.: 50100-603-41773, sklicna št. 610, do 6. 11. 1997.

Prosimo, da se za seminar prijavite pisno do 6. 11. 1997 na naslov:
INŠTITUT ZA VAROVANJE ZDRAVJA RS, »Enota za izobraževanje«
Trubarjeva 2, 1000 Ljubljana, tel.: 061/1327-259, fax.: 061/323-955

Predvideno število udeležencev je 20.

PRIJAVNICA

Prijavljam se na seminar
HIGIENA PREHRANE – DIETETIKA

Ime in priimek: _____

Naslov: _____

Zaposlen: _____

Telefon / telefaks: _____

Datum: _____ Podpis: _____

INTERNISTIČNA SEKCIJA SLOVENSKEGA ZDRAVNIŠKEGA DRUŠTVA

vabi zdravnike interniste in zdravnike splošne medicine

na

STROKOVNI SESTANEK

24. in 25. oktobra 1997
v veliki dvorani Poslovno informacijskega centra tovarne zdravil LEK, Ljubljana, Verovškova 57

NAJNOVEJŠA DOGNANJA NA PODROČJU INTERNE MEDICINE

PROGRAM

Petek, 24. oktobra 1997

9.30	**Uvodno predavanje**	
	P. Vidali	Začetek in usklajevanje programa internističnega izobraževanja z EU
10.00–13.00	**Kardiologija**	
	Strokovni vodja: *P. Rakovec*	
	N. Ružič-Medveščck	Novosti na področju srčnega popuščanja
	P. Rakovec	Novosti na področju zdravljenja aritmij
	M. F. Kenda	Inhibitorji konvertaze pri ishemični bolezni srca
	I. Kranjec	Novosti na področju invazivnih intervencijskih posegov
		Razprava
13.10–15.00		Kosilo
15.00–18.00	**Hematologija**	
	Strokovni vodja: *P. Černelč*	
	D. Andoljšek	Hemofilija – novosti zdravljenja hemofilije z inhibitorji
	P. Černelč	Nova zdravila pri zdravljenju hiperproliferativnih boleznih
	J. Pretnar	Sedanji dosežki pri presaditvi kostnega mozga
		Razprava

Sobota, 25. oktobra 1997

9.00–12.00	**Nefrologija**	
	Strokovni vodja: *A. Bren*	
	S. Kaplan-Pavlovčič	Novosti pri glomerulni bolezni
	M. Benedik	Novi pogledi na zdravljenje uremične osteopatije
	A. Guček	Novosti pri nadomestnem zdravljenju s peritonealno dializo
	R. Ponikvar	LDL afereza – Zdravljenje hiperlipedimij
		Razprava
	Urgentna medicina	
	Strokovni vodja: *A. Bručan*	
	A. Bručan	Pomen čim hitrejše zgodnje defibrilacije pri zastoju srca
	M. Gričar	Pristop k življenjsko ogroženemu bolniku
		Razprava
	Društvene informacije in problematika	
	Sprejetje Pravilnika o častnih članih Internistične sekcije SZD	

Udeležbo na strokovnem sestanku priznava Zdravniška zbornica Slovenije kot strokovno izpopolnjevanje zdravnikov in jo upošteva pri podaljševanju licence (št. odločbe: 97081).

Kotizacijo 10.000,00 SIT (vključno s certifikatom ZZS) plačate pred pričetkom predavanj.
Študentje, sekundariji in upokojenci kotizacije ne plačajo.

ŠOLA KLINIČNE RADIOLOGIJE

VNETNI IN DEGENERATIVNI REVMATIZEM

Klinični center Ljubljana, 23.–24. oktober 1997

Organizatorji
KATEDRA ZA RADIOLOGIJO MF V LJUBLJANI
REVMATOLOŠKA SEKCIJA SZD
PNEVMOLOŠKA SEKCIJA SZD

Strokovni odbor
prof. dr. ***Vladimir Jevtič,*** *prof. dr.* ***Blaž Rozman,*** *doc. dr.* ***Stanislav Šuškovič,*** *mag.* ***Jurij Zalar***

Tehnična organizacija
MERIDIANA d.o.o. Ljubljana

Šola je namenjena radiologom, fiziatrom, ortopedom, revmatologom, pnevmologom in splošnim zdravnikom

Četrtek, 23. oktober 1997

8.00–9.00		Registracija udeležencev	
9.00–9.05	***B. Rozman***	*Ljubljana*	Uvodne misli
	Vnetni revmatizem		
9.05–9.30	***B. Rozman***	*Ljubljana*	Revmatoidni artritis (klinična problematika)
9.30–10.00	***M. Kos-Golja***	*Ljubljana*	Seronegativni spondiloartritisi (klinična problematika)
10.00–10.30			Odmor za kavo (vključeno v kotizacijo)
10.30–10.50	***A. J. Freemont***	*Manchester*	Rheumatoid arthritis (pathoanatomic considerations)
10.50–11.10	***A. J. Freemont***	*Manchester*	Seronegative spodyloarthropathies (pathoanatomic considerations)
11.10–11.40	***V. Jevtič***	*Ljubljana*	Revmatoidni artritis (radiološka problematika)
11.40–12.10	***V. Jevtič***	*Ljubljana*	Seronegativni spondiloartritisi
12.10–12.30	***L. Stegel***	*Ljubljana*	Vnetni in degenerativni revmatizem (ultrazvočna diagnostika)
12.30–15.00			Odmor (prosto)
15.00–15.20	***E. Mušič***	*Ljubljana*	Pljuča pri vnetnem revmatizmu (klinična problematika)
15.20–15.40	***E. Mušič***	*Ljubljana*	Pljuča pri vnetnem revmatizmu (radiološka problematika)
15.40–16.00			Odmor za kavo (vključeno v kotizacijo)
16.00–17.15	Učna delavnica		
	(delo v skupinah, vodje skupin: ***V. Jevtič, B. Rozman, M. Kos-Golja****)*		
17.15–18.30	Učna delavnica		
	(delo v skupinah, vodje skupin: ***V. Jevtič, B. Rozman, M. Kos-Golja****)*		
20.00	Skupna večerja (vključeno v kotizacijo)		

Petek, 24. oktober 1997

	Degeneratvni revmatizem		
9.00–9.30	***B. Čurković***	*Zagreb*	Degenerativni reumatizam (klinička problematika)
9.30–9.50	***A. J. Freemont***	*Manchester*	Osteoarthritis (patoanatomski pogled)
9.50–10.20	***K. Potočki***	*Zagreb*	Degenerativni reumatizam (radiološka problematika)
10.20–10.50			Odmor za kavo (vključeno v kotizacijo)
10.50–11.50	Učna delavnica		
	(delo v skupinah, vodji skupin: ***K. Potočki, B. Čurković****)*		
11.50–12.50	Učna delavnica		
	(delo v skupinah, vodji skupin: ***K. Potočki, B. Čurković****)*		
12.50–13.30	***V. Jevtič***	*Ljubljana*	Rezultati kviza in zaključek

Kotizacija in vplačila:
25.000,00 SIT (žiro račun MERIDIANA d.o.o. Ljubljana št. 50100-601-134414, sklic na št. 9708)

Informacije v zvezi s strokovnimi vprašanji:
Prof. dr. ***Vladimir Jevtič,*** Katedra za radiologijo MF, tel. 061 / 323 556, faks 061 / 13 31 044

Ostale informacije in prijave:
MERIDIANA d.o.o. Ljubljana, Župančičeva 7, 1000 Ljubljana
tel. 061 / 217 905, 12 11 380, faks 061 / 217 905, 12 11 381

GORENJSKO ZDRAVNIŠKO DRUŠTVO

Vas obvešča, da bo

6. TRADICIONALNI

DRUŽABNI MEDICINSKI PLES

v »Casino« na Bledu
v soboto, dne 18. oktobra 1997 ob 19.30 uri

Cena vstopnic je 4.000,00 SIT po osebi

Vikend paket v hotelu Park – 12.500,00 SIT. Vključuje 2 polpenziona (nočitev, zajtrk in večerja – 1-krat penzionska in 1-krat skupna, turistična taksa), uporabo bazena s termalno vodo in vstopnino.

Prijave (in predhodne rezervacije) pošljite na naslov:
Hotel PARK, Cesta svobode 15
tel.: 064 / 79 30, fax: 064 / 741 505

Program in družabni del srečanja bo vodil g. Slavko Podboj.
V programu bodo nastopili plesni par Primož Ramovš – Petra Vidmar in Blejski plesni studio.

Za ples bo poskrbel ansambel Music Box.
Prost bo vstop v igralnico Casino s cocktail party.
Organizirali bomo tudi srečolov.

Vljudno vabljeni

ZDRUŽENJE ZA PEDIATRIJO
SLOVENSKEGA ZDRAVNIŠKEGA DRUŠTVA

STROKOVNI SESTANEK

Ljubljana, 6. decembra 1997

TEMA

CEPLJENJE IN ANTIBIOTIČNO ZDRAVLJENJE

1. ***Rasta R. Rakar*** Uvodne misli
2. ***Milan Čižman*** Novosti v antibiotičnem zdravljenju v pediatriji
3. ***Breda Zakotnik*** Novosti pri cepljenju otrok

ZDRUŽENJE ZA PEDIATRIJO SLOVENSKEGA ZDRAVNIŠKEGA DRUŠTVA

STROKOVNI SESTANEK

Slovenj Gradec, 24. oktobra 1997

TEMA

INTERDISCIPLINARNA OBRAVNAVA BOLEZNI OTROK V KOROŠKI REGIJI

1.	**40 let otroškega oddelka Splošne bolnišnice Slovenj Gradec**	
2.	***Pavle Kornhauser***	Oblikovanje medicinsko-arhitekturnega programa otroške bolnice v Slovenjem Gradcu
3.	***Marjan Kos***	Predstavitev Koroške regije
4.	***Elizabeta Vravnik***	Interdisciplinarna obravnava otrok z redkejšimi diagnozami: AIDS, erlihioza, Kawasakijeva bolezen V razpravi bodo sodelovali: ***Vesna Glavnik, Milan Čižman, Tatjana Bufon-Lužnik, Breda Zakotnik-Vihar, Dušica Pleterski***
5.	***Zdenka Lužnik, Nedeljko Krevs***	Motnje srčnega ritma – prikaz nekaterih primerov
6.	***Ljuba Gangl, Dušanka Mičetić-Turk, Gordana Logar-Car, Andreja Knol***	Brata dvojčka s cistično fibrozo in celiakijo
7.	***Milan Špegel***	Absence
8.	***Cita Burnik***	Analiza ankete o obiskih in počutju otrok, staršev in osebja na otroškem oddelku
9.	***Marija Vodnjov***	Prikaz onesnaževanja okolja v Mežiški dolini v zadnjih 30 letih
10.	***Alenka Florjančič-Košuta***	Kirurško zdravljenje otrok

ZDRUŽENJE ZA PEDIATRIJO SLOVENSKEGA ZDRAVNIŠKEGA DRUŠTVA

PULMOLOŠKA SEKCIJA SLOVENSKEGA ZDRAVNIŠKEGA DRUŠTVA

SEKCIJA ZA ŠOLSKO IN VISOKOŠOLSKO MEDICINO SLOVENSKEGA ZDRAVNIŠKEGA DRUŠTVA

STROKOVNI SESTANEK

Ljubljana, 14. novembra 1997

TEMA

TUBERKULOZA V PEDIATRIJI

1.	***Jurij Šorli***	Epidemiologija in preventivni ukrepi pri tuberkulozi
2.	***Vasilja Maček, Matej Kunaver, Jurij Šorli, Dunja Piškur-Kosmač***	Delitev dela med pediatričnim in pnevmološkim dispanzerjem, vloga Pediatrične klinike v Ljubljani
3.	***Vasilja Maček***	Klinična slika tuberkuloze pri otroku
4.	***Silvester Kopriva***	Zdravljenje tuberkuloze pri otroku
5.	***Manca Dovč-Žolnir***	Možnost laboratorijske diagnostike tuberkuloze pri otroku

Pismo uredništvu/Letter to the editor

Poučevanje splošne/družinske medicine
OCENJEVANJE KAKOVOSTI DELA V AMBULANTI

Mateja Bulc

Zdravstveni dom Ljubljana, enota Šiška, Derčeva ul 5, 1000 Ljubljana

Uvod

Kakovost zdravstvene oskrbe je bila tema 11. Učne delavnice za zdravnike splošne medicine v Gozdu Martuljku pred dobrima dvema letoma. Namen učne delavnice je bil opozoriti sodelujoče na pomen izboljševanja, zagotavljanja in ocenjevanja kakovosti zdravstvene oskrbe in jih opremiti z novimi znanji in spretnostmi. Udeleženci, specialisti splošne medicine iz več evropskih držav, so kot končni izdelek skupinskega dela pripravili učne modele. Namen učnega modela je bil vgrajevanje stalnega ocenjevanja kakovosti v ambulante splošne medicine in v učenje študentov Medicinske fakultete, ki opravljajo praktični del sedemtedenskega ciklusa v ambulantah, ob mentorjih, specialistih splošne medicine.

Izdelava učnega modela

Učni model, ki ga predstavljamo, je izdelala delovna skupina zdravnikov splošne medicine: Jaime Correia de Sousa (Portugalska), Nada Prešeren, Darinka Šoln, Miha Demšar, Marko Kocijan, Adrian Wirthner (Švica), Matjaž Lesjak in Mateja Bulc (Slovenija).
Zagotavljanje kakovosti je dinamični postopek, ki naj bi uporabnikom zagotavljal kakovostni sistem zdravstvenega varstva. Sistem sestavljajo trije členi: zdravniki, bolniki in snovalci zdravstvene politike, vsak s svojimi stališči o kakovosti.
Postopek ocenjevanja kakovosti lahko razdelimo na tri stopnje.
Prva je izbira primerne snovi (indikatorja) v zdravstveni oskrbi in izdelava meril oziroma navodil (kriterijev) za dobro delo.
Druga stopnja je ocenjevanje zdravstvene oskrbe s sprejetimi merili.
Tretja stopnja pa je uvajanje potrebnih izboljšav in spremljanje izidov.

Izbira primerne snovi za ocenjevanje

Za izdelavo učnega modela si je skupina morala izbrati snov za ocenjevanje kakovosti dela v splošni ambulanti. Pri izbiri je treba upoštevati naslednje pogoje: tema mora biti dovolj pogosta, vplivati mora na zbolevnost in umrljivost, biti mora zanimiva tudi za druge medicinske strokovnjake, njeno reševanje mora biti smotrno in skupina jo mora biti sposobna rešiti.
Sodelujoči v skupini smo se ob iskanju teme spraševali:
– Kateri so dejanski medicinski problemi v večini ambulant?
– Ali se jih da prilagoditi in kako?
– Kako pomembni so?
– Ali so obvladljivi?
– Kakšne so sociološke, biološke in druge značilnosti populacije, za katero skrbimo?
– Kateri so najpogostejši zdravstveni problemi v tej populaciji?
– Ali imamo dovolj informacij o svojih bolnikih?
– Kakšna so naša opravila v ambulanti?
– Kako lahko izboljšamo svoje delo?
– Kakšen je pomen preprečevanja bolezni in zdravstvena vzgoja v ambulanti splošne medicine?

Po »prevetrenju« in iskanju idej se nam je ponujalo veliko tem (Zdravljenje arterijske hipertenzije v ambulanti splošne medicine; Ugotavljanje koncentracije lipidov v ambulanti splošne medicine; Timsko delo v ambulanti splošne medicine; Dobrobit preventive v ambulanti splošne medicine; Pomoč pri prenehanju kajenja v ambulanti splošne medicine). Z glasovanjem smo se odločili za »Ugotavljanje koncentracije holesterola v krvi pri 20 do 40 let starih moških v ambulanti zdravstvenega doma«.

Izbira meril (kriterijev)

Za merjenje kakovosti zaznavanja zvišanih koncentracij maščob v krvi mladih moških obiskovalcev ambulante smo postavili poseben protokol z 11 stopnjami (»criteria mapping«) – glej Učni model.

Zunanji nadzor s svetovanjem

Naša »izvedenska« skupina je napovedano obiskala ambulanto enega od zdravnikov v bližnjem zdravstvenem domu.
Ob obisku ambulante smo pregledali zdravstvene kartoteke vseh moških pacientov, ki so bili rojeni med letoma 1954 in 1974, torej so bili v opazovanem obdobju stari 20 do 40 let.
Upoštevali smo vse obiske v ambulanti v zadnjih dveh letih, torej od 10. septembra 1972 do 8. septembra 1974.
Ukrepanje zdravnika smo vpisovali v formular Protokol meril, ki smo ga poprej izdelali.
V omenjenih zdravstvenih kartotekah smo po izoblikovanem protokolu iskali podatke o določanju koncentracije holesterola v serumu, podatke o lipidnem statusu, o načrtnem iskanju napovednih dejavnikov za zvišani holesterol, o iskanju drugih dejavnikov tveganja za razvoj bolezni srca in ožilja ter o ustreznosti ukrepanja oziroma zdravljenja.
Kot kakovostno ravnanje bi ocenili, če bi se v 40 ali več odstotkih ravnanje zdravnika (razvidno iz pregledanih kartotek) ujemalo z našimi merili. To pomeni, da bi bil postopek od točke 1 do točke 2 oziroma 4 ustrezen: odgovor NE v točki 2 oziroma v točki 4. Kot slabo ravnanje bi ocenili ravnanje zdravnika, ki bi se v manj kot 40 odstotkih ujemalo z našimi merili.
Kot dobro zdravljenje zvišanega holesterola v krvi moških, starih od 20 do 40 let, bi ocenili, če bi se postopek pri vseh varovancih, ki so potrebovali zdravljenje, ujemal s protokolom (od točke 1 do točke 11 odgovori DA) v 60 odstotkih ali več.
Kot nekakovostno zdravljenje bi ocenili tisto, kjer bi se postopek pri vseh varovancih, ki so potrebovali zdravljenje, v manj kot 60 odstotkih ujemal s protokolom (od točke 1 do točke 11 odgovori DA).

Rezultati

Po pregledu kartotek smo izračunali, v koliko odstotkih se je ravnanje zdravnika ujemalo z izoblikovanimi kriteriji, in objavili rezultat:
»Ugotavljanje koncentracije holesterola pri moških med 20. in 40. letom starosti v ambulanti dr. ... Zdravstvenega doma ... je po oceni skupine izvedencev ... (ne)kakovostno, saj se v ... % njegovo ukrepanje ujema z merili kakovosti detekcije in zdravljenja hiperholesterolemije, ki jih je izoblikovala ta izvedenska skupina.«

Izdelek
Izdelek

Učni model

Zdravstveni problem

Kako dr. X ugotavlja in zdravi holesterol pri svojih bolnikih

Metodologija

1. ***Načrt meril za ocenjevanje (Protokol meril)***
2. ***Zunanji nadzor s svetovanjem***

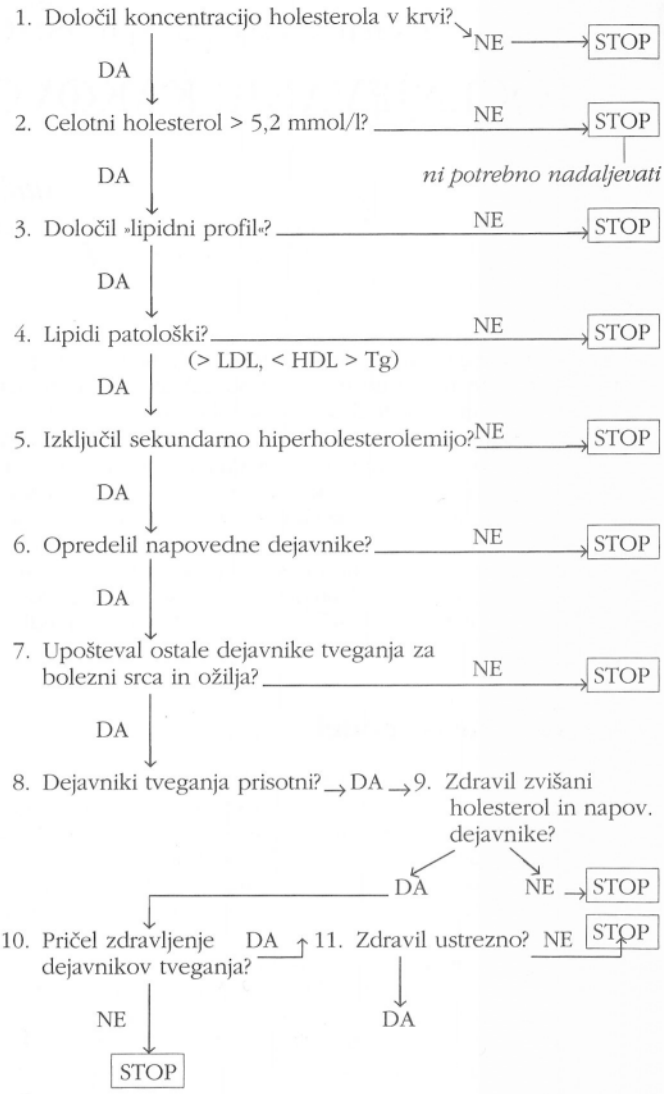
   Ocena zdravstvene oskrbe

– lokacija zdravstvene dejavnosti:	ambulanta splošne medicine
– zdravstvena dejavnost:	preventiva, presejanje, diagnostika, zdravljenje, zdravstvena vzgoja
– zdravstveni problem:	zvišan holesterol v krvi, spremenjen lipidni profil
– populacija:	moški, stari od 20 do 40 let
– koga ocenjujemo:	dr. X
– čas ocenjevanja:	obdobje dveh let (10. 9. 1992 do 8. 9. 1994)
– kaj ocenjujemo:	ustreznost ukrepanja, vodenja
– vir podatkov:	zdravstveni karton

3. ***Zbiranje podatkov*** iz klasičnih zdravstvenih kartonov na posebne obrazce (Protokol meril)
   Varianta: računalniško zbrani podatki in računalniška obdelava.

Merila

Protokol meril za ocenjevanje kakovosti



Merila kakovostnega ravnanja:

Pri več kot 40% obiskovalcev ambulante v opazovanem obdobju je bilo ravnanje pravilno:
stopnja 1–2 → NE
stopnja 1–4 → NE
Nekakovostno ravnanje:
<40%

Merila kakovostnega zdravljenja:

Pri več kot 60% bolnikov, ki so potrebovali zdravljenje, je bil odgovor v Protokolu od stopnje 1 do 11: DA.
Nekakovostno zdravljenje:
<60%

Rezultati

a)
Dr. X je ukrepal v skladu s Protokolom od stopnje 1 do 2 oziroma od stopnje 1 do 4 v 56%.
Njegovo ravnanje za ugotavljanje lipidnega statusa je bilo torej kakovostno.

b)
Dr. X je zdravil zvišano koncentracijo holesterola pri svojih bolnikih v skladu s Protokolom od točke 1 do točke 11 le v 58%. Njegovo zdravljenje je bilo torej neustrezno, nekakovostno.

Ponujeni model naj služi zgolj v didaktične namene!

Strokovno izpopolnjevanje

SEMINAR »CORNELL« IZ GINEKOLOGIJE IN PORODNIŠTVA V SALZBURGU

Salzburg, 16.–22. februarja 1997

Boštjan Lovšin, Barbara Požlep

Seminarji »Cornell« v Salzburgu so od leta 1993 oblika izobraževanja zdravnikov iz Srednje in Vzhodne Evrope v organizaciji Medicinske fakultete Univerze Cornell in Sorosove fundacije iz New Yorka. Enotedenska predavanja potekajo v čudovitem gradu Leopoldskron v predmestju Salzburga. Letošnjega seminarja s področja ginekologije in porodništva sva se med 50 zdravniki iz Srednje in Vzhodne Evrope udeležila tudi dva iz Slovenije. Predavali so štirje ugledni strokovnjaki z Univerze Cornell v New Yorku, vsak je imel vsak dan približno enourno predavanje, ki mu je sledilo intenzivno razpravljanje.

Vodja programa, profesor dr. William J. Ledger, je prikazal širše področje okužb v ginekologiji in porodništvu. V predavanju o profilaktični uporabi antibiotikov ob operativnih posegih je izluščil smernice smiselne profilakse. Antibiotična profilaksa bo uspešna, če je endogena okužba z bakterijami velika, če je koncentracija antibiotika v rani v času reza dovolj velika ter ob kratkotrajnem načinu jemanja. Zadostovalo naj bi, če je antibiotik učinkovit le na nekatere bakterije. Antibiotična profilaksa je smiselna pri vaginalni histerektomiji, urgentnem carskem rezu, radikalni histerektomiji ter prekinitvi nosečnosti. Pred operacijo (pri carskem rezu pa ob prekinitvi popkovnice) je priporočal antibiotike cefoksitin, cefotetan, piperacilin ali cefazolin, ponovitev odmerka pa pride v poštev le ob daljšem trajanju operacije. Ob morebitni okužbi po operaciji je priporočal uporabo drugega antibiotika. Pri histerektomiji prek trebušne stene je priporočal profilakso pri večji ogroženosti (debelost, predhodna vnetja v mali medenici, rakave bolezni, bakterijska vaginoza). Sledilo je predavanje o predčasnem razpoku plodovih ovojev, kjer je predavatelj poudaril, da je sam prezgodnji porod in z njim povezana dihalna stiska precej večji problem od morebitne sepse novorojenčka, zatorej naj se nam ne mudi s porodom pri prezgodnjem predčasnem razpoku. Pomembno je iskanje prisotnosti bakterijske vaginoze (ki jo spoznamo po alkalnem pH vaginalnega izcedka, vonju po ribah ob kapanju kalijevega hidroksida, ob pregledu pod mikroskopom vidimo značilne celice ter odsotnost levkocitov), trihomonasa vaginalis (zanesljivo ga dokažemo s polimerazno verižno reakcijo – PCR) in klamidije trahomatis (prav tako jo zanesljivo dokažemo s PCR). Nad profilaktičnim dajanjem antibiotikov pri grozečem prezgodnjem porodu pa ni bil navdušen. Sledilo je predavanje o sindromu kroničnega vulvovaginitisa, ki se kaže v različnih oblikah: kondilomi (tu je priporočil zdravljenje z interferonom, milijon enot, 4 tedne, pričakovano izboljšanje čez 6 tednov), labialna mikropapilomatoza, vestibularni adenitis, alergični in kandidiazni vulvovaginitis, bakterijska vaginoza in druge. Omenil je zanimiv problem vaginitisa pri ženskah, katerih partnerji so bili vazektomirani, kjer so opazili porast IgE protiteles v semenski tekočini, zato nekaj časa priporočajo uporabo kondoma.

Dr. Steven R. Inglis je prikazal problematiko prezgodnjega poroda in nadzora plodovega stanja v nosečnosti. V predavanju o biokemičnih kazalnikih prezgodnjega poroda je predstavil citokine, elastazo, proteaze, fosfolipazo A-2, prolaktin, estriol, metaloproteinaze, serumski alfa-fetoprotein, TNF-alfa in fetalni fibronektin. Le zadnja preiskava se je izkazala kot kar zanesljiv kazalnik začetka poroda, ob terminu ali prezgodnjega. Priporočal je tedensko jemanje vzorcev pri zelo tveganih nosečnostih. Končalo se je z večnim vprašanjem: kaj sproži začetek poroda pri človeku? V krajšem predavanju o izoimunizaciji v nosečnosti je povedal nekaj besed o uporabi eritropoetina ob intrauterinih transfuzijah, ker te zavirajo eritropoezo. Eden največjih problemov porodništva je preprečevanje prezgodnjega poroda, o čemer je govoril v naslednjem predavanju. Celo tedenski ginekološki pregledi bistveno ne pripomorejo k zmanjšanju pojavnosti prezgodnjega poroda. Trenutno obeta nekaj več ultrazvočni pregled cervikoistmičnega dela maternice, ko se bodo ustalili kriteriji s poznejšim sledenjem izida nosečnosti. Nadzor aktivnosti maternice na daljavo se je izkazal koristen le pri večplodnih nosečnostih. Pomembno je iskanje okužb in zdravljenje teh. Najbolje je ločiti manj in bolj tvegane nosečnosti in slednje intenzivneje nadzorovati. Vplivati je treba na možne dejavnike ogrožanja: kajenje, zloraba drog, slaba predporodna oskrba, težko fizično delo, stres, higiena, več partnerjev. Zelo dobra je negativna napovedna vrednost testa s stimulacijo bradavic na dojkah. Če ob tem ne pride do krčenja maternice, je zelo majhna verjetnost poroda v naslednjih petih tednih. V predavanju o okužbi z virusom HIV v nosečnosti je bilo zanimivo slišati novost o določanju antigena HIV p24, ki zmanjša okno med okužbo in pojavom protiteles. Novorojenčku je mogoče antigen najti že sedmi dan po porodu, če je HIV pozitiven. Možnost okužbe med porodom je manjša ob ohranitvi integritete plodove kože, izogibati se je treba instrumentalnega poroda, skalp elektrod in določanja pH krvi iz skalpa. Vsaki HIV pozitivni nosečnici ponudijo terapijo z zidovudinom, ki zmanjša navpični prenos okužbe. Američani imajo seveda izdelane natančne protokole ravnanja tudi za zaščito zdravstvenih delavcev.

Najbolj slikovito je bilo predavanje o nadzoru plodovega stanja v nosečnosti. Vzrok mrtvorojenosti je asfiksija v 30%, maternalni dejavniki v 25%, malformacije v 20%, okužba v 5%, ostali vzroki niso znani. Zato so pred leti ustanovili enoto za predporodno nadzorovanje in zmanjšali popravljeno perinatalno umrljivost na 9 promilov, mrtvorojenost pa na 3 promile. Za odlično metodo nadzora še vedno velja kardiotokografija z analizo reaktivnosti. Pri nereaktivnem kardiotokografskem zapisu je predavatelj priporočal vibroakustično stimulacijo ali fetalni biofizični profil. Prva metoda je zelo enostavna in jo mogoče pri nas premalo uporabljamo. Druga metoda zahteva več časa, vendar je precej zanesljiva. Štetje gibov ploda s strani nosečnice še ni za odmet, saj je metoda enostavna, varna in poceni. Nad vrednostjo indeksov pretokov umbilikalne arterije ni bilo navdušenja, razen seveda pri odsotnem ali obratnem pretoku v diastoli. Glavne indikacije za nadzor so znane: nosečnost čez porodni termin, hipertenzivne bolezni v nosečnosti, sladkorna bolezen, zastoj rasti ploda, zmanjšani gibi ploda, poprejšnja mrtvorojenost, večplodna nosečnost, Rh izoimunizacija, kolagenoze ter druge bolezni matere. Začetek nadzora je predavatelj priporočil nekako okrog 32. tedna nosečnosti, štetje gibov naj bo dnevno, kardiotokografija pa dvakrat tedensko. V neuradnem delu je bilo zanimivo slišati, da delajo pH med porodom zadnji v Ameriki, amnioskopij pa sploh ne več. Res pa je tudi, da se 25% vseh porodov konča s carskim rezom. Porode v zadnjični vstavi praviloma končajo s carskim rezom.

Dr. Zev Rosenwaks je imel več predavanj o asistirani reprodukciji s takšnimi rezultati, da smo se kar malo čudili. V prvem je analiziral pomen starosti ženske za uspeh. Kazalnika ovarijske rezerve sta predvsem koncentraciji FSH in estradiola 3. dan ciklusa. Malo je uspešnih nosečnosti ob koncentraciji FSH nad 20 mIU/mL ali estradiola nad 75 pg/mL. V njihovi seriji pade odstotek nosečnosti s porodom (na transfer) s 53,5% pri ženskah pod 30 let na 11,4% pri 43-letnih. Problem predstavljajo ženske z nezadovoljivo ovarijsko stimulacijo ob standardnem protokulu, tam si pomagajo z znižanjem odmerkov GnRH-agonistov. V koristnost rastnega hormona ne verjame in ga ne uporablja. Pri starejših je težišče raziskav na izboljšanju nadzirane ovarijske stimulacije, asistirani implantaciji in možnosti preimplantacijske biopsije zarodka za odkrivanje anevploidij. Z uporabo FISH tehnike so samo s štirimi kromosomskimi sondami odkrili značilne razlike: pri ženskah, mlajših od 39 let, so odkrili 21% kromosomskih nepravilnosti (9% anevploidij), pri starejših od 39 let pa 48% kromosomskih nepravilnosti (42% anevploidij). Iz tega je zaključil, da večji uspeh omejuje sama biologija, ne pa tehnika zunajtelesne oploditve, zato bi

pač ženske morali začeti zdraviti bolj zgodaj. Sledilo je pregledno predavanje o darovanju oocitov, ki je bilo zaradi razpravljanj ob pripravi novega zakona o asistirani reprodukciji pri nas še posebej zanimivo. Naj navedeva le nekaj primerov, kako ravnajo ob določenih problemih. Večino dajalk oocitov predstavljajo plačane prostovoljke in sestre pacientk, novost predstavlja gojenje nezrelih oocitov iz nestimuliranih ovarijev, dobljenih ob operacijah. Pri pacientkah z ovarijsko odpovedjo stimulirajo naravni ciklus s transdermalno uporabo estradiola, 15. dan pa začnejo z intramuskularnimi injekcijami progesterona. V predhodnih pripravljalnih ciklusih potrdijo ustrezen odgovor endometrija z biopsijo. Ključ do uspeha je učinkovita sinhronizacija ovarijskega, embrionalnega in endometrijskega statusa. Najboljše rezultate daje prenos zarodkov s štirimi ali več blastomerami v endometrij histoloških značilnosti 17. do 19. dneva ciklusa, predvsem pa so uspehi odvisni od izbire dajalk oocitov. Uspešnost je večja kot pri običajnem programu zunajtelesne oploditve zaradi mlajših oocitov in odsotnosti hiperstimulacije pri prejemnicah.

Tudi v naslednjem predavanju o indukciji ovulacije je bilo slišati nekaj zanimivih stvari: indukcija ovulacije je ravno toliko umetnost kot znanost, dajanje gonadotropinov mora biti individualno, monitorirano in uravnavano. Za zgodnji razvoj foliklov so nujne meritve koncentracije estrogenov, za število in velikost zrelih foliklov pa ultrazvočni pregledi. Zagovarjajo protokol z relativno visokimi začetnimi odmerki gonadotropinov, ki jih nato postopno znižujejo. Pri bolnicah s policističnimi jajčniki trenutno dosti uporabljajo protokol, kjer 25-dnevni uporabi hormonskih kontracepcijskih tablet sledi levprolid acetat in nato gonadotropini. Zadnje predavanje je bilo o intracitoplazmatski injekciji spermijev (ICSI) oziroma mikromanipulaciji, ki predstavlja revolucijo na področju asistirane reprodukcije. Do septembra lani so imeli 763 kliničnih nosečnosti v 2000 ciklusih po ICSI postopku. Natančno so analizirali rezultate in ugotovili, da stopnja oploditve ni odvisna od kakovosti semena, prav tako ne od tega, ali je bilo dobljeno z ejakulacijo ali aspirirano iz epididimisa, pač pa je manjša po aspiraciji iz testisa. Stopnja oploditve pa je seveda odvisna od starosti ženske. Precej boljši so rezultati po agresivni imobilizaciji spermijev v primerjavi s standardno. Ena od smeri razvoja v prihodnosti bo mogoče tudi transplantacija spermatogonijev in zorenje v testisu gostitelja.

Dr. Steven S. Witkin je predaval o imunologiji v ginekologiji in porodništvu. Poudaril je, da lahko neplodnost povzročijo tudi protitelesa na semenčice. Ob določenih indikacijah je priporočil testiranje, ki se opravi navadno s testom Mar. Zdravljenje lahko predstavlja intrauterina inseminacija ali ICSI. Tudi asimptomatska klamidijska okužba v ženskem genitalnem traktu lahko povzroči neplodnost in zgodnji splav. Zunajcelična elementarna telesca aktivirajo imunski sistem, interferon gama in drugi citokini sicer povzročijo krajevno vnetje in fagocitozo, vendar znotrajcelična telesca ostanejo. Ponovljeni ciklusi rasti nato vedno bolj okvarijo jajcevode. Klamidijski antigen »heat-shock-protein« (hsp60) ima kar polovico aminokislinskih zaporedij homolognih s človeškim hsp60, zato lahko pride do imunske odzivnosti na človeški hsp60. V nosečnosti lahko pride do reaktivacije limfocitov in vnetnega odgovora. Edina zanesljiva diagnostika asimptomatske klamidijske okužbe je verižna polimerazna reakcija, priporočeno je široko presejanje vseh spolno aktivnih žensk pod 25. letom starosti, nosečnic, bolnic s spolno prenosljivo boleznijo, žensk ob menjavi partnerja, ob nepojasnjeni neplodnosti, po spontanih splavih. V predavanju o imunskih mehanizmih v povezavi s prezgodnjim porodom je povedal, da je najbolj zanesljiv in specifičen kazalnik intraamnijske okužbe in napovedni dejavnik prezgodnjega poroda le interlevkin 6 v plodovnici, nekaj manj pa tumorski nekrozni dejavnik alfa v cerviksu. Še enkrat je poudaril pomen iskanja okužbe s trihomonasom in klamidijo v nosečnosti z imunološkega vidika. V živahni razpravi o zdravljenju asimptomatskih okužb v nosečnosti so priporočili zdravljenje bakterijske vaginoze z metronidazolom per os 5 dni 500 mg dvakrat dnevno. Priporočili so tudi zdravljenje kolonizacije s streptokoki skupine B, nato pa ponovni odvzem brisa že čez dva tedna, ker so lahko spet prisotni. Zdravljenje kolonizacije z enterokoki je potrebno le ob prisotnem serklažnem šivu, ker ta predstavlja tujek.

V okviru programa je bil en popoldan rezerviran za računalniško izobraževanje ter deskanje po internetu, en popoldan pa za voden ogled Salzburga. Po zaključnem razpravljanju in podelitvi diplom sva se polna novih spoznanj veselo odpravila domov. Zahvaljujeva se Zavodu za odprto družbo – Slovenija, gospe Neli Dimc in vsem, ki so nama omogočili to strokovno izpopolnjevanje.

Delo SZD

PREDSTAVITEV KNJIG

Bogdan Leskovic

Predsednica Komisije za stike z javnostjo pri SZD dr. Tatjana Zorko in predsednik SZD prof. dr. Pavel Poredoš sta pripravila na sedežu društva 19. 6. 1997 predstavitev štirih novih knjig slovenskih zdravnikov.

Anton Dolenc: *Medicinska etika in deontologija II. Razprave, izbrana poglavja*. Mihelač. Ljubljana 1997. 620 strani.

Knjiga je nadaljevanje istoimenskega dela, označenega z I, ki je izšlo 1993. leta na 556 straneh (spoznavanje temeljev medicinske etike) in pomeni nadaljevanje tradicije dela Inštituta za sodno medicino ter Katedre za sodno medicino in deontologijo Medicinske fakultete v Ljubljani. V obravnavi so aktualna vprašanja medicinske morale in etike ter skrb za deontološko vzgojo slovenskih zdravnikov.

V sedanjem, drugem delu je obsežnejši del medicinske etike in deontologije namenjen izbranim poglavjem tega področja. Pisec v svojem uvodu pravi, da je bil pred dilemo: ali učbenik napisati povsem na novo, ali pa zbrati lastne, po strokovnih revijah in časopisju raztresene prispevke. Uresničitev v predloženem delu je nekje vmes: nekatera poglavja so napisana za knjigo »namensko«, izbrani prispevki pa so »neredigirani« tako, da neposredno kažejo na ljubljansko deontološko šolo tudi z vso specifičnostjo, ki so jih ta prizadevanja imela pri uveljavljanju medicinske etike v tistem času.

Izbrana poglavja bodo dala slušateljem temelje za kritično razmišljanje o vlogi in pomenu medicine in zdravnika nasploh v preteklosti in sedanjosti ter jih soočila s potmi in razhajanji v medicinski teoriji in praksi doma in po svetu.

Vsebina je razdeljena na štiri dele. I. del, ki ima 8 poglavij, se začne s poglavjem Kodeks medicinske deontologije Slovenije. II. del ima 3 poglavja z začetnim Spoštovanje življenja. III. del je najobsežnejši in ima 41 poglavij. Uvaja ga poglavje Poklicna odgovornost zdravnika. V IV. delu pa so v glavnem deklaracije.

Obe knjigi tako zaključeno prikazujeta aktualna vprašanja medicinske morale in etike na Slovenskem, pa tudi razvoj deontološke misli po svetu.

Recenzenta sta bila prof. dr. Jože Drinovec in dr. Jože Trček. Slednji je knjigo tudi predstavil poleg avtorja samega.

Velimir Vulikić, urednik, in Zvonka Zupanič Slavec, sourednica: *Prof. dr. Jože Rant – organizator slovenskega zobozdravstva*. Zbornik spominskega simpozija ob 100-letnici rojstva prof. dr. J. Ranta z mednarodno udeležbo. Četrti Pintarjevi dnevi 1996. Inštitut za zgodovino medicine Medicinske fakultete v Ljubljani. Ljubljana 1997. 228 strani.

Zbornik je predstavil urednik. Z vidika polpretekle zgodovine predstavlja življenje in delo prof. dr. J. Ranta, po drugi strani pa

razvoj zobozdravstva in strokovnega šolstva na naših tleh. Objavljenih je 22 referatov z obravnavo teh dveh tem. Bogato slikovno gradivo popestri vsebino in ponazori marsikatero trditev.
Devet referatov je vezano neposredno na prof. dr. J. Ranta, ostalih trinajst pa le posredno na njegovo delo in osvetljujejo razvoj zobozdravstva na naših tleh, vzgojo kadrov in sodelovanje s hrvaškimi kolegi v okviru tedanje skupne države. Sestavki v zborniku in obsežna literatura ob njih odkrivajo polpreteklo zgodovino in dokazujejo prizadevanje in delo tega velikega moža. Zbornik je dragocen dodatek k njegovemu biografskemu romanu izpod peresa prim. dr. Velimira Vulikića, ki je izšel lani ob simpoziju.
Obe knjigi sta pomemben doprinos k ohranjanju spomina na prof. dr. J. Ranta in na razvoj zobozdravstva pri nas ter prispevata k boljšemu razumevanju dogajanj in pojmovanj v tistem času.
Recenzijo zadnje knjige sta opravila prof. dr. Zvone Žajdela in prim. dr. Zoran Arnež.

Zvonka Zupanič Slavec: *Z očmi zdravnice. Ugledni pisci družno z medicino.* Znanstveno društvo za zgodovino zdravstvene kulture Slovenije, Ljubljana 1997. 150 strani s portreti piscev.

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Izbor ni bil narejen po v naprej pripravljenem načrtu, ampak svobodno in spontano, z osebnim odnosom do ustvarjalcev. Razmišljanje o piscih in njihovih delih je predvsem povzeto po nemških prevodih tujih raziskovalcev in publicistov, a spet svobodneje, s potrebnim in smiselnim poseganjem v izvirno pisanje.
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Knjiga se zaključuje z navedbo literature, kar ji daje še posebno vrednost.
Avtorico je na zavihkih knjige lepo predstavila dr. Ana Krušič Kaplja in odkrila njeno življenjsko razpetost med medicino in njeno zgodovino ter umetnostjo.
Knjigo je predstavil prof. Jaro Dolar, ki je napisal tudi spremno besedo in jo zaključil z mislijo, da ne bo knjiga zanimiva le za zdravnike, temveč za vse, ki jim je literatura pri srcu.

Pavle Kornhauser, urednik in oblikovalec: *Almanah ob 40-letnici zavoda v Šentvidu.* Več avtorjev. Center za zdravljenje bolezni otrok Šentvid pri Stični, Ljubljana, Šentvid 1997. 104 strani, ki so bogato ilustrirane in opremljene s preglednimi razpredelnicami in grafikoni.

Almanah se začne z uvodnimi besedami pokroviteljev ob 40-letnici zavoda. Referati, ki slede, pojasnjujejo zgodovino zavoda in njegovega dela. Urednik opisuje njegovo prvo dobo od 1957. do 1967. leta, ko mu je bil prvi strokovni vodja in se je imenoval »Zavod za revmatične in srčne rekonvalescente za mladino dr. Marko Gerbec«. Nadaljnje strokovno vodstveno delo prof. dr. Leva Matajca med letoma 1967 in 1990 je opisala dr. Ana Videnič. V tem času se je že spremenila patologija in so preimenovali zavod v »Center za zdravljenje bolezni otrok Šentvid pri Stični« glede na njegovo novo, razširjeno zdravstveno dejavnost. Prim. mag. dr. Štefan Kopač, ki ga od leta 1990 strokovno vodi, je napisal s sodelavkama zadnji del zgodovine zavoda, ki je sedaj specialna bolnišnica za podaljšano zdravljenje, rekonvalescenco in rehabilitacijo ter redno šolanje otrok iz vseh bolnišnic v Sloveniji. Slede še sestavki Etiopatogeneza in zdravljenje juvenilnega revmatoidnega artritisa, Penicilin – še vedno najprimernejše zdravilo za zdravljenje streptokokne angine in v preprečevanju revmatične bolezni, Služba nege v zavodu, Doživljanje bolezni in kakovost življenja kronično bolnega otroka, Dr. Marko Gerbec naš znameniti rojak ter Šolska in vzgojna dejavnost v zavodu.
Almanah daje lep prikaz štiridesetletnega dela zavoda, ki se je vseskozi prilagajal spremenjenim zdravstvenim potrebam in plemenito skrbel za bolno, zaupano mu mladino.
Bogato predstavitev knjig sta popestrili še dve glasbeni točki, ki jih je izvedla na kitari kolegica dr. Alenka Okorn z dvema svojima učenkama na glasbeni šoli.

Založba Forma 7, d. o. o. iz Ljubljane je poslala Zdravniškemu vestniku v predstavitev dve svoji najnovejši izdaji iz serije uspešnic ameriške založbe Publications International, Ltd., Lincolnwood, Illinois.
Gre za poljudni, zdravstvenovzgojni knjigi, ki služita kot priročnika pri vsakdanjem življenju in težavah. Vsaka zase daje po 50 praktičnih nasvetov. Obe sta bogato ilustrirani, besedilo je kratko in pregledno. Prevedel ju je Bojan Ilich. Format knjig je kvadraten, videz je ličen in vezava trda.

Hermine Hilton: *50 poti do boljšega spomina.* 68 strani.

Avtorica je direktorica svetovalne organizacije Hilton Memory s sedežem v Los Angelesu in se uspešno ukvarja s tehnikami za izboljšanje spominskih zmogljivosti pri ljudeh vseh starosti s pomočjo predavanj, programov in seminarjev. Svoje strokovno znanje s področja urjenja spominov je doslej posredovala mnogim pomembnim organizacijam v ZDA.
Številne vsakdanje informacije, tudi važne, človek hitro pozabi, če jih ne »zaklene« v svoj spomin. Ta knjiga pokaže, kako se to stori, da ostanejo informacije zasidrane v spominu. Zato je knjiga dobrodošel pripomoček v življenju tako šolarja kot aktivnega človeka in v starosti.
Knjiga ima naslednja poglavja:
Uvod. Kako vključite svoje spominske zmogljivosti. Mnemonika. Tehnike za zbiranje informacij. Povezava z novimi informacijami. Nasveti za urjenje spomina glede številk. Nasveti za »zaklepanje« dejstev in seznamov. Kako si laže zapomnite priimke. Kako si zapomnite besede. Nasveti proti raztresenosti. Kako si zapomnite svoj govor. Vaje vašega spomina.

Billy Glisan s sodelovanjem Stephena Hochschulerja: *50 načinov lajšanja bolečin v hrbtenici.* 88 strani.

Glavni avtor je doktor fizioloških znanosti in sodelavec Inštituta za hrbtenico v Teksasu. Je avtor programa za rehabilitacijo hrbtenice tega inštituta. Drugi soavtor pa je doktor medicine in ortopedski kirurg, ki se je specializiral za hrbtenično kirurgijo. Je ustanovitelj

razvoj zobozdravstva in strokovnega šolstva na naših tleh. Objavljenih je 22 referatov z obravnavo teh dveh tem. Bogato slikovno gradivo popestri vsebino in ponazori marsikatero trditev.
Devet referatov je vezano neposredno na prof. dr. J. Ranta, ostalih trinajst pa le posredno na njegovo delo in osvetljujejo razvoj zobozdravstva na naših tleh, vzgojo kadrov in sodelovanje s hrvaškimi kolegi v okviru tedanje skupne države. Sestavki v zborniku in obsežna literatura ob njih odkrivajo polpreteklo zgodovino in dokazujejo prizadevanje in delo tega velikega moža. Zbornik je dragocen dodatek k njegovemu biografskemu romanu izpod peresa prim. dr. Velimira Vulikića, ki je izšel lani ob simpoziju.
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Almanah daje lep prikaz štiridesetletnega dela zavoda, ki se je vseskozi prilagajal spremenjenim zdravstvenim potrebam in plemenito skrbel za bolno, zaupano mu mladino.
Bogato predstavitev knjig sta popestrili še dve glasbeni točki, ki jih je izvedla na kitari kolegica dr. Alenka Okorn z dvema svojima učenkama na glasbeni šoli.

Založba Forma 7, d. o. o. iz Ljubljane je poslala Zdravniškemu vestniku v predstavitev dve svoji najnovejši izdaji iz serije uspešnic ameriške založbe Publications International, Ltd., Lincolnwood, Illinois.
Gre za poljudni, zdravstvenovzgojni knjigi, ki služita kot priročnika pri vsakdanjem življenju in težavah. Vsaka zase daje po 50 praktičnih nasvetov. Obe sta bogato ilustrirani, besedilo je kratko in pregledno. Prevedel ju je Bojan Ilich. Format knjig je kvadraten, videz je ličen in vezava trda.

Hermine Hilton: *50 poti do boljšega spomina.* 68 strani.

Avtorica je direktorica svetovalne organizacije Hilton Memory s sedežem v Los Angelesu in se uspešno ukvarja s tehnikami za izboljšanje spominskih zmogljivosti pri ljudeh vseh starosti s pomočjo predavanj, programov in seminarjev. Svoje strokovno znanje s področja urjenja spominov je doslej posredovala mnogim pomembnim organizacijam v ZDA.
Številne vsakdanje informacije, tudi važne, človek hitro pozabi, če jih ne »zaklene« v svoj spomin. Ta knjiga pokaže, kako se to stori, da ostanejo informacije zasidrane v spominu. Zato je knjiga dobrodošel pripomoček v življenju tako šolarja kot aktivnega človeka in v starosti.
Knjiga ima naslednja poglavja:
Uvod. Kako vključite svoje spominske zmogljivosti. Mnemonika. Tehnike za zbiranje informacij. Povezava z novimi informacijami. Nasveti za urjenje spomina glede številk. Nasveti za »zaklepanje« dejstev in seznamov. Kako si laže zapomnite priimke. Kako si zapomnite besede. Nasveti proti raztresenosti. Kako si zapomnite svoj govor. Vaje vašega spomina.

Billy Glisan s sodelovanjem Stephena Hochschulerja: *50 načinov lajšanja bolečin v hrbtenici.* 88 strani.

Glavni avtor je doktor fizioloških znanosti in sodelavec Inštituta za hrbtenico v Teksasu. Je avtor programa za rehabilitacijo hrbtenice tega inštituta. Drugi soavtor pa je doktor medicine in ortopedski kirurg, ki se je specializiral za hrbtenično kirurgijo. Je ustanovitelj

teksaškega inštituta za bolezni hrbtenice, ki uspešno pomaga tisočem bolnikom, ki jih mučijo tozadevne težave.
Bolečine v hrbtenici in težave z njo so v naši sodobni družbi zelo pogosta nadloga. Ta knjiga daje 50 praktičnih nasvetov, kako zmanjšati tveganje za poškodbe in kako olajšati manjše bolečine v hrbtenici. Kombinacija preventivnih ukrepov in enostavnih zdravil pomaga ohranjati zdravje hrbtenice ali lajšati bolečine, nikakor pa ne more nadomestiti zdravnika, terapevta ali drugega strokovnega medicinskega osebja.
Knjiga je razdeljena na šest poglavij. Poglavje z naslovom Spoznavajte svojo hrbtenico predstavi sestavne dele hrbtenice za boljše poznavanje povezave med ukrepi in tem, kako hrbtenica deluje. Naslednje poglavje Neposredno lajšanje bolečin opisuje nekaj enostavnih pripomočkov za takojšnje lajšanje bolečin v hrbtenici, vključno s pravilnimi ukrepi prve pomoči, z uporabo zdravil, vaj, masaže in svetuje, kdaj so bolečine dovolj resne, da je treba poiskati zdravnika. Poglavje Vaša vsakodnevna rutina obravnava tveganja v vsakdanjih dejavnostih oziroma preprečuje negativne učinke na hrbtenico. Poglavje z naslovom Vaje za vašo hrbtenico daje navodila za vaje, s pomočjo katerih se lahko obdržita moč in zdravje hrbtenice. V poglavju Telesna mehanika so opisane pravilne tehnike dviganja bremen in drugi vidiki telesne mehanike. Zadnje poglavje Drugi dejavniki življenjskega sloga razpravlja o vlogi prehrane in stresa ter o negi hrbtenice.
Obe knjigi sta koristen pripomoček pri vsakdanjih težavah in nadlogah ter zapolnjujeta vrzel v poljudnem zdravstvenovzgojnem slovstvu.

Zanimivo je vedeti

MEDICINCI 45 V NOVEM MESTU

Zlata Črepinko-Stropnik

Pred letom dni so se člani Društva Medicinci 45 sestali na 1. redni skupščini v štajerski metropoli. Letos jih je pomladansko sonce zvabilo v živo, utripajoče srce Dolenjske. In tako je na stežaj odprta dvorana farmacevtske tovarne Krka v Novem mestu sprejela 66 od 115 vpisanih članov društva. Pozdravil jih je namestnik generalnega direktorja Krke g. Slavko Plavec. Ni mu bilo težko s ponosom govoriti o razvoju Krke, ki je v 43 letih delovanja prerasla v vodilno farmacevtsko kemijsko industrijsko podjetje, uveljavljeno v Sloveniji, v Srednji in Vzhodni Evropi. Prestrukturirana v delniško družbo proizvaja Krka zdravila za humano in veterinarsko uporabo, kozmetične izdelke, ukvarja pa se tudi s termalno zdraviliško turistično dejavnostjo.
Danes je Krka predvsem izvozno usmerjeno podjetje, eno izmed najuspešnejših izvoznikov v državi. Tri četrtine proizvodov izvaža v več kot 70 držav. Usklajevanje proizvodnje uresničuje z normami Evropske Unije in ZDA. Njene naložbe v izgradnjo sodobnih obratov pa že ustrezajo zahtevam novega tisočletja. Vodstvo se zaveda, da sta varnost in učinkovitost proizvodov nujna za vstopanje na svetovna tržišča. Temu cilju je namenjeno tudi kontinuirano izobraževanje kadrov. V Sloveniji zaposluje Krka 3500 ljudi. V tujini ima 30 podjetij in predstavništev z 250 zaposlenimi, predvsem strokovnjaki s področja medicine in farmacije.
Dipl. ekon. ga. Janja Požar je s projekcijami na platnu podrobneje predstavila današnjo Krko, ki je v preteklosti usmerjala svoje interese proti vzhodu, sedaj pa prevladujejo težnje po širjenju v zahodno Evropo in na druge kontinente.
Prof. dr. Jože Drinovec je predstavljene dejavnosti dopolnil še s sponzorsko in donatorsko politiko, ki jo vodi Krka na področju štipendiranja, raziskovalnega dela (Krkine nagrade), kulturnih in humanitarnih programov, športnih prireditev in mnogih drugih akcij.
Predsednik društva dr. Zvonimir Hönigsman je povedal, da sponzorska dejavnost Krke omogoča tudi naši generaciji zdravnikov strokovna srečanja že polnih 30 let in tudi današnjo skupščino. V imenu društva se je zahvalil za dosedanjo materialno pomoč in vsestransko naklonjenost. G. Plavcu je izročil oljno sliko »Modri cvet«, umetniško delo ge. dr. Mire Cepudrove, ki je darovala sliko za ta namen. G. Plavec je nato poklonil ge. dr. Cepudrovi knjigo »Krka od izvira do izliva«.
Prof. dr. Aleksej Kansky je za dopolnilno izobraževanje strokovnjakov v Krki izročil g. Plavcu Zbornik 4. Kogejevih dnevov in Zbornik simpozija o lymski boreliozi. Za isti namen je prof. dr. Miroslav Kališnik, glavni urednik Medicinskega terminološkega slovarja, ki ga tudi sponzorira Krka, poklonil novo izdajo Pravopisa medicinskih izrazov, pri katerem je sodelovalo šest članov društva.
Temu uvodnemu delu je sledil formalni del skupščine z izvolitvijo delovnega predsedstva, poročili o opravljenem delu in sprejemanje delovnih programov. V tem letu ima društvo v načrtu izdajo suplementa ZV, za katerega zbira prispevke članov in drugih kolegov, ki so se odzvali vabilu k sodelovanju, nekateri pa so pristopili v društvo kot člani.
Že kmalu po ustanovitvi društva so nekateri kolegi iz drugih letnikov pokazali zanimanje za članstvo v društvu. Drugi pa so bili mnenja, da bi taka sestava članstva pomenila podvajanje Zdravniškega društva. Zato so na prejšnji skupščini sklenili, da bodo o predlogu še razpravljali in se odločili letos. Po temeljitem premisleku je upravni odbor ugotovil, da širjenje članstva z vpisovanjem kolegov, ki niso ravno »letnik 45«, a želijo koristno sodelovati, ni v nasprotju s statutom. Poleg tega pa se namen in cilji Zdravniškega društva in Društva Medicinci 45 ne izključujejo, ampak se dopolnjujejo, gledani iz različnih izhodišč. Zato je sodelovanje obeh društev lahko v obojestransko spodbudo. O usmeritvi naših interesov priča že dosedanje sodelovanje z Zdravniškim društvom, Zdravniškim vestnikom, Medicinsko fakulteto in drugimi ustanovami s podobnimi programi.
O zgodovini našega zdravstva je bilo že veliko napisanega, vendar se vedno najde še marsikaj zanimivega. Naše društvo se ne želi omejiti le na pretekle dogodke, ampak tekoče spremlja dogajanja v sedanjosti in jih želi tudi v prihodnje. Ne more nam biti namreč vseeno, kaj se dogaja z našim zdravstvom, ki smo ga ustvarjali 50 let. Zato se društvo ne sme zapirati vase, ampak mora sprejemati mlajše člane, ki bodo nadaljevali naše delo.
To je tudi eden od razlogov, zakaj želi naše društvo še naprej sodelovati z Medicinsko fakulteto in z drugimi ustanovami, saj poslanstvo in dolžnost zdravnika – prizadevanje za zdravje bolnikov – ne preneha z upokojitvijo. Spodbud za izboljšanje zdravstva pa tudi ni ravno v izobilju.
Društvo si prizadeva popestriti svojo dejavnost tudi s kulturnim programom. Lansko leto je pripravilo enodnevni izlet v Čateške Toplice z obiskom Kostanjevice, Pleterij in Otočca. Letos pa pripravlja etnografsko umetnostno ekskurzijo po Ziljski dolini z vodstvom dr. Marije Makarovič. Poleg tega se pripravlja na Zlato promocijo, ki bo v letu 2000. To bo slovesno obeležje 50-letnice promocije prvih študentov medicine, ki so začeli in končali študij na popolni slovenski medicinski fakulteti po 2. svetovni vojni. Ta dogodek bo prav gotovo vreden pozornosti v okviru celotne slovenske univerze.
Nadaljnje razprave, ki jih je usmerjala prim. dr. Marinka Kremžar, niso mogle obiti pritožb v dnevnem tisku zaradi razmer v zdravstvu, ki ne morejo zadovoljiti potreb bolnikov. Od mnogih problemov, ki se pojavljajo, so se dotaknili le nekaterih.
Vsi vemo, da če kdo potrebuje zdravniško pomoč, jo potrebuje takoj, ali pa je ne potrebuje. Dandanes pa se marsikomu večkrat upravičeno vsiljuje vprašanje, ali še velja obljuba, da je zdravnik dolžan pomagati bolnemu človeku v stiski. Ali sploh še velja Hipokratova prisega? S temi besedami je prim. dr. Maks Pen sprožil razpravo o razmerah v zdravstvu, ki je sledila.
Medicinske storitve so se zelo podražile po vsem svetu. Niti najbogatejše države ne zmorejo plačevati vseh stroškov brez sponzor-

jev. Zato si pomagajo na najrazličnejše načine, vendar nimajo povsod enakih možnosti. Za stike med bolniki in zdravstveno službo si ponekod pomagajo s prostovoljci. Tudi pri nas se že organizira na nekaterih področjih zdravstva vključevanje posameznikov v prostovoljno delo, vendar v večjem obsegu še ni uveljavljeno.

Naša zdravstvena služba je v zadnjih letih preživela veliko preizkušnjo. Brez hujših nalezljivih bolezni je šlo skozi Slovenijo 170.000 beguncev, največ iz Bosne. Vsiljuje se vprašanje, kakšen bi lahko bil rezultat te preizkušnje, če bi bilo to naše zdravstvo v zasebnih rokah.

V časopisih se stalno pojavljajo pritožbe zavarovancev na čakalno dobo v zdravstvenih ustanovah. Res je, da ima Zavod za zdravstveno zavarovanje (ZZZS) močan vpliv na delo v zdravstvu. Ko si je dovolil ukiniti nadure, so se čakalne dobe podaljšale. Še dodatno se podaljšujejo, če splošni zdravniki pri tem ne omejijo pošiljanja na specialistične preglede. Razen tega ZZZS plačuje samo storitve, izpolnjene po planu, ostale gredo v breme zdravstvenih ustanov in bolnikov. Ministrstvo za zdravstvo se mora čimprej odločiti, katere zdravstvene storitve sodijo v obseg splošnega zdravstvenega varstva, kar gre v breme skupnosti, in kaj sodi v zasebni sektor.

Delovno predsedstvo je po tej razpravi predlagalo, da bi imenovali odbor članov društva, ki bi na osnovi dokumentiranih pritožb zavarovancev oblikoval okvirni pogram, kako izboljšati razmere v zdravstvu, in ga posredoval ministrstvu in ZZZS.

Ker je dosedanjemu upravnemu odboru potekel mandat, so sledile volitve. Ponovno je bil izvoljen dosedanji odbor, ki bo nadaljeval z začetim delom.

Po zaključku skupščine so udeleženci odšli na skupno kosilo v hotel Krka. Preostanek dneva so popestrili z obiskom arheološkega muzeja, ki je vreden ogleda. Bogate najdbe iz starejše železne dobe na ozemlju Novega mesta in okolice pričajo, da je bilo v 7. do 5. stoletju pred našim štetjem tukaj pomembno evropsko središče halštatske kulture. Zanimiv je bil tudi ogled poznogotske Kapiteljske cerkve, ki je sama kulturnozgodovinski spomenik, s Tintorettovo oltarno sliko sv. Nikolaja in kripto. Preden so zapustili Novo mesto, so si ogledali še galerijo z obsežnim in dragocenim opusom slikarske poti Božidarja Jakca v Jakčevem domu.

Novo mesto so zapuščali z dobrim občutkom, da so društveno organizacijsko obveznost dopolnili in polepšali z zanimivim kulturnim programom in tovariškim srečanjem. Takšna srečanja so za upokojene zdravnike prijetna tudi zaradi priložnosti za izmenjavo mnenj med kolegi, ki pridejo iz različnega okolja.

Kot že večkrat je Krka tudi tokrat pripravila in omogočila nepozabno srečanje, ki so ga sklenili na Otočcu, kjer so se ustavili v čudovitem grajskem parku za čim lepše slovo od kolegov in prijateljev.

Pogovori z bralci

BOLNIŠNICA IZOLA KONČNO POD SKUPNO STREHO

Drago Kocjančič

Za Splošno bolnišnico Izola je znan prilastek »bolnišnica na razdalji 35 km«. To izvira še iz obdobja po priključitvi »cone B« k Jugoslaviji. Namesto tržaške bolnišnice, kjer so se dotlej zdravili bolniki iz Slovenske Istre, je bilo treba organizirati bolnišnične kapacitete na tem območju. Tako so se v le delno primernih objektih od Ankarana do Pirana na hitro organizirali razni »začasni« bolnišnični oddelki. Hkrati pa je bilo že oktobra 1954 sklenjeno, da je takoj pristopiti k izgradnji nove splošne bolnišnice za celotno južnoprimorsko območje. Po tem, ko so bili v letih 1958 do 1962 (tedaj je bil ravnatelj Splošne bolnice Koper pediater dr. Branko Šalamun) izdelani vsi izvedbeni projekti in izvršena vsa pripravljalna dela za izgradnjo bolnišnice v Škocjanu pri Kopru, vključno z že podpisano gradbeno pogodbo, je »državna reforma« ustavila izgradnjo.

Po večletnem zastoju so v sedemdesetih letih ponovno oživela prizadevanja za izgradnjo nove splošne bolnišnice. Da bi se priprave izvajale bolj strokovno in intenzivno, je bil leta 1972 ustanovljen Sklad za izgradnjo splošne bolnišnice Koper. Na podlagi študij in mučnih razprav o možni lokaciji so se odločili za lokacijo v Izoli. Temu je sledil javni natečaj za izbor projektanta, na katerem je bil izbran arhitekt Stanko Kristl. Takoj nato je stekla izdelava izvedbenih projektov; v tej fazi je bila postavljena definitivna lokacija objekta. Glede na odmik objekta na vrh hriba je bilo treba najprej zgraditi 1,5 km dolgo dostopno cesto. Na njej je prvi buldožer zaoral 5. 10. 1974, temeljni kamen za objekt bolnišnice pa je bil položen na svečani otvoritvi 28. 11. 1974.

Idejni projekt je predvidel izgradnjo bolnišnice s 630 posteljami na 38.000 m^2. Finančno je bil to prevelik zalogaj, da bi zmogli zgraditi celoten načrtovani objekt hkrati. Zato se je tedanji upravni odbor Sklada za izgradnjo splošne bolnišnice odločil, da se bo gradnja izvajala v dveh večjih etapah, znotraj teh pa se bodo v manjših fazah po določeni prioriteti usposabljali prostori za posamezne oddelke. Tako smo 3. 7. 1975 začeli z izgradnjo 1. etape objekta površine 18.000 m^2.

Predvsem zaradi finančnih težav je gradnja samo 1. faze, v kateri smo funkcionalno usposobili 14.080m^2, trajala celih sedem let. Tako se je 27. 11. 1982 v novi objekt prvi preselil kirurški oddelek iz docela dotrajanih prostorov v mestu Izola. Čez dve leti smo dogradili in opremili še 4000 m^2, v katere se je preselil internistični oddelek iz Ankarana. S sredstvi iz prodaje dela izpraznjenih objektov v Ankaranu smo naslednje leto dogradili še koronarno enoto in dializni oddelek.

S finančnimi sredstvi za izgradnjo so bile stalne težave in temu smo morali prilagoditi tempo del. Konec leta 1985 pa je financiranje povsem ugasnilo. Tedanji Zdravstveni center Koper je predlagal uvedbo samoprispevka, vendar predlog ni bil sprejet. Intenzivnejši izgradnji smo se morali odreči in nadaljevati z majhnimi koraki. Prvega je naredila Splošna banka Koper, ki nam je po zaključnem računu za leto 1985 dala del sredstev za nadaljevanje izgradnje. Nato smo SGP »Gorica« prodali še ostale objekte in zemljišča v Ankaranu in tako zasnovali gradnjo 3. faze, v kateri smo zgradili drugi diagnostično-poliklinični objekt v skupni površini 3600 m^2 (centralni laboratorij, RTG in poliklinične ambulante piranskih oddelkov). Po preselitvi RTG iz začasnih prostorov na novo lokacijo smo preuredili še severni del pritlične hospitalne etaže in vanjo septembra 1988 preselili oddelke iz piranske bolnišnice – okulistični, ORL in infekcijski oddelek. Nato smo z lastnimi sredstvi bolnišnice uredili še začasne prostore za radioizotopni laboratorij v okviru RTG etaže (spomladi 1989). S tem smo v celoti zaključili izgradnjo 1. etape (v treh fazah smo usposobili 21.675 m^2).

S prodajo objektov v Ankaranu smo se obvezali, da bomo do konca 1989 izpraznili vse objekte, med drugim tudi kuhinjo. Zato je bilo treba takoj nadaljevati z njeno izgradnjo. Mislili smo, da bomo denar za to dobili s prodajo objektov piranske bolnišnice, toda zaradi nerazumevanja piranske občine nam to ni uspelo. Kljub vsem tem težavam smo z drugimi finančnimi viri zmogli dograditi in opremiti (junija 1990) tudi kuhinjo s površino 1800 m^2. Še isto leto smo s finančnimi sredstvi treh obalnih občin začeli z izgradnjo gradbene konstrukcije objekta 2. etape v skupni površini 10.500 m^2. Ker tudi v tem obdobju nismo uspeli dobiti načrtovanih finančnih sredstev od prodaje objektov bolnišnice v Piranu, se je gradnja zavlekla za nekaj let. Šele konec leta 1993 smo z izredno dotacijo občin Koper in Piran ter sredstvi Ministrstva za zdravstvo (za streho in zaporo fasade) končali grobo izgradnjo tega objekta.

Med zgoraj navedeno gradnjo pa se je leta 1991 ponovno zaostril problem adaptacije starega objekta Oddelka za transfuzijo krvi v Izoli. Da ne bi vlagali sredstev v neprimeren in od bolnišnice dislociran objekt, smo se odločili urediti nov oddelek v že izgrajenih prostorih pod novo kuhinjo. S sredstvi Ministrstva za zdravstvo in sredstvi od prodaje starega objekta transfuzijske postaje v Izoli ter delno tudi lastnimi sredstvi smo jeseni 1992 začeli z izgradnjo in objekt površine 500 m^2 predali v uporabo že junija 1993.

Konec leta 1993, ko so se zaključevala dela na izgradnji skeleta, strehe in fasade objekta 2. etape, smo Ministrstvu za zdravstvo predložili program t. i. »preselitvene« faze, v kateri naj bi dogradili in funkcionalno usposobili ca. 6600 m^2 površin za potrebe koprskih oddelkov (ginekološko-porodniški in otroški oddelek ter pato-citološki laboratorij) z ocenjeno vrednostjo 1540 mio SIT. Na podlagi te ocene in nadaljnjih usklajevanj s predstavniki Ministrstva za zdravstvo oz. njegovega Odbora za investicije v zdravstvu so bila z Zakonom o investicijah v javne zdravstvene zavode za obdobje 1994–1999 zagotovljena sredstva za izgradnjo »preselitvene« faze v višini 891 mio SIT.

Takoj za tem smo začeli s konkretnimi postopki za realizacijo te velike investicije. S projektnima organizacijama Invest biro Koper (za novi objekt) in Medicoengineering Ljubljana (preureditev starega objekta) smo junija 1994 sklenili pogodbo za izdelavo razpisne dokumentacije. Čez en mesec pa smo že objavili javni razpis za izbor izvajalca, na podlagi katerega je bil jeseni 1994 izbran GIP »Stavbenik« Koper, s katerim je bila 28. 11. 1994 podpisana splošna gradbena pogodba za kompletni projektni in izvajalski inženiring za pogodbeno vrednost 750 mio SIT. Proti koncu izvajanja gradbenih del je bil v juliju 1996 izvršen tudi javni razpis za dobavitelja pohištvene in medicinske opreme, na katerem je bila izbrana firma Mollier iz Celja, ki je dobavila in zmontirala vso pogodbeno opremo v roku treh mesecev, tj. do 31. 3. 1997.

V 22 letih gradnje smo dogradili in opremili 28.000 m^2 bolnišničnih površin v skupni vrednosti ca. 10 milijard SIT. V drugačnih pogojih oz. če bi bila vsa finančna sredstva zagotovljena ob začetku gradnje, bi taka gradnja trajala le nekaj let. Žal pa smo morali tempo gradnje stalno prilagajati finančnim možnostim. Sicer pa je sedaj najpomembneje, da je bil zastavljeni cilj »združiti vse bolnišnične oddelke od Ankarana do Pirana na eni lokaciji« končno le dosežen.

Zdravniški vestnik pred 60 leti

ŠTEVILKA 8–9/1937

Anton Prijatelj

Dvojna številka 8–9 Zdravniškega vestnika, strokovnega glasila zdravništva v Dravski banovini, je izšla avgusta–septembra. Uredništvo in uprava: dr. R. Neubauer – Golnik.

- Dr. Bogdan Brecelj: Kolaps v športu
- Dr. ing. Ladislav Klinc: Nova klinična metoda določitve celokupnega acetona v urinu
- Dr. Igor Tavčar: Ukluzova bolezen kot alergoza – smeri tozadevne moderne terapije. Nadaljevanje in konec
- Dr. Josip Vrtovec: Prispevek k epidemiologiji trebušnega legarja
- Dr. Rudolf Leskovar: Balneoterapija v Rogaški Slatini pred 250 leti v luči sodobne znanosti. Predavanje o priliki obiska graških zdravnikov v Rog. Slatini 5. junija 1937
- Dr. Franjo Smerdu: Zdravniki in časnikarji. (Nekaj misli ob časnikarski razstavi)
- Dr. Mirko Černič: Naše zdravniško poslanstvo in novi stanovski red

O zdravnikih in zdravilstvu

Sloves zdravnika so ozdravljeni bolniki.

Paracelsus

Ne računaj na hvaležnost; kar se ti posreči, to bodo prezrli, kar se ti ponesreči, o tem bodo govorili.

W. Klausmann

Štiri vrste zdravnikov so:
1. Ti, ki imajo malo zdravniškega pogleda in malo znanosti. Prava muka je to.
2. Ti, ki imajo malo zdravniškega pogleda, pač pa mnogo znanosti. Muka je še večja, ker je njihova samozavest večinoma ogromna.
3. Ti, ki imajo pravi zdravniški pogled in malo znanosti. Uspešno delajo, toda ovira jih večinoma negotovost.
4. Zdravniki z dobrim zdravniškim pogledom in temeljitim obvladovanjem znanosti. To je blagoslovljeno sigurno delo.
Pravilno je: ločiti medicinsko vedo od zdravniške umetnosti. Lahko se je kdo naučil iz knjig neskončno mnogo medicinskega znanja, tudi tehniko pri uporabi svojega znanja je iz knjig lahko utisnil svojemu spominu, mnogo medicinskega bo potem vedel in znal, toda s tem še nikakor ni postal zdravnik.

Teodor Billroth

Posamezni primeri – pravila – umetnost – posamezni primeri. To je veliki krog.

G. Much, Hippokrates der Grosse

Eksaktna znanost in zdravniška umetnost si ne stojita sovražno nasproti, nobeni od njiju ne bo usojena izključna zmaga. Ideal ostane njuna harmonična zveza.

G. Donzellini

Zdravniški poklic daje svojemu nosilcu gotovo oblast, ki pomeni, če jo zlorablja, hudo nevarnost za družbo. Na nobenem drugem področju nimata nevednost in lakomnost tako usodnih posledic kakor prav v medicini.

Sigerist, Antike Heilkunde

Kratko je življenje, dolgotrajna pa umetnost; bežna je ugodna prilika, poskus ni brez nevarnosti in težavna je sodba. Potrebno je, da stori zdravnik vse, ne le kar zahteva slučaj, temveč tudi bolnik sam in njegova okolica, pri čemer ne smemo pustiti vnemar niti vplivov zunanjega sveta.

Hippokrates, aforizmi

Iz vsakega zdravega lahko napraviš bolnika; samo ponavljati mu moraš, da je bolan.

Po Sieku

Medicine se zares nikdar ne izučimo in ta ni zdravnik, ki je vsak dan na novo ne študira.

Indijska medicina, po H. Muchu

Tajna osebnosti ni v glavnem, vse drugo prevpijočem prevladovanju enega določenega zvoka, temveč v zmesi, v preobilju zvokov, vezanih v akord.

Buttersack, Aerztliche Weisheit

Mene pusti misel na smrt popolnoma mirnega; zakaj trdno sem prepričan, da je naš duh nekaj čisto nerazrušljivega, nekaj, kar deluje naprej od večnosti do večnosti; podoben je soncu, ki zahaja samo našim zemeljskim očem, ki pa nikdar ne zaide, temveč sveti neprestano.

Goethe 1824 napram Eckermannu

Kaj pa je vse zdravilstvo, če ne iskanje poti, kako bi mogli podpirati one zdravilne moči, ki v telesu delujejo.

W. Klausmann (Das Ärztebüchlein)

Zdravnik naj bo vzor vzvišenega človeštva. *H. Much*

Zdravnik bodi človek, ki se ne boji odgovornosti, skratka – osebnost.
Pomni: brez tople ljubezni do ljudi, brez dobrotljivega srca, si lahko odličen kirurg, nikdar pa dober zdravnik.
Bodi zdravnik, ne sodnik.
Bodi zdravnik, ne propovédnik. *W. Klausmann*

S pravico so trdili, da dobrega kirurga manj spoznamo po tem, kar operira kot po tem, kar ne operira.
E. Liek

Quod medicamenta non sanat, verbum sanat.
Star pregovor

Kdor tuje rane obvezuje, lastnih pozabi.
Zdravnik Karl Theodor, vojvoda bavarski

Pravi zdravnik se nikoli ne izuči. *Klausmann*

Samo ta je pravi zdravnik, ki je obenem pravi duhoven in pravi umetnik.
H. Much

Zdravnik naj bo: umetnik, rokodelec, znanstvenik, toda prav pred vsem naj bo človek.
Po E. Lieku

Operirati smemo samo, ako imamo vsaj nekaj upanja na uspeh; brez tega upanja operirati se pravi: prostituirati prelepo umetnost in znanost kirurgije, osumiti jo pri laikih in kolegih. Kje pa je mera, po kateri lahko upamo na uspeh? V neumornem študiju naše znanosti, v ostri kritiki naših lastnih in tujih opazovanj, v najnatančnejši preiskavi vsakega poedinega primera, v kritični rabi naše skušnje.
Billroth

Iz »Das Aerztebüchlein« od W. Klausmann. Založba: G. Thieme – Leipzig.

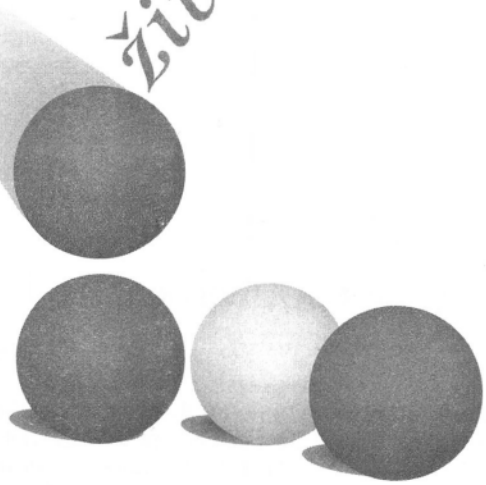
Pentilin® forte

SAMO DVAKRAT NA DAN!

retardne tablete po 600 mg pentoksifilina

- ***hemoreološko in antitrombocitno zdravljenje periferne arterijske obliteracijske bolezni***
- ***podaljšuje hojo brez bolečin***
- ***izboljšuje periferno cirkulacijo na kritičnih mestih***

Živahna misel in korak



Skrajšano navodilo

Indikacije: *Motnje perifernega arterijskega obtoka in mikrocirkulacije zaradi ateroskleroze, sladkorne bolezni in vnetij (intermitentna klavdikacija, diabetična makro- in mikroangiopatija, endangiitis obliterans); distrofične motnje (potrombotični sindrom, varikozni ulkus na goleni, gangrena, zmrzline); angionevropatije (redkeje); motnje možganskega krvnega obtoka (prehodni ishemični napadi, posledice možganske tromboze in krvavitve ter kronična cerebrovaskularna insuficienca) in motnje prekrvljenosti očesa (akutna in kronična stanja zaradi nezadostnega krvnega obtoka v mrežnici).*

Doziranje in uporaba

PERORALNO		
Pentilin, tablete po 400 mg		*3-krat 1 tableta na dan*
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PARENTERALNO		
i.v. infuzija	*100—400 mg v 250—500 ml infuzijske raztopine*	*90—180 minut*
i.v. injekcija	*100 mg/dan*	*5 minut*

Bolniki s hudo ledvično okvaro (kreatininski očistek manjši kot 10 ml/min; serumski kreatinin večji kot 9 mg/100 ml ali 800 µmol/l) smejo dobiti le 50 do 70 % običajne doze. ***Kontraindikacije:*** *Preobčutljivost za Pentilin in podobna zdravila oziroma snovi iz skupine ksantinskih derivatov, kot so teofilin, kofein, holin teofilinat, aminofilin ali teobromin. Pentilina ne dajemo ob akutnem srčnem infarktu, pri porfiriji, zelo močnih krvavitvah in bolezenskih stanjih z veliko nevarnostjo krvavitev. Za parenteralno dajanje so relativne kontraindikacije huda koronarna ali možganska ateroskleroza ob povečanem krvnem tlaku in hude motnje srčnega ritma.* ***Stranski učinki:*** *Stranski učinki so zelo redki. Najpogosteje se pojavljajo prebavne motnje (tiščanje v žlički, slabost, bruhanje, napenjanje), redkeje pa rdečica obraza, glavobol, omotica, nespečnost, tremor, bolečina v prsih ter neredno ali močno utripanje srca. Pri daljšem zdravljenju priporočamo pogostejše kontrole krvnega sladkorja, protrombinskega časa, levkocitov in trombocitov.*
Oprema: *20 retardnih tablet po 400 mg in 600 mg, 5 ampul po 100 mg/5 ml.*

Podrobnejše informacije so na voljo pri proizvajalcu.

KRKA
SLOVENIJA

23. Annual Scientific Meeting of the European Underwater and Baromedical Society

on

Diving and Hyperbaric Medicine

EUBS 97

Bled, Slovenia
September 22 - 26, 1997

PROGRAMME & ABSTRACTS

Editors:
Igor B. Mekjavić
Ola Eiken
Michael J. Tipton

Welcome Address

(on the occasion of the Opening Ceremony, XXIII Annual Scientific Meeting of the European Underwater and Baromedical Society, Bled, Slovenia)

Dr. L. Marinček
Minister of Science and Technology, Republic of Slovenia

Dear ladies and gentleman, dear guests from abroad.

Allow me to welcome you here at Bled on behalf of the Ministry of Science and Technology and my own behalf.
We appreciate indeed that Slovenia, actually Dr. Mekjavic and his colleagues, were chosen by the European Underwater and Baromedical Society to organize this meeting. We expect the outcomes and the messages from this meeting with great interest. Although my professional expertise covers quite a different field of science, the available information has convinced me about the broad importance of baromedicine, either in terms of medical research or as a much needed service, which Slovenia has to regulate according to the standards in the European Union and NATO. In this sense I am satisfied that the Ministry of Science and Technology has supported baromedical research in the past years and will continue to support it in the future.
International scientific cooperation and connections are of primary importance for Slovenian research policy. Slovenia is a small country, characterized by scarce human and economical potential. Therefore, it is a very important task for our scientists and other professionals to keep up contacts with the development of science and technology and other professional skills worldwide, especially if they are of importance for the foreseen development of Slovenia, including international alliances. We are committed therefore to support all activities, which will result in the improvement of the reputation and relevance of the research of our research community in Slovenia, and which will contribute to the treasury of knowledge of mankind.
I believe that this meeting is an excellent opportunity to meet colleagues, get aquainted with the state of the art, discuss the problems and in this way find new solutions and achieve deeper understanding.
Therefore, I wish you a successful work during the following days, to strengthen old and establish new personal relationships. I wish you plenty of new ideas for your work in the future and successful cooperation for the mutual benefit.
At the end, I sincerely hope that you will spend a very pleasant time here at Bled and bring nice impressions back home.

Tit Turnšek
Minister of Defense, Republic of Slovenia

Dear participants of the EUBS '97 Congress,

I was very happy to hear that you have decided to organize such an important scientific meeting for underwater and hyperbaric medicine in Slovenia.
The Ministry of Defense is aware of the significance of underwater and hyerbaric medicine and supports the development of this branch of science in the Republic of Slovenia as well. An effective defense system for the Republic of Slovenia requires and demands an effective coastal defense, capable of being included into systems of collective defense and security within the European integration framework. The system of national health care, especially underwater and hyperbaric medicine, plays an important role in the provision of an effective coastal defense. This medicine, which is prescribed in regulations and carried out throughout the world, includes the provision of an equivalent level of health care for all participants in coastal defense activities.
The extreme physical and psychological pressures that occur during diving have brougth about the development of a special branch of medicine, that deals with the analysis of the changes that take place in the human body under water. Today, hyperbaric medicine is a recognized, important branch of medicine throughout the world. Treatment in pressure chambers is essential in order to treat a number of health problems that may occur during diving. Scientific research, which confirms the success of treatment in pressure chambers for a variety of medical conditions, are also being carried out. The use of pressure chamber oxygenation for treatment of some cases of poisoning, infection, burns, disturbances in blood circulation and other diseases has been introduced throughout the world.
Pressure chambers provide possibilities for research, testing and the determination of the psychophysical abilities of amateur and professional divers, as well as the testing of underwater equipment. The Ministry of Defense has cooperated successfully with local experts and institutions in the field of hyperbaric medicine for several years. Our wish is to strengthen and extend this cooperation in the future, as well as to immediately integrate the findings of modern underwater and hyperbaric medicine into our daily practice.
I am convinced that the findings and conclusions of this congress will contribute significantly to the recogntion of the importance of hyperbaric medicine in the Republic of Slovenia as well. They will also provide effective health care for everyone involved in diving, either professionally or as an amateur.
The Ministry of Defense will continue to support these efforts and will cooperate willingly in the development of underwater and hyperbaric medicine in the Republic of Slovenia.
In conclusion, allow me to wish all of the conference participants every success in their research and a pleasant stay in Slovenia.

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The 23rd Annual Scientific meeting of the European Underwater and Baromedical Society is hosted jointly by the Institute of Physiology (Faculty of Medicine, University of Ljubljana), National Institute of Biology and the Department of Automatics, Cybernetics and Robotics (Institute Jožef Stefan) in collaboration with:

- Ministry of Science and Technology *(Slovenia)*
- Slovene Science Foundation
- University Clinical Centre, Ljubljana
- Slovene Physiological Society
- Slovenian Aeronautical & Underwater Medical Society
- Divers Alert Network (DAN) - Europe / Slovenia
- School of Physiotherapy
- Biomed d.o.o.

We are honoured that the European Underwater and Baromedical Society has delegated Slovenia as the site for this year's Annual Scientific Meeting. Organising a meeting, such as EUBS 97, in a country where Diving and Hyperbaric Medicine is neither recognised nor officially approved was not a promising proposition. We are therefore grateful to the EUBS membership, and particularly to the Executive Committee, for their support and trust throughout the organisation of this year's meeting. We are indebted to the organisations and institutions listed above for their contributions and support. We wish to particularly acknowledge the assistance of the Ministry of Science and Technology. Their continued support and guidance has been instrumental in the development of Diving and Hyperbaric Medicine in Slovenia. They have not only assisted in the establishment of the only Baromedical Laboratory in Slovenia, provided funds for research projects, but have also provided a generous grant for the publication of the Abstracts and Proceedings.

Finally, we are indebted to all the EUBS 97 participants. Your participation at the meeting provides much needed encouragement and support for our continued effort to ensure that Diving and Hyperbaric Medicine recieves official recognition and approval in Slovenia in the near future.

Igor B. Mekjavić
Secretary General, EUBS 97

Pre-Congress Course on

CLINICAL HYPERBARIC MEDICINE

September 16–19, 1997

Course directors:

Eric P. Kindwall
Igor B. Mekjavić
Žare Finderle

Accreditation:

The Undersea & Hyperbaric Medicine Society *(U.S.A.)*, which is accredited by the ACCME to sponsor continuing medical education (CME) for physicians, has approved this course for 40 CME credits. Participants will receive CME certificates upon completion of the course. The course is also approved by the Slovene Medical Association for continuing medical education.

TUESDAY, September 16, 1997

8:00 • Course overview
8:15 • History of Hyperbaric Oxygen (HBO) Therapy
• The Role of the European Underwater Baromedical Society (EUBS) and the Undersea Hyperbaric Medicine Society (UHMS)
• The European Consensus Committee on Hyperbaric Medicine
9:30 Physics of Diving
10:30 *Break*
11:00 Hyperbaric Physiology
12:00 *Lunch*
13:00 Decompression Sickness
14:00 Decompression Tables
15:00 *Break*
15:30 Design of Hyperbaric Facilites
16:30 Ancillary equipment
17:30 Medical evaluation for diving
18:00 Sham treatments & Assign Coursework
19:00 *Dinner*

WEDNESDAY, September 17, 1997

8:00 Oxygen Toxicity
9:00 Risks and side effects of HBO
10:00 Hyperbaric Fire Control
10:30 *Break*
11:00 Contraindications to HBO
12:00 *Lunch*
13:00 Barotrauma
14:00 Air Embolism
15:00 *Break*
15:30 Carbon Monoxide Poisioning
Cyanide Poisoning
Hydrogen Sulfide Poisoning
Carbon Tetrachloride Poisoning
16:30 Mechanisms of Wound Healing
17:30 Osteomyelitis
18:00 Sham Treatments & Coursework (assignment & review)
19:00 *Dinner*

THURSDAY, September 18, 1997

8:00 Trauma, Crush Injury & Compartment Syndrome
9:00 Wound Infections and Sepsis
10:00 *Break*
10:30 Management of Chronic Wounds
11:30 Gas Gangrene
12:00 *Lunch*
13:00 Drugs and HBO

14:00 Radionecrosis
15:00 *Break*
15:30 Burns
16:30 Exceptional Blood Loss Anemia and Bowel Disorders
17:00 Cerebral Edema, Spinal Cord Injury, Frostbite, Decubitus Ulcers and Other Investigative Areas
18:00 Sham Treatments & Coursework (assignment & review)
19:00 *Dinner*

FRIDAY, September 19, 1997

8:00 Demonstration of operation of monoplace chamber
9:00 Demonstration of operation of multiplace chamber
10:00 *Break*
10:30 Transcutaneous PO_2 monitoring
11:30 Sudden Deafness
12:30 *Lunch*
13:30 • Hands-on Chamber Time
• Demonstration of Transcutaneous PO_2 monitoring
15:30 *Break*
16:00 Insurance and Reimbursement Considerations
17:00 Economics of Chamber Operations
18:00 Professional and Educational Requirements for the Staff of a Hyperbaric Facility
19:00 *Dinner*

SATURDAY, September 20, 1997

The self-assessment examination is scheduled later in the day, to allow participants to attend the Trinational (Switzerland-Austria-Slovenia) Satellite Meeting on Diving and Hyperbaric Medicine.
17:00 Self-Assessment Examination
19:00 Review of Final Examination and Course Critique
20:00 *Dinner*

SATURDAY, September 20, 1997

Pre-Congress

TRINATIONAL (CH-A-SLO) SATELLITE MEETING ON HBO AND DIVING MEDICINE

Organising Committee:

I. B. Mekjavić & B. Brodnik *(SLO)*
G.B. Friehs & C. Mader *(A)*
P. Knessl & J. Wendling *(CH)*

Time	Abstract number	
		INTRODUCTION **Moderators: I.B. Mekjavić & B. Brodnik** *(SLO)*
8:00		**Registration**
8:45		**Welcome address**
9:00	70	**Trials and tribulations of diving and hyperbaric medicine in Slovenia.** I. B. Mekjavić & B. Brodnik *(SLO)*
9:15	71	**Development of diving medicine and hyperbaric oxygenation in Austria.** G. B. Friehs & H. Kovac *(A)*
9:30	72	**Diving and hyperbaric medicine in Switzerland.** P. Knessl *(CH)*
		HBO **Moderators: G. B. Friehs** *(A)* **& L. Travnik** *(SLO)*
9:50	73	**Clinical application of hyperbaric oxygen.** J. Schmutz, W. Müller, K. W. Grätz & J. Vavrina *(CH)*
10:10	74	**CO intoxication and HBO** A. Offer *(A)*
10:30	75	**Treatment of frostbite injury with HBO** F. Bajrović *(SLO)*, M. J. Tipton *(UK)* & I. B. Mekjavić *(SLO)*
10:50		**Discussion**
11:00		*Coffee break*
		FITNESS TO DIVE **Moderators: J. Schmutz** *(CH)* **& E. Schenk** *(A)*
11:30	76	**Diving with diabetes** E. Schenk *(A)*
11:50	77	**Diving and cardiological problems** E. Schenk *(A)*
12:10	78	*Standards for fitness to dive* J. Wendling *(CH)*
12:30		**Discussion**
12:40		*Lunch*
		DIVING RELATED PROBLEMS **Moderators: C. Mader** *(A)* **& J. Wendling** *(CH)*
13:40	79	**Dehydration as a possible cause of decompression sickness** F. Dietzel, S. Koegel, F. M. Smolle-Jüttner, H. Kovac & G. B. Friehs *(A)*
14:00	80	**Evaluation of decompression stress with tear film bubbles** P. Jaki, P. Dovšak *(SLO)*, E. P. Kindwall *(USA)* & I. B. Mekjavić *(SLO)*
14:20	81	**Pulmonary edema in divers** D. Blickenstorfer *(CH)*
14:40	82	**Nitrogen narcosis potentiates hypothermia** I. B. Mekjavić *(SLO)* & O. Eiken *(S)*
15:00		**Discussion**
15:10		*Coffee Break*

RECREATIONAL DIVING TRENDS
Moderators: P. Knessl *(CH)* **& Ž. Finderle** *(SLO)*

1540 83 **Diving for the handicapped.**
W. Beuster *(A)*
1600 84 **Should children dive?**
M. Kraus *(CH)*
1620 85 **Diving emergencies in remote areas.**
J. Wendling *(CH)*
1640 **Discussion**

16:50 - 17:10 **Closure and final statements**

19:00 *Dinner*

SUNDAY, September 21, 1997

Pre-Congress

TECHNICAL DIVING SYMPOSIUM

Organising Committee:

R. W. Hamilton *(U.S.A.)* **& J. P. Imbert** *(France)*
J. Wenzel *(Germany)* **& I. B. Mekjavić** *(Slovenia)*

9:00–9:15 **Welcome address**
E. Kobal, Director, Slovenian Science Foundation

MORNING SESSION
Chairperson: J. Wenzel (Germany)

- **History of technical diving.**
  R. W. Hamilton *(U.S.A.)*
- **Overview of technical diving in Europe**
  J. P. Imbert *(France)*
- **BSAC, enriched air (Nitrox), and technical diving**
  Chris Allen *(United Kingdom)*
- **Fontaine de Vaucluse**
  F. Badier *(France)*
- **Technology of Doux de Coly**
  Olivier Isler (with J. P. Imbert) *(Switzerland & France)*

AFTERNOON SESSION
Chairperson: I. B. Mekjavić (Slovenia)

- **Technical diving decompression**
  J. P. Imbert *(France)*
- **The DCAP approach**
  R. W. Hamilton *(U.S.A.)*
- **Saturation procedures for technical diving**
  A. O. Brubakk *(Norway)*
- **Oxygen toxicity**
  Y. Melamed *(Israel)*
- **The practice of oxygen measurement for divers**
  J. S. Lamb *(United Kingdom)*
- **Rebreather for recreational diving**
  C. Schult *(Germany)*
- **Diving at Altitude**
  E. Murat *(Turkey)*

Hosted by:
- **Marine Biology Station Piran, National Institute of Biology**
- **BIOMED d.o.o.**

Supported by:
- **The Slovenian Science Foundation**
- **Divers Alert Network (DAN) - Europe / Slovenia**
- **BAROTECH d.n.o.**
- **Slovenian Diving Federation**

ANNUAL SCIENTIFIC MEETING OF THE

EUROPEAN UNDERWATER & BAROMEDICAL SOCIETY

ON DIVING AND HYPERBARIC MEDICINE

EUBS 97

Organising Committee:

Igor B. Mekjavić, *Secretary General (SLO)*
O. Eiken *(S)* **M.J. Tipton** *(U.K.)*
E. P. Kindwall *(U.S.A.)* **R. W. Hamilton** *(U.S.A.)*
Ž. Finderle *(SLO)* **V. Starc** *(SLO)*

MONDAY, September 22, 1997

Time	Abstract number	
8:00		**Registration**
9:00	1	**Welcome Address** L. Marinček Minister for Science and Technology *(Slovenia)*
		HYPERBARIC OXYGEN: experimental studies **Moderators: E. P. Kindwall** *(U.S.A.)* **& G. B. Friehs** *(Austria)*
9:15	2	**The effect of repetitive exposures to hyperbaric oxygen on TNFα mRNA, TNF-α secretion & mononuclear subsets in the spleen.** Bitterman N., M.A. Rahat, D. Zisman, H. Bitterman, A. Kinarty & N. Lahat *(Israel)*
9:30	3	**Differences in regional endothelium dependent control of vascular tone may underlie HBO induced redistribution of blood flow in hemorrhagic shock.** Bitterman H., H. Levy, R. Goldstein, N. Bitterman & V. Brod *(Israel)*
9:45	4	**Effects of nitric oxide synthase inhibition upon neural transmission in the dentate area during hyperbaric oxygen exposure.** Jellestad F. K. & F. A. S. Hanssen *(Norway)*
10:00	5	**Hyperbaric oxygen therapy for thrombotic complications in patients with antiphospholipid antibodies.** Nogay H.A. & M. Çimsit *(Turkey)*
10:15		*Coffee break*
		HYPERBARIC TECHNOLOGY **Moderators: J. Cl. Pechon** *(France)* **& J. Lenarčič** *(Slovenia)*
10:45	6	**Interior design of hyperbaric living chambers.** Bolstad G., H. Ryvarden & B. Benum *(Norway)*
11:00	7	**Real cause and process of a chamber combustion mishap.** Takahashi H. *(Japan)*
11:15	8	**Development of prototype Hyperbaric Environmental Control System (HECS) for Nitrox saturation diving system.** Okamoto M. & H. Yamagichi *(Japan)*
11:30	9	**A new airlock system for a tunnel boring machine (TBM).** Le Pechon J. C., L. Boulestreau & E. Larue (*France)*
11:45		*Lunch*
		DIVING MEDICINE - I **Moderators: P. Germonpré** *(Belgium)* **& M. Hadravsky** *(Czech Republic)*
13:15	10	**Labyrinthine hydrops as a cause of cochleo-vestibular problems after SCUBA diving: a »new« diving syndrome.** Vander Eecken P. & P. Germonpre *(Belgium)*
13:30	11	**Decompression sickness during a breath-hold dive: A case report.** Arance, I. G., G. Garcia-Franco & J. D. Gonzalez Aquino *(Spain)*
13:45	12	**Diving profiles and decompression risk in occupational SCUBA divers.** Nashimoto I., T. Mochizuki & Y. Hagihara *(Japan)*
14:00	13	**Testicle implants - diving exposure.** Peusch-Dreyer D., J. Ahrens, K. H. Dreyer & K. H. Männche (*Germany)*
14:15		*Break*

DIVING MEDICINE - II
Moderators: A. Marroni *(Italy)* **& Z. Sićko** *(Poland)*

14:30 14 **Dive history: a predictive factor in relapse after treatment of decompression illness.**
Stephenson R. N., D. J. Godden, P. J. Lonsdale, A. G. Murchison, S. J. Watt, C. M. Wilson & J. A. S. Ross (*United Kingdom*)

14:45 15 **Incidence of decompression illness among HBO nurses.**
Brattebø G., L. Aanderud, J. Risberg, E. Thorsen & M. Forland (*Norway*)

15:00 16 **Fatal diving accidents in recreational and sport diving in Northern Adriatic.**
Barković D., R. Dobi & D. Cuculić (*Croatia*)

15:15 17 **Outcome of dysbaric disorders is not related to delays in treatment. Preliminary results of a multivariate analysis of 466 cases following a prospective study.**
Desola J., J. Sala, J. Bohé, A. Garcia, C. Geronimo, M. Gomez, S. Graus, E. Martinez, J. Montanya & A. Rabella (*Spain*)

15:30 *Coffee*

15:30 **Joint meeting of the Medical Subcommittee of EDTC and Educational / Training Subcommittee of ECHM (closed meeting)**

19:00 ***Reception at Castle Bled***
Bus departures from Hotel Golf: *19:00, 19:15 & 19:30*
Departures from Castle Bled: *22:00, 22:30 & 23:00*

TUESDAY, September 23, 1997

HYPERBARIC PHYSIOLOGY - I
Moderators: R. W. Hamilton *(U.S.A.)* **& H. Takahashi** *(Japan)*

8:30 18 **The effect of exercise on decompression bubbles - a theoretical study.**
Flook V. *(United Kingdom)*

8:45 19 **A theoretical study on the extent and duration of decompression bubbles following a submarine escape.**
Flook V. *(United Kingdom)*

9:00 20 **Effects of diving and diving accidents on supraspinal MR-imaging compared to normal, healthy controls.**
Sipinen S. & J. Ahovuo (*Finland*)

9:15 22 **The effect of reduced blood flow on local inert gas content, and bubble formation during decompression.**
Koteng S., I.M.H. Geving, A.L. Ustad, V. Flook & A.O. Brubakk (*Norway*)

9:30 23 **Two-dimensional imaging ultrasound monitoring of gas phase emboli after decompression dives.**
Brauzzi M., M. Merli & M. Rizzo (*Italy*)

10:00 *Coffee break*

HYPERBARIC PHYSIOLOGY - II
Moderators: V. Flook *(United Kingdom)* **& S. Sipinen** *(Finland)*

10:30 24 **Persistence of tear film bubbles.**
Mekjavić I.B., P. Jaki, & E.P. Kindwall (*Slovenia & U.S.A.*)

10:45 25 **Assessment of visual function in divers by contrast sensitivity.**
Garcia-Franco Zuñiga F., I. G. Arance, M. P. Ruiz, E. T. Alfaro & I. J. Lopez (*Spain*)

11:00 26 **Serotyping is not adequate for epidemiological studies in saturation environments.**
Ahlen C., L. Mandal & O.J. Iversen (*Norway*)

11:15 27 **Evaluation of decompression sickness risk in saturated air and nitrox divers judged on the basis of changes in haemostasis.**
Olszanski R., Z. Baj, A. Buczynski, M. Konarski, R. Klos & S. Skrzynski (*Poland*)

11:30 28 **Body fluid loss during 4 hours head out immersion (HOI) in 38°C fresh water (FW) and sea water (SW).**
Hope A., L. Aanderud & A. Aakvaag (*Norway*)

11:45 29 **Hot water burn during an excursion diving in 400 m saturation dive.**
Ikeda M., A. Akagi, Y. Shigemitsu, S. Suzuki & A. Ito (*Japan*)

12:00 *Lunch*

PROGRESS REPORTS
Moderators: J. Wendling *(Switzerland)* **& J. Desola** *(Spain)*

13:30 **Personal, professional and educational requirements for the staff of a hyperbaric medical centre. Conclusions of the I. European Consensus Congress of the European Committee for Hyperbaric Medicine (E.C.H.M.).**
J. Desola *(Spain)*,
Member of E.C.H.M. & Chairman of the Medical Subcommission of the European Diving Technology Committee (E.D.T.C.).

1350 **An educational European programme on hyperbaric medicine. A joint work between the E.C.H.M. and the European : Diving Technology Committee (E.D.T.C.). A preliminart report.**
J. Wendling *(Switzerland)*
Member of E.C.H.M. & Chairman of the Medical Subcommission of the E.D.T.C.

POSTER PRESENTATIONS

14:15 **Oral presentations of posters**
Moderators: S. Gošović *(Croatia)* **& T. Lah** *(Slovenia)*

Diving: 30 **Bubble detection in isolated tissue based on the Cartesian diver principle.**
Hink J. & J. Madsen (*Denmark)*

31 **The effect of water hyperbaria on the cardiorespiratory system.**
Gulyar S. A., A. L. Evtushenko, V. N. Ilyin, R. Olszanski & S. Skrzynski (*Ukraine & Poland)*

32 **The effect of PO_2 on tear bubble formation.**
Jaki, P. , P. Fidler, P. Jurič, P. Dovšak & I. B. Mekjavić (*Slovenia)*

33 **Manned work of breathing in underwater breathing apparatus.**
Louise A. Gay *(United Kingdom)*

34 **Pulmonary function in divers after an intensive training programme.**
Olea Gonzalez A., I. Martinez Gonzalez-Moro, J.D. Gonzalez Aquino, A. Pujante Escudero, I. Arance Gil & M. Ruiz Pardo *(Spain)*

21 **Acent rate, age, weight, precentage of fat tissues and aerobic capacity: influence on the grades of circulating bubbles detected with echography and Doppler.**
Carturan D., A. Boussuges, H. Burnet, P. Vanuxem, B. Gardette & J. M. Sainty (*France)*

HBO: 35 **HBOT in monoxide poisoning: A 10 years' experience at A.T.I.P. Hyperbaric Medical Centre in Padua (Italy); 719 cases are under examination.**
Zanon V., F. Rusca, G. Garetto, R. Scappatura & G. Giron (*Italy)*

36 **Cost - benefit analysis of hyperbaric oxygen therapy for post-irradiation injuries.**
Vesnaver, A. & I.B. Mekjavić (*Slovenia)*

37 **Hyperbaric oxygen therapy of pseudomonas dermatitis in the dog: a case study.**
Tozon N., D. G. Campbell & J. A. Exner *(Slovenia & Canada)*

56 **HBO rationale in surgical reconstruction of pharyngostoma.**
Sparacia B., G. Gulotta, A. Alongi & A. Sansone (*Italy)*

58 **The role of HBO in the treatment of anorectal and colic diseases determined by clostridium difficile.**
Sparacia B., F. Piazza, A. Alongi & A. Sansone (*Italy)*

Equipment:

38 **Sydney Hyperbaric Centre - Relocation.**
Gibbons B. D. *(Australia)*

39 **Adaptation of the hyperbaric ventilator Sechrist 500A for the air filled hyperbaric chamber.**
Hadravsky M., J. Ružička, M. Emmerova & V. Suchy (*Czech Republic)*

40 **Field evaluation of a prototype diver thermal monitoring system.**
I. B. Mekjavić, F. Gider, M. Tomsic, F. S. C. Golden, C. Franks & M. J. Tipton (*Slovenia & United Kingdom)*

41 **OXYNET: Development of an internet information network for hyperbaric oxygen therapy.**
P. Germonpre & R. Houman (*Belgium)*

14:45 **Poster viewing**
Coordinators: L. Travnik *(Slovenia)* **& P. Jaki** *(Slovenia)*

15:30 **EUBS Executive Commitee Meeting**

17:00–23:00 ***Evening stroll through Ljubljana.***
A tour through the Old Town of Ljubljana.
Buses will depart from Hotel Golf.

WEDNESDAY, September 24, 1997

HYPERBARIC PHYSIOLOGY - III
Moderators: G. Bolstad *(Norway)* **& M. Gensser** (Sweden)

8:30 42 **»Helium in - hydrogen out« a new diving technique.**
Gardette B., C. Gortan & H. G. Delauze (*France)*

8:45 43 **Saturation decompressions using trimix with nitrogen content between 16 and 44%.**
Sicko Z., J. Kot & T. Doboszynski (*Poland)*

9:00 44 **Inner ear barotrauma complicated with compressive myelopathy in a hypothermic diver.**
Nogay H. A. *(Turkey)*

9:15 45 **Morphological (semiquantitative) assessment of the changes in the lungs after experimental pulmonary barotrauma.**
Siermentowski P., W. Kozlowski, R. Koktysz, A. Kulig, R. Olszanski & M. Konarski (*Poland)*

9:30 46 **Macroscopic and microscopic indices of changes in experimental pulmonary barotrauma.**
Siermentowski P., W. Kozlowski, R. Koktysz, A. Kulig, R. Olszanski & M. Konarski *(Poland)*

9:45 47 **Computer tomography and autopsy features of pulmonary barotrauma and air embolization in a diver.**
Longobardi P., M. G. Amorico, C. Morisi, S. Maitan & F. De Pasquale (*Italy)*

10:00 *Coffee Break*

HYPERBARIC OXYGEN THERAPY - I
Moderators: N. Bitterman *(Israel)* **& M. Živković** *(Yugoslavia)*

10:30 48 **The British Hyperbaric Association Carbon Monoxide Database, 1993-6: delay to delivery to hyperbaric facilities.**
Hamilton-Farrell M. R. *(United Kingdom)*

10:45 49 **Hyperbaric oxygenation and blood flow velocity of vertebral artery.**
Franinović-Marković, J. & H. Kovačević (*Croatia)*

11:00 50 **Treatment of frostbite with hyperbaric oxygen therapy.**
Bajrović F., M. J. Tipton & I. B. Mekjavić (*Slovenia & United Kingdom)*

11:15 51 **Dynamic modelling of transcutaneous oximetry.**
Ružička J., M. Hadravsky, M. Emmerova & J. Cendelin (*Czech Republic)*

11:30 *Lunch*

HYPERBARIC OXYGEN THERAPY - II
Moderators: O. Eiken *(Sweden)* **& Z. M. Arnež** *(Slovenia)*

13:00 ***Invited lecture:***
52 **Hyperbaric oxyen poteniates wound healing.**
J. J. Gibson & T. K. Hunt (*U.S.A.)*

14:00 *Break*

14:15 53 **Hyperbaric oxygen therapy in the management of clostridial gas gangrene.**
Korhonen K.& J. Niinikoski (*Finland)*

14:30 54 **Pyoderma gangrenosum and hyperbaric oxygen therapy: a case report.**
Ruiz Pardo M., I. Arance Gil, F. Garcia-Franco, M. D. Alcalde Molina, M. Á. Arance Gil & A. Olea Gonalez (*Spain)*

14:45 55 **Mortality risk factors and predictive prognostic evaluation based on stratification of severity levels (phases 1, 2, 3, 4) in progressive necrotizing infections of soft-tissue.**
Longobardi P., Calandra G., C. Morisi, W. Zabberoni & G. Oriani (*Italy)*

15:00 57 **Indication about hyperbaric treatment of asceptic necrosis of the femoral head (NATF).**
Montanari M. & N. Bronzini (*Italy)*

15:15 *Coffee Break*

HYPERBARIC OXYGEN THERAPY - III
Moderators: T. K. Hunt *(U.S.A.)* **& J. Wendling** *(Switzerland)*

16:00 59 **Sudden death after hyperbaric oxygen therapy - a case report.**
Hamilton-Farrell M. R. & M. May *(United Kingdom)*

16:15 60 **Sudden sensorineural deafness: treatment with hyperbaric oxygen therapy after failure of a ten day course of »classical« drug therapy.**
Desloovere C. & P. Germonpre *(Belgium)*

16:30 61 **How many HBO treatments are necessary for the therapy of sudden deafness and acute tinnitus?**
Welslau W., A. Lammerding, M. Almeling, R. Busch, G. Trombitas & G. Hesse *(Germany)*

16:45 62 **Treatment of psoriasis by hyperbaric oxygenation combined with Psoralen + ultraviolet light (PUVA) therapy.**
Živković M., I. Dostanić, Ž. Kanjuh & V. Gajić *(Yugoslavia)*

17:45 ***Wine Tasting.***
Participants wishing to sample the wines of Slovenia, please assemble at the Conference Centre. The tour consists of a trip to the island in the middle of Lake Bled, followed by sampling of wine and food in a Wine Cellar near Villa Zaltorog. The tour is limited to 30. Participants that pre-registered for this tour have priority. (Price = 40 DM).

20:00 ***Cocktail party at Villa Zlatorog***
(No host bar)

THURSDAY, September 25, 1997

HYPERBARIC PHYSIOLOGY
Moderators: M. J. Tipton *(United Kingdom)* **& R. Zorec** *(Slovenia)*

8:30 ***Invited lecture:***
63 **Synapses under pressure: the Ca2+ channels enigma.**
Y. Grossman, H. golan, Y. Etzion & A. E. Talpalar *(Israel)*

9:30 *Break*

9:45 64 **The intracerebral microdialysis technique used for *in vivo* receptological studies in the hyperbaric field.**
Risso J. J., A. Saget, N. Turle & J. L. Meliet *(France)*

10:00 65 **High pressure of heliox induced striatal glutamatergic hyperactivity: a microdialysis and behavioural study.**
Darbin O., J. J. Risso & J. C. Rostain *(France)*

10:15 66 **HPNS induced morphological changes in rat brain.**
Wenzel J., H. D. Mennel & G. Stumm *(Germany)*

10:30 *Coffee Break*

HYPERBARIC PHYSIOLOGY - III
Moderators: J. Wenzel *(Germany)* **& Y. Grossman** *(Israel)*

11:00 67 **Latency to CNS oxygen toxicity in rats as a function of CO_2 production and PO_2.**
Arieli, R. *(Israel)*

11:15 68 **Comparison between nitrogen narcosis and normobaric nitrous oxide narcosis. Neurochemical and behavioural aspects.**
Turle N., A. Saget, J. L. Méliet & J. J. Risso *(France)*

11:30 69 **Neurochemical and behavioural studies of an eventual adaptation to narcosis.**
Saget A., A. Courtiére, J. Hardouin, N. Turtle, J. L. Méliet & J.J. Risso *(France)*

11:45 *Lunch*

13:00 **ANNUAL GENERAL MEETING OF THE EUROPEAN UNDERWATER & BAROMEDICAL SOCIETY**

15:30 ***EUBS picnic-in-lieu-of-banquet on Mt. Vogel***
Buses depart from Hotel Golf.

FRIDAY, September 26, 1997

08:30 ***EUBS Excursion to Postojna Cave and Piran.***
The afternoon is free for leisure activities in Piran (swimming, diving, sightseeing etc.)
Buses will return to Bled at 1800.
Price: 80 DM (includes tour of Postojna Cave, lunch and refreshments)

2

THE EFFECT OF REPETITIVE EXPOSURES TO HYPERBARIC OXYGEN ON TNFα mRNA, TNF-α SECRETION & MONONUCLEAR SUBSETS IN THE SPLEEN

N. Bitterman[1], M. A. Rahat, D. Zisman, H. Bitterman, A. Kinarty & N. Lahat

[1] Israel Naval Medical Institute, Medical Corps, IDF & Carmel Medical Center, Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel

INTRODUCTION: We studied immunological parameters of the spleen, a major component of the immune system, to further evaluate molecular mechanisms underlying the effects of exposure to therapeutic profiles of HBO on the immune system.

METHODS: Nine rats were exposed to 0.28 MPa oxygen for 90 minutes twice daily for a total of 10 exposures, and 9 rats served as air controls. Immediately after the last exposure, the spleen was prepared for immunological assays of mononuclear subsets. Secretion of TNFα from cultured splenic monocytes was determined with and without stimulation with PHA (phytohemagglutinin). Total RNA was extracted from isolated splenocytes, and quantitative RT-PCR analysis was performed on RNA samples.

RESULTS: Our results demonstrate an increase in TNFα mRNA after 10 exposures to HBO. A highly significant correlation (R^2 = 0.91) was observed after exposure to HBO between TNFα mRNA and stimulated secretion of TNFα. A negative correlation (R^2 = 0.7) was found between TNFα mRNA and CD4/CD8 ratio.

CONCLUSIONS: Our results demonstrate variations in splenic molecular mechanisms of immune response to repeated HBO, expressed by significant individual correlations in each rat between changes in TNFα mRNA, CD4/CD8 ratio and TNFα secretion.

3

DIFFERENCES IN REGIONAL ENDOTHELIUM DEPENDENT CONTROL OF VASCULAR TONE MAY UNDERLIE HBO INDUCED REDISTRIBUTION OF BLOOD FLOW IN HEMORRHAGIC SHOCK

H. Bitterman, H. Levy, R. Goldstein, N. Bitterman[1] & V. Brod

Carmel Medical Center, Technion – Israel Institute of Technology & [1] Israel Naval Medical Institute, IDF, Haifa, Israel

INTRODUCTION: We evaluated changes in regional endothelium-NO-dependent control of vascular tone and HBO induced redistribution of blood flow in shock.

METHODS: Shock was induced in rats by withdrawal of 30% of the total blood volume. This was followed by an infusion of acetyl choline (ACh) (1mg/kg/min. for 15 min. and 10 mg/kg/min. for 30 min.). HBO (0.3 MPa) was started in the middle of high dose Ach infusion and continued after its cessation. Ultrasonic flow meters were used to monitor blood flow in the distal aorta (DA) and the superior mesenteric artery (SMA).

RESULTS: ACh at both doses decreased mean arterial blood pressure and DA vascular resistance and increased DA blood flow significantly (by 12±4 & 25±5% at 1 & 10 mg/kg/min., respectively, $p < 0.01$). SMA resistance and flow did not change after low dose ACh. During high dose ACh, SMA flow decreased significantly by 27±5% ($p < 0.01$). After cessation of ACh, HBO induced a significant increase in mean arterial blood pressure, a decrease in distal aortic flow and an increase in SMA flow.

CONCLUSIONS: Neutralization of NO seems to be one of the mechanisms of the hemodynamic effects of HBO. It is suggested that different degrees of NO production and/or vascular endothelial dysfunction in the splanchnic and muscle beds may underlie HBO induced redistribution of blood flow in hemorrhagic shock.

4

EFFECTS OF NITRIC OXIDE SYNTHASE INHIBITION UPON NEURAL TRANSMISSION IN THE DENTATE AREA DURING HYPERBARIC OXYGEN EXPOSURE

Finn K. Jellestad & Fredrik A. S. Hanssen

Department of Biological and Medical Psychology, University of Bergen, Norway

INTRODUCTION: Hyperbaric oxygen (HBO) exposure may lead to epileptic seizure activity. Inhibition of Nitric Oxide Synthase (NOS) delays the onset of seizures and reduces the duration in rats. The aim of the present project was to investigate, whether inhibition of NOS inhibits or facilitates neuronal transmission in the dentate area in rats.

METHODS: Twelve male Sprague Dawley rats (350±40 g) were used. Six rats recieved-systemic i.p. injections of Nw-Nitro-L-Arginine (L-NNA), while the other six rats recieved saline injections. All rats were implanted with a teflon coated stainless steel electrode in the perforant path (stimulation electrode) and another electrode in the granule cellular layer of the dentate area (registration electrode). Monosynaptic neuronal transmission was tested in a paired-pulse paradigm with stimulus delay intervals of 20, 100 and 300 ms to test early inhibition, facilitation and late inhibition, respectively. Measurements were done with drugs followed by HBO exposures to 0.3 MPa.

RESULTS: The results suggest that L-NNA prevents a reduction of early inhibition (20 ms delay interval) seen in the saline injected rats during HBO exposure. The L-NNA also significantly reduced the large individual variation seen during adaptation and baseline measurements.

CONCLUSIONS: It is concluded that one protective effect of L-NNA may be mediated through the prevention of reduced early inhibition during HBO exposure.

5

HYPERBARIC OXYGEN THERAPY FOR THROMBOTIC COMPLICATIONS IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES

Hasan A. Nogay[1] & Maide Çimsit[2]

[1] Department of Immunology, Institute for Experimental Medicine and Research & [2] Department of Underwater and Hyperbaric Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey.

INTRODUCTION: Circulating antiphospholipid antibodies (aPL) that activate vascular endothelial cells are associated with severe thrombosis, which is amenable to hyperbaric oxygen (HBO). The present study was conducted to describe the efficacy and benefit of HBO as an immunotherapy in patients with aPL-thrombosis syndrome.

METHODS: Three female patients (aged 22 to 30 years) with central retinal artery occlusion (CRAO) and a 11 month old female with severe purpura fulminans (PF), who underwent HBO therapy were prospectively studied. On admission, two patients with CRAO had visual acuities with 'no light perception', while the third had 'light perception only'. An average of 40 sessions of HBO were applied.

RESULTS: In the patients with CRAO, vision improved an average of 3.6 visual acuity gradations. One patient with PF was cured with HBO and careful wound care. In this patient 1 digit spontaneously amputated and degenerated completely.

CONCLUSIONS: We conclude that in combination with the other noninvasive treatment modalities, HBO should be administered as early as possible for thrombotic complications in patients with aPL-thrombosis syndrome.

6

INTERIOR DESIGN OF HYPERBARIC LIVING CHAMBERS

Greta Bolstad, G. B. Benum & Helga Ryvarden

SINTEF Unimed, Section of Extreme Work Environments, 7034 Trondheim, Norway.

INTRODUCTION: Saturation divers in the North Sea spend up to 24 consecutive days in hyperbaric chambers, performing work tasks as well as leisure time activities within these closed environments. Although diving equipment, in general, has undergone substantial improvements since saturation diving first started, very little emphasis has been placed on the divers living quarters.

METHODS: Based on user input from experienced saturation divers and technicians and ergonomic know-how, we have developed a set of design requirements for hyperbaric living chambers. Accepting the limitations and restrictions given by the physical framework that existing hyperbaric diving chambers represent, we have suggested how the living conditions of saturation divers may be significantly improved with simple means.

RESULTS: Sketches and drawings, presenting how a living chamber of limited size and with a rather non-user friendly overall layout, may be rearranged and redecorated to present a more pleasant, although far from optimal interior.

CONCLUSIONS: With these simple and non-costly means, the divers may be offered a living and working interior which may stimulate safety and efficiency, as well as improve comfort.

7

REAL CAUSE AND PROCESS OF A CHAMBER COMBUSTION MISHAP

Hideyo Takahashi
Department of Hyperbaric Medicine, University of Nagoya School of Medicine, Showaku, Nagoya, 466 Japan

ACCIDENT: On February 21, 1996, an acrylic monoplace hyperbaric chamber exploded in a Japanese hospital and killed two and injured two other people.

CAUSE OF FIRE: According to the investigative research of an *ad hoc* committee within the Japanese Society for Hyperbaric Medicine (JSHM), a disposable chemical pocket warmer was identified as the possible igniting source. This warmer can generate moderate heat by using the oxidizing effect of iron powder contained within it and oxygen in the air. JSHM committee proved, that in a 2.7 ATA oxygen enriched atmosphere, the same pressure at which the mishap took place, the warmer could catch fire spontaneously.

COMBUSTION PROCESS: A simulation experiment was conducted with a miniature acrylic chamber. The simulation revealed that, once the warmer caught fire, the intense flame reacted with flammable substances in the chamber, including the chamber shell, and created an enormous amount of combustible gas. When the internal pressure exceeded the durable point, an explosion occurred suddenly. All proceeded within a short period of time, within ten seconds.

STATIC ELECTRICITY: JSHM committee also performed a series of studies to examine whether static electricity could be the cause of chamber fire. However, static electric energy accumulating in the chamber proved to be insufficient to catch fire even under hyperbaric and oxygenated conditions.

8

DEVELOPMENT OF A PROTOTYPE HYPERBARIC ENVIRONMENTAL CONTROL SYSTEM (HECS) FOR A NITROX SATURATION DIVING SYSTEM

Mineo Okamoto & Hitoshi Yamagichi

JAMSTEC 2-15, Natsushima Yokosuka 237, Japan

INTRODUCTION: An automated hyperbaric environmental control system (HECS) for a nitrox diving system is under development since 1994. Major parts of the system have been manufactured and are in preparation for evaluation.

METHODS: HECS was planned to be operated automatically by supplying electricity and cooling water. To realize this, a reusable carbon dioxide removal method and a 100 V electrically powered blower system was developed as a key technology. Major parts, including these systems, were completed in March 1997.

RESULTS: By using molecular sieves as an absorbent material for carbon dioxide, an automated sequence for absorbent renewal could be successfully implemented. Also, by using solid state conductor circuitry, a 100 V type blower for hyperbaric conditions could be developed. Components of the HECS have been manufactured and are under preparation to be equipped inside the JAMSTEC diving simulator for further evaluation.

CONCLUSIONS: An automated environmental control system HECS has the possibility of being used for undersea laboratory systems, hyperbaric oxygen treatment chambers for long exposure, hyperbaric treatment chambers, etc.

9

A NEW AIRLOCK SYSTEM FOR A TUNNEL BORING MACHINE (TBM)

Jean-Claude Le Pechon[1], Luc Boulestreau[2] & Eric Larue[3]

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INTRODUCTION: After completion of the first gallery of the Lyon-Nord boulevard project and before undertaking the second tunnel, an evaluation of works carried out in compressed air demonstrated that the need to increase the capabilities and to improve the working conditions, meant an airlock exchange. The new airlock should be more comfortable, and should allow back to back interventions, saving stand-by time between shifts in the range of pressures from 1.5 to 2.7 bars(g).

METHODS: A feasibility study was performed to find out the best way to accommodate and install a twin lock chamber in the small room available in the TBM. Among several options, the most suitable was designed in detail and finally constructed and installed during the U turn of the TBM.

RESULTS: A description of the new airlock system is presented with the major innovations. In particular, the twin compression chambers connected to a single emergency entrance chamber and to an ante-chamber giving access to the cutter head of the TBM.

CONCLUSIONS: An overview of the new capabilities of the airlock are presented, together with the results collected during the first phase of the second tunnel boring operation.

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LABYRINTHINE HYDROPS AS A CAUSE OF COCHLEO-VESTIBULAR PROBLEMS AFTER SCUBA DIVING: A "NEW" DIVING SYNDROME

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INTRODUCTION: Labyrinthine Hydrops is, until now – to our knowledge, an undescribed cause of vertigo and hearing problems after SCUBA diving. This "Meniere"-like syndrome occurs in divers who have moderate to severe middle ear equalisation problems, but is not associated with true inner ear barotrauma. Instead, the repeated oval window movements and perilymphatic changes of pressure induced by forceful Valsalva manoeuvres, probably induce a reactive rise in peri- and/or endolymphatic fluid production, causing a syndrome of acute vertigo, tinnitus and low-frequency hearing loss in the hours after surfacing.
The prognosis seems to be excellent, and eventually only classical anti-vertiginous drug therapy (type Beta-histine) is indicated.

RESULTS: We present three case reports of divers who suffered from labyrinthine hydrops after SCUBA diving.

CONCLUSIONS: The pathophysiology, symptoms and various differential diagnostic elements are discussed.

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DECOMPRESSION SICKNESS DURING A BREATH-HOLD DIVE: A CASE REPORT

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INTRODUCTION: Usually the amount of N_2 transferred to the circulation during a breath-hold (B-H) dive is very small. However, it is theoretically possible to accumulate enough N_2, if the diver repetitively dives to considerable depths with very short surface intervals.

METHODS: A diver, completing about 25 B-H dives to 32 metres in 90 min., with the help of a scuba scooter, developed Decompression Sickness (DCS). Each dive lasted approximately 2 min. with surface intervals of less than 2 min. During the last dive, the diver became tired and experienced pain in the lumbar column and right shoulder. Within 5 min. of completing the last dive he exhibited facial paralysis, confusion and disorientation.

RESULTS: These symptoms did not progress to more severe ones. The diver was treated with US Navy Treatment Table 6 and experienced relief of all symptoms following the treatment. An additional treatment on Table 6 was required, as the symptoms reappeared after 10 hours. Partial facial paralysis persisted following the second treatment.

CONCLUSIONS: DCS is a possible medical complication of breath-hold diving, particularly after unusually frequent dives to relatively deep depths.

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DIVING PROFILES AND DECOMPRESSION RISK IN OCCUPATIONAL SCUBA DIVERS

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INTRODUCTION: In Japan, some divers are engaged in establishing man-made gathering places for fish. We conducted a preliminary survey to assess their diving profiles and decompression risk from the viewpoint of prevention of decompression related illness.

METHODS: Two male scuba divers, aged 21 and 35 years, participated in the survey. They were engaged in directing a crane operator, via an underwater communication system, to set concrete blocks at correct points for the fish gathering place. Their diving profiles were recorded by a Citizen diving watch, HYPER-AQUA-LAND. Immediately after surfacing from each dive, they were examined by the precordial Doppler bubble detector.

RESULTS: The maximal dive depth for both divers was 26m, and dive durations ranged from 21 to 31 minutes. They conducted two dives daily. Bubbles were not detected, nor was decompression sickness encountered after surfacing, in any of the dives. Analyzed diving profiles showed longer decompression times than those in the J-2 table issued by the Ministry of Labor in Japan, but some exceeded the safety ascent depth (SAD) of the DCIEM model.

CONCLUSIONS: Results indicate that the conventional J-2 table could be improved and that analysing recorded diving profiles is a useful tool for improvement of diving tables.

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TESTICLE IMPLANTS – DIVING EXPOSURE

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INTRODUCTION: Many users of testicle implants have doubts whether the hyperbaric environment (inside a pressurised chamber or underwater) can damage or affect testicle implants. We have analysed products of the company HEYER-SCHULTE under different pressure exposures.

METHODS: The testicle implants were exposed to several defined pressures in water and air. The pressure environment was controlled and recorded by the chamber's control computer and a diving-computer (UWATEC Aladin Air X). Diving profiles used during the tests were: 2.4 bar – simulating profiles normally applied during HBOT (Hyperbaric Oxygenation Therapy); 6 bar – a repetitive dive profile, conducted in conformance with the calculated computer profile; 6 bar – repetitive dive profile; the first dive was conducted in conformance with the calculated computer profile, which was followed by a repetitive dive with a significant deviation from the correct computer profile; 9 bar – dive profile normally not used by recreational divers.

RESULTS: Only the exposure to 9 bar (40 minutes) resulted in singular air bubbles inside the testicle implants.

CONCLUSIONS: There appears to be no risk of damage to testicle implants during dives to a depth of 50m. Also, the exposure to negative pressure (pressurised aircraft cabins) has no effect on the implants.

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DIVE HISTORY: A PREDICTIVE FACTOR IN RELAPSE AFTER TREATMENT OF DECOMPRESSION ILLNESS

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METHODS & RESULTS: A retrospective audit, with regard to relapse after recompression therapy, was conducted on the records of 150 cases of decompression illness treated during the years December 1991–April 1997. Relapse after treatment was noted in 17 (11.3%) patients. Dive history was examined and the amount of omitted decompression over the three days prior to onset of symptoms was calculated using RNPL '74 tables. In patients who had not relapsed, 68 had been diving for more than one day prior to symptoms and 65 had only dived during this period. In contrast, in patients who relapsed after initial therapy only 2 had not been diving more than one day. This difference in pattern of diving was significant ($p = 0.004$ chi^2). Although the mean decompression omitted was greater in the relapse group at 24 hours (96.5 minutes) and 24–72 hours (187.7 minutes) than in control (58.8 at 24 hours and 107.4 at 24–72 hours) this was not significant. The points of interest are that omitted decompression was common. Only 22.9% of patients had no omitted decompression for the first day prior to symptoms and 21.4% had no omitted decompression time for the two days prior to that.

CONCLUSION: Relapse is more likely in people who dive for more than just one day.

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INCIDENCE OF DECOMPRESSION ILLNESS AMONG HBO NURSES

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INTRODUCTION: Decompression illness (DCI) among attending nursing personnel after hyperbaric oxygen (HBO) therapy in multiplace chambers has been reported. To estimate the effect of modifying the decompression procedure, we monitored the incidence of DCI among attending nursing personnel after elective HBO therapy.

METHODS: 18 registered nurses have been attending althogether 1, 534 HBO treatment sessions (414 patients) for a period of 30 months. Patients are treated daily in a multiplace chamber for 90 min. at a pressure of 240 kPa (14 msw), involving two 5 min. air breaks between 30 min. periods of oxygen breathing. Attending nurses breathed oxygen during the 7 min decompression time according to table. After 3 DCI cases (395 sessions), the procedure was modified by adding a period of oxygen breathing (5 or 10 min., depending on the compression time) before start of decompression.

RESULTS: 3 cases of DCI were registered after the first 395 HBO sessions; all involving skin only, resulting in an overall incidence of 7.6 per 1000 compressions. After modifying the decompression procedure for the nurses, no cases of DCI have been reported after 1,139 subsequent treatment sessions ($p = 0.02$ Fisher's exact test).

CONCLUSIONS: Prolonging the period of oxygen breathing significantly reduced the incidence of DCI in attending nursing personnel, after HBO therapy with the osteoradionecrosis treatment table to 240 kPa for 90 min.

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FATAL DIVING ACCIDENTS IN RECREATIONAL AND SPORT DIVING IN THE NORTHERN ADRIATIC OVER A 3 YEAR PERIOD (1994–1996)

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INTRODUCTION: The number of individuals becoming involved with diving as a sport and recreational activity, is increasing substantially in Croatia. Croats and many foreign tourists visit the Adriatic coast in great numbers. The latter are usually not familiar with the conditions in the sea, dive rarely, and have no proper knowledge about the dive sites.

METHODS: We analysed forensic medicine protocols, and collected data of casualties, which were put to coroner's inquest.

RESULTS: In the three year period from 1994 to 1996, an estimated 10,000 recreational dives were conducted in the region. Death occurred in 17 accidents. Cause of death was: hypoxia in 8 cases, barotrauma with gas embolism in 7 cases, DCI in 2 cases. Among them, there were 8 breath hold divers and 9 scuba divers; 8 novice and 7 experienced divers, and 2 instructors; 5 divers were Croats and 12 foreigners; 11 dove with organised groups and 6 dove alone.

CONCLUSIONS: The number of fatal diving accidents in the Croatian Adriatic is increasing. A considerable number of victims are breathhold divers. The most common causes of accident were poor diving techniques, mistakes in diving procedures and inadequately prepared divers. The co-operation, co-ordination, reporting and investigation of accidents have to be improved to prevent accidents in the future.

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OUTCOME OF DYSBARIC DISORDERS IS NOT RELATED TO DELAY IN TREATMENT. PRELIMINARY RESULTS OF A MULTIVARIATE ANALYSIS OF 466 CASES FOLLOWING A PROSPECTIVE STUDY

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INTRODUCTION: It is generally believed that the sooner you treat a Dysbaric Disorder(DD), the better the outcome will be; however this assumption has never been proven. METHODS: A logistic regression analysis of 466 cases of DD corresponding to the period 1969–1995 was conducted following a prospective model, in an attempt to relate all variables to the final outcome of the patient.

RESULTS: The average time elapsed from when the divers experienced the first symptom to their arrival at our Unit was 19.7±53.7

(1–750) hours. The outcome of the patients was satisfactory after the first hyperbaric treatment in 39.4% of the cases, in 58.7% upon completion of the entire therapeutic protocol, and in 90.0% in a long term control. Neither a bivariate, nor a multivariate analysis revealed any relation between the number of hours of delay in the treatment and the initial, medium or final outcome.

CONCLUSIONS: These results confirm our old suspicion that therapeutic urgency in DD is more dependent on the first minutes than on hours elapsed. Dysbaric disorders induce local tissue hypoxia and thus generally result in neurological impairment. If hyperbaric treatment can be initiated immediately, the outcome would probably be better, but after the first few minutes, the final result depends more on the quality of the treatment than on the urgency.

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THE EFFECT OF EXERCISE ON DECOMPRESSION BUBBLES – A THEORETICAL STUDY

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INTRODUCTION: A mathematical model of decompression, which has a physiological and anatomical basis, is an ideal method of making a rapid, relatively cheap, systematic study of the effect of physical activity on the degree of post-decompression bubbling. This paper describes some early results from such a study.

METHODS: The model uses physiological, anatomical and physical data to describe the inert gas movement and bubble development in the body. In its basic state, it describes the body at rest, with appropriate levels of tissue blood flow and metabolic gas exchange; because each tissue type is identifiable, it is possible to change these values to simulate different physiological conditions. Bubble production has been computed for generalised physical activity, at levels corresponding to 20 and 40% VO_2max during bottom time only, and throughout the whole hyperbaric exposure, including decompression. Non-saturation hyperbaric profiles have been studied.

RESULTS: The effect of exercise can be dramatic. For example, following 40 minutes at 110 feet using USN in-water decompression profile, the lower level of activity during the time at maximum depth increases the volume of gas in bubbles in muscle by 93 % and in pulmonary artery blood by some 40 %. If activity is continued at the same level throughout decompression, the values drop by 52 and 22 % below those for the exposure at rest.

CONCLUSION: This type of model could be used to draw up guidelines relating to physical activity during diving.

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A THEORETICAL STUDY OF THE EXTENT AND DURATION OF DECOMPRESSION BUBBLES FOLLOWING A SUBMARINE ESCAPE PROCEDURE

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INTRODUCTION: This paper reports the predicted magnitude and duration of bubbles following very brief exposure to high pressure, as used in submarine escape procedures.

METHODS: A mathematical model is used to calculate inert gas levels and bubble formation in the body; the tissues grouped according to the time constant for gas dynamics. The model uses published physiological, anatomical and physical data to calculate the volume of gas in bubbles for each compartment, pulmonary artery inert gas load and pulmonary artery bubble counts derived from an empirically determined relationship between predicted gas load and bubble counts. Three depths have been studied; 220, 250 and 280 msw. Time from compression to the start of decompression ranged from 20 to 25 seconds, decompression was at a rate of 0.275 $bar.s^{-1}$.

RESULTS: The results indicate that there is considerable bubble formation even in animals completely at rest. Bubble numbers increase with depth from 2.7 to 10 $bubbles/cm^2$. The duration for which bubbles are predicted to remain in the pulmonary artery ranges from 148 to 270 minutes.

CONCLUSIONS: These calculations suggest that bubbles can last for several hours following a very brief exposure to high pressure, without the need to invoke any concept of stabilisation of bubbles.

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EFFECTS OF DIVING AND DIVING ACCIDENTS ON SUPRASPINAL MR-IMAGING COMPARED TO NORMAL HEALTH CONTROL

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INTRODUCTION: Diving accidents with symptoms of DCS and/or AGE increase the amount of pathological changes in EEG compared to healthy divers (Sipinen & Halonen, UHMS 1987). Diving itself, even without known symptoms of DCS, has been suggested to increase the amount of central nervous system lesions using MR-imaging (Reul *et al*, Lancet 1995). Whether the pathological changes, are proof of functional deficit, is still an open question (Wilmshurst, BMJ 1977).

METHODS: A brain MR-imaging was made for three groups of volunteers: 25 divers, who were treated for DCS in a pressure chamber, 29 divers, who had never had symptoms of DCS (and/or AGE) and 24 healthy, age matched non-diving controls.

RESULTS: Our preliminary results do not verify evidence of increased amount of central nervous lesions found in MR-imaging of normal divers as compared to non-diving healthy control subjects, whereas 16% of divers treated for DCS in a pressure chamber had hyperintense lesions in brain white matter.

CONCLUSIONS: The risk of accumulating lesions in the central nervous system by uncomplicated diving could not be proven in our study group, but the opposite findings support the evidence of brain lesions even after recompression treatment of DCS. Peer review of the MR-images of the examined three groups and testing of the affected divers is in progress.

REFERENCES:

1. Sipinen S. A. & J. P. Halonen (1987). Effects of recompression treatment on EEG in diving accidents. In: Underwater and Hyperbaric Physiology IX. Eds.: A. A. Bove, A. J. Bachrach, and L. J. Greenbaum, Jr. Undersea Hyperbaric Medical Society, Bethesda, Maryland, pp. 887–892.
2. Reul J., A. Weis, A. Jung, A. Willmes, & A. Thron (1995). Central nervous system lesions and cervical disc herniations in amateur divers. The Lancet 345: 1403–1405.

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ASCENT RATE, AGE, WEIGHT, PERCENTAGE OF FAT TISSUES AND AEROBIC CAPACITY: INFLUENCE ON THE GRADES OF CIRCULATING BUBBLES DETECTED WITH ECHOGRAPHY AND DOPPLER

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INTRODUCTION: We communicated at the 1996 EUBS congress in Milan the preliminary results of a study about the "influence of ascent rate, age and weight on the grades of circulating bubbles in recreational divers" carried out with 20 subjects. We continued this study with 17 new subjects, in an attempt to further elucidate the influence of age and weight.

METHODS : We conducted detections of bubbles at 10 min intervals after surfacing by means of a continuous wave-doppler with a new group of divers. A total of 37 subjects paricipated in 80 dives. We applied an analysis of variance to our results.To emphasise the effect of ascent rate (9m/min and 17m/min) on our oldest and heaviest subjects, we applied a Wilcoxon test on the grades of bubbles of our subjects aged over 40 and weighing more than 76 kg. Furthermore, one of the effects of age being a reduction of VO_2max and an increase of adiposity, we included ascent rate, VO_2max and percentage of fat tissues in a multiple linear regression. We then compared the kinetics of bubbles related with the 2 ascent rates.

RESULTS: Our preliminary results were confirmed: age : $P < 0.001$, weight: $P < 0.001$, ascent rate $P = 0.062$. Effect of ascent rate on subjects aged over 40 and weighing more than 76 kg: $P = 0.031$. Significant effect of ascent rate ($P = 0.036$), percentage of fat tissues ($P = 0.036$), and VO_2max ($P < 0\ 00\ 1$). The comparison of the kinetics of bubbles showed a higher grade of bubbles for a longer period of time with 17m/min than with 9m/min.
CONCLUSIONS: A slow ascent (9m/min) offers more security to divers than a fast ascent, particularly divers presenting risk factors of DCS.

REFERENCES:

1. Carturan D., A. Boussuges, G. Habib, B. Gardette & J. M. Sainty (1996). Influence of ascent rate on venous bubbles detected after recreational dives. Proc. XXII Annual EUBS Meeting, Milan, Italy, pp. 499–503.

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THE EFFECT OF REDUCED BLOOD FLOW ON LOCAL INERT GAS CONTENT, AND BUBBLE FORMATION DURING DECOMPRESSION

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INTRODUCTION: Both blood flow and bubble formation influence tissue and venous inert gas levels. The extent of bubble formation is dependent on blood flow and inert gasload. This paper describes experiments designed to examine these relationships in the hind leg of anaesthetised pigs.

METHODS: Pigs exposed for 3 hours to 40 metres, on heliox, followed by a 2 hour continuous decompression had femoral artery blood flow restricted in the left hind legduring decompression only. Bubble levels were recorded in the femoral vein of both legs. Dissolved helium content was measured in the venous blood sampled downstream from the Doppler probes in each leg. The more severe reduction in flow resulted in too little venous flow to allow samples to be drawn for helium analysis.

RESULTS: 70% and 90% reduction in flow in the femoral artery resulted in 46% and 63% reduction in femoral venous flow. Comparison of the ratio of peak amplitude in bubbles left leg to right showed average ratios to be significantly greater than 1 for both groups. The lesser reduction in flow did not affect venous helium levels compared to controls.

CONCLUSIONS: Blood flow restrictions during decompression increases the number of bubbles in the venous blood without any measureable differences in the helium content.

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TWO-DIMENSIONAL IMAGING ULTRASOUND MONITORING OF GAS PHASE EMBOLI AFTER DECOMPRESSION DIVES

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INTRODUCTION: In the post-decompression assessment of undissolved circulating gas phase emboli with two-dimensional imaging ultrasound monitoring, examination of the various cardiac chambers and the inferior vena cava has proven useful. The aim of this study was detection, by means of echocardiographic images, the changes of volume of cardiac chambers and the presence of gas phase emboli in the cardiac flow, after a decompression dive performed inside the hyperbaric chamber.

METHODS: The dives were conducted by 5 professional divers. The dive profile was 40 msw for 15 min., using the French Navy professional decompression schedules. The device used was a mono and two-dimensional imaging system. For qualitative comparison of circulating bubbles, we used the classification of Powell, Spencer and Von Ramm.

RESULTS: We detected bubbles on two of the divers, grade 2–3 on the Spencer scale, without signs or symptoms of decompression illness. We also detected volumetric changes in the right atrium.

CONCLUSIONS: The two-dimensional imaging system may be more sensitive than Doppler in the detection of bubbles. It is far larger and more costly than the Doppler instrumentation, but we hope that technological improvements will provide smaller instrumentation for field use.

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PERSISTENCE OF TEAR FILM BUBBLES

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INTRODUCTION: We have previously demonstrated that counting bubbles forming in ocular tear film following decompression is more sensitive than rating the formation of venous gas emboli with Doppler ultrasonic surveillance in the precordial region. The aim of the present study was to monitor the persistence of tear film bubbles following a compressed air dive.

METHODS: Five subjects (4 females and one male) paricipated in two compressed air dives: 30 msw for 15 min., and 15 msw for 3 hrs. The dives were spaced one week apart. Subjects tear film was examined with a slit-lamp microscope prior to each dive, immediately after the dive, and for up to 5 days following the dive.

RESULTS: Tear film bubbles increased following decompression to the surface in both dives. The number of bubbles forming in the tear film remained elevated for up to two days, before decreasing towards pre-dive levels. The number and persistance of tear film bubbles was significantly greater for the dive to 15m for 3 hrs.

CONCLUSIONS: If, indeed, tear film bubbles reflect the process of denitrogenation, then the present results suggest that current estimations may overestimate the rate of decrease in tissue residual nitrogen following a dive. Tear film bubbles appear to reflect the saturation of faster and slower tissues after a dive: the 3 hr. dive to 15m would have caused saturation and near saturation of the fast and slow tissues, respectively. In contrast, the 15 min. dive to 30 msw would have resulted in near saturation of only the fasted tissues. The increased persistence and greater number of bubbles formed in the former dive, compared to the latter suggests that the eye as a site, and tear film bubble formation as a measurement method, provide a good indication of the level of inert gas partial pressure in the different tissues.

ACKNOWLEDGEMENT: The support of the Ministry of Science and Technology (Slovenia) is gratefully acknowledged.

REFERENCES:

1. Campbell D. G., P. Jaki, P. Dovšak & I. B. Mekjavić (1996). Ocular bubble formation as a method for evaluating decompression tables. Proc. XXII Annual EUBS Meeting, Milan, Italy, pp. 505–508.

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ASSESSMENT OF VISUAL FUNCTION IN DIVERS BY CONTRAST SENSITIVITY

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INTRODUCTION: Retinal disorders in divers have previoulsy been reported, but with no repercussions in vision. Changes in the optical system of the eye, due to hyperoxia was also noticed. Contrast sensitivity (C.S.) is a subjective method, which is very sensitive and which measures visual function. The low spatial frequencies assess the whole of the retina, whereas high spatial frequencies assess foveal vision and optical system. The purpose of this study was to evaluate, whether there is any visual change by C. S. after diving courses performed in the Navy.

METHODS: 48 divers, including professional military divers (25 years diving experience) and novice divers attending a variety courses were studied. The courses were: air scuba diving (8 weeks), and a course (6 months) involving semiclosed and closed-circuit oxygen apparatus. The American Optical Test developed by Arden was our choice of measurement. The test was carried at the begining and at the end of each course.

RESULTS: C.S. is not decreased during the shorter courses. Nonetheless C.S. is decreased at the end of the longer courses, mainly in the high spatial frecuencies. There is no difference in C.S. between professional military divers and non-divers.

CONCLUSIONS: During the longer courses, where oxygen mixture systems were breathed, C.S. decreased immediately after the course. The consequences of this could be myopia, but without any clinical or functional consequences.

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SEROTYPING IS NOT ADEQUATE FOR EPIDEMIOLOGICAL STUDIES IN SATURATION ENVIRONMENTS

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INTRODUCTION: External otitis and other skin infections have been a true challenge for operational saturation divers in the North Sea. *Pseudomonas aeruginosa* is the most prominent microorganism in skin infections. In order to prevent infections, determination of possible sources and means of spread of the infection-related microbes have regularily been done by use of classic epidemiological methods (biotyping and serotyping) extended by "ABF-marker". Regular environmental control over the last ten years has resulted in unique microbiological material for retrospective epidemiological analyses.

METHODS: In 1996, a first mini-epidemiological study (one vessel/one season) was performed by use of the molecular-genetic method Pulsed Field Gel Electrophoresis (PFGE).

RESULTS: A microbiological relationship could be demonstrated between infection-related microbes and between infection isolates and environmental isolates. The results further indicate that certain infection-related strains remain in the saturation environment for longer periods. Last, but not least, four separate strains of one and the same serotype as the infection strain were present in the saturation environment by the time of infection.

CONCLUSIONS: PFGE is a powerful tool for demonstrating the true relationship between infection and environmental isolates in a saturation environment. Serotyping, the most commonly used epidemiological marker for *Pseudomonas aeruginosa* world-wide, seems to be inadequate for epidemiological studies in saturation environments.

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EVALUATION OF DECOMPRESSION SICKNESS RISK IN SATURATED AIR AND NITROX DIVES JUDGED ON THE BASIS OF CHANGES IN HAEMOSTASIS

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INTRODUCTION: The goal of the study was evaluation of decompression stress after saturation (air and nitrox) dives, according to selected parameters of haemostasis.

METHODS: 38 divers participated in 16 saturation air and nitrox exposures. Before and after each exposure the following examinations of haemostasis were performed: blood platelet count and their aggregation, PTT (caoline-kefaline time), prothrombine time, thrombine time, fibrinogen level, coagulation factors VII, X, XII, complement level C3 and C4.

RESULTS: After the air dives, there was a considerable decrease in blood platelet count, an increase in the proportional values of aggregation, and a drop in the level of coagulation factors X, XII and of fibrinogen. An increase of complement level was observed after both, air and nitrox saturation dives. The differences were statistically significant.

CONCLUSIONS: Evaluation of haemostasis may be an important factor in determing the risk of decompression sickness.

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BODY FLUID LOSS DURING 4 HOURS HEAD OUT IMMERSION (HOI) IN 38°C FRESH WATER (FW) AND SEA WATER (SW)

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INTRODUCTION: We have previously observed body fluid losses of more than 4 kg, or 5.5% of the body weight (BW), during 4 hours of diving with the open hot water suit (HWS). In addition to sweating, we postulated that this dehydration could, in part, be explained by osmotic effects of the hyperosmotic SW flushing the skin surface.

METHODS: To test the hypothesis that osmotic effects are involved in the fluid loss processes, 8 subjects participated in 38°C FW and SW HOI lasting for 4 hours. BW, rectal temperature (T_{re}), water temperature (T_w) and heart rate (HR) were determined and venous blood and urine were collected prior to, during, and after HOI.

RESULTS: T_w and T_{re} were 0.05 and 0.15°C lower, respectively, during SW compared to FW HOI, and HR increased more in FW. However, average BW reduction was significantly greater during SW compared to FW HOI (2.49 versus 1.90 kg). The increase in hemoglobin, plasma osmolality and protein concentration also indicated a more pronounced dehydration during SW HOI. Diureses and electrolyte excretion were significantly lower during the last 2 hours of both SW and FW HOI.

CONCLUSIONS: During sweating in warm water, body fluid loss is significantly greater in SW compared to FW indicating different osmotic effects. This may explain why BW losses of more than 4 kg are observed during dives with HWS.

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HOT WATER BURN DURING AN EXCURSION DIVING IN 400 M SATURATION DIVE

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INTRODUCTION: A diver suffered a hot water burn to his extremities during an excursion dive to 42 ATA in the course of a 400 m heliox saturation dive simulation. The volume and temperature of hot water supplied to his hot water suit were suddenly increased, immediately after locking out into a wet pot, following the first diver. He had a grade IId burn to his left third finger and a grade I burn to his forehead and left first toe, where hot water tube openings were located. The first diver, who also noticed the increase in water temperature, immediately shut off the hot water supply to his hot water suit and had no burn.

METHODS: The treatment was conducted by colleague divers in the deck decompression chamber (DDC) under the direction of a medical doctor, who monitored the treatment through an observation port. Our previous studies demonstrated that the bacterial flora of DDC under the 41 ATA heliox condition is quite different from 1 ATA air, and that the control of *Pseudomonas aeruginosa* infection is difficult under hyperbaric conditions. The *Pseudomonas aeruginosa* infection was severe and uncontrollable in his left third finger, while he received ordinary oral antibiotics for three days.

RESULTS: With daily medical care, such as cleansing, and povidone-iodine ointment, which was continued for about a week, the infection disappeared.

CONCLUSIONS: The healing of the non-infectious wound under the hyperbaric condition seemed to be much faster than at 1 ATA air.

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BUBBLE DETECTION IN ISOLATED TISSUE BASED ON THE CARTESIAN DIVER PRINCIPLE

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INTRODUCTION: Separation of a free gas phase in a tissue will reduce the specific gravity of the tissue. The specific gravity of a lipid rich tissue such as spinal cord will also vary with the water concentration of the tissue (edema). Consequently a simple determination of specific gravity is not suited to demonstrate the presence of minute amounts of free gas in the tissue.

METHODS: We have devised a translucent column in which the hydrostatic pressure of a density gradient can be increased or reduced suddenly. The density gradient is made of kerosene/brombenzol mixtures giving specific gravities between 1.0365 and 1.0572 $g.ml^3$ (Neslon *et al.*, 1971). It is calibrated with K_2SO_4 solutions (Weast, 1975). The specific gravity of a sample can be read to 4 decimals.

RESULTS: Samples of rat spinal cord, injected with a microbubble about 0.005 of the sample, change specific gravity immediatly, when the column is pressurized. This is not the case with uninjected control samples.

CONCLUSION: The ability of the method to demonstrate decompression induced bubbles in rat spinal cord is being tested. Results of these experiments will be reported.

REFERENCES:
1. Nelson SR, M. L. Mantz & J. A. Maxwell (1971). Use of specific gravity in the measurement of cerebral edema. J. Appl. Physiol. 30: 268–271.
2. Weast RC (1975). Handbook of Chemistry and Physics. 56th ed. Cleveland, Ohio: Chemical Rubber Co., D-246/247.

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THE EFFECT OF WATER HYPERBARIA ON THE CARDIORESPIRATORY SYSTEM

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METHODS: We examined the ventilatory and gas exchange characteristics, and cardiac haemodynamics in divers (N = 38) during a series of experimental dives: to 30 m (4 ATA) in water, to 21 ATA in air and gas mixtures of varying PO_2, PN_2 and PHe. In this mannerwe were able to exclude the influence of factors associated with immersion in water.

RESULTS: Hyperoxia had the greatest effect on the respiratory system (46.0%), followed by density of the breathing medium (26.4%), and thermal conductivity of the water medium (18.9%). With regards to the circulation, the most significant factors were hypo-gravitation and the hydrostatic pressure gradient between different parts of the body (59.4%). Increased density was responsible for 20.3% of the observed variance, and hyperoxia (compressed air) for 10.7%. Changes in central haemodynamics were most notable during the dives in water.

CONCLUSIONS: At depths to 30m, stress is exerted primarily on the circulatory system at the expense of central haemodynamics (stroke volume, cardiac output, periphery vascular resistance).

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THE EFFECT OF PO_2 ON TEAR FILM BUBBLE FORMATION

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INTRODUCTION: We have previously demonstrated that tear film bubble formation is dependent upon the depth and duration of a dive. Consequently, we conlcuded that it may serve as a useful index of decompression severity. The aim of the present study was to confirm that tear film bubbles are a consequence of PN_2.

METHODS: Eight subjects (4 males and 4 females) were compressed to 2.0 ATA for 60 minutes on two separate occasions. On one occasion they inspired the ambient air, and on the other occasion 100% oxygen, while wearing an oxygen hood. Prior to, and immediately after the hyperbaric exposure, their tear film was examined with a slit-lamp microscope. For each subject, the hyperbaric exposures were separated by at least 7 days. The order of the two hyperbaric exposures was randomised.

RESULTS: There was a significant increase in tear film bubble count following the dive, during which the subjects inspired ambient air ($p < 0.05$, t test), whereas there was no significant difference between the tear film bubble count observed before and after the dive, during which subjects inspired 100% oxygen.

CONCLUSIONS: The results confirm that the tear film bubbles previously observed following decompressions from compressed air dives reflect the process of denitrogenation. The sensitivity, objecivity and simplicity of the method suggests that it may be useful in monitoring decompression stress in divers. Since the present dive profiles simulated hyperbaric oxygen treatments, we anticipate that the method might also be useful for monitoring the decompression stress of personnel attending patients during HBO treatments.

The support of the Ministry of Science and Technology (Slovenia) is gratefully acknowledged.

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MANNED WORK OF BREATHING IN UNDERWATER BREATHING APPARATUS

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INTRODUCTION: This study investigated the use of respiratory-inductive plethysmography (RIP) for the generation of respiratory pressure-volume (P-V) loops and hence manned work of breathing (WOB) measurement for the evaluation of diving sets.

METHODS: The divers (13 males) were service personnel. Dives were conducted in thewet compartment of a compression chamber to 39 msw (0.49 Mpa) on nitrox and heliox, and 79 msw (0.89 Mpa) on heliox. P-V loops and derived measurements (e.g. WOB, respiratory rate, respiratory pressures, minute ventilation) were displayed in real time. This data was obtained on three diving sets with open, closed and semi-closed circuit systems. Minute averaged manned WOB measured during a graded exercise test at depth was compared with unmanned WOB and UK DEn/NPD performance guidelines.

RESULTS: For closed and open circuit sets, both unmanned and manned WOB were well within the DEn/NPD preferred limit on the densest bretahing gas (nitrox at 39 msw) and was less than unmanned WOB: on this equipment WOB is dependent on the setting of a diver operated buoyancy control valve.

CONCLUSIONS: RIP provides a practicable means of producing P-V loops for real-time diagnosis of equipment problems and diver-equipment interactions. Manned WOB used with DEn/NPD guidelines is a good index of equipment performance during dives.

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PULMONARY FUNCTION IN DIVERS AFTER AN INTENSIVE TRAINING PROGRAMME

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INTRODUCTION: Respiration is one of the main physiological functions that is affected by the physical adaptation to diving. Diving with compressed air induces a series of changes in respiratory function due to: an increase in the resistance to breathing, an increase in the density of the mixture, as well as modifications in the pulmonary volume and flow rates. These changes can be observed by periodic spirometric tests.

METHODS. A sample of 83 military divers starting an eight week initiation course in diving, under an intensive training programme

on land and in water, were given weekly spirometric tests. The parameters FVC, FEVI, FEVI/FVC, FEF 25–75% were analysed. The variation in each parameter of each individual was studied, as well as the average variation of the group.

RESULTS: A decrease in the following parameters was observed: FVC (4.5%), FEV1 (11.03%), FEV1/FVC (5.9%), FEF 25–75% (15.74%).

CONCLUSIONS: This decrease can be expalined by different phenomena, amongst which we can highlight toxic phenomena, due to the different gases in the breathing mixture, mainly oxygen. Irritative phenomena, because of the presence of contaminants in the breathing mixture and lastly a muscular phenomenon due to the adaptation period to diving that results in changes to the respiratory muscles.

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HBOT IN MONOXIDE POISONING: A 10 YEARS' EXPERIENCE AT A.T.I.P. HYPERBARIC MEDICAL CENTRE IN PADUA (ITALY); 719 CASES ARE UNDER EXAMINATION

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INTRODUCTION: From March 6th 1985 to March 31st 1995 we treated 719 cases suffering from acute monoxide poisoning with hyperbaric oxygen therapy, at an average of approximately 60 cases/year. In the 16 month period from January 1st 1993 to May 24th 1994 we treated more than half of the total cases of the previous seven years.

METHODS: Hyperbaric oxygen (HBO) treatments were conducted at 2.8 ATA for 75 min, for all cases where at least one of the following criteria were met: 1) anamnestical proof of toxic exposure. 2) COHb-aemia ≥ 25%; 3) significant neurological and/or cardiac clinical conditions.

RESULTS: With a single (HBO) treatment (2.8 ATA or 18m: 25 min. of 100% O_2 + 5 min. air break + 25 min. of 100% O_2 + 5min. air break + 25 min. of 100% O_2) we did not observe any symptoms of O_2 toxicity and, as per neurological sequelae, our results are within bounds previously reported: 0.03% Schillito (1963), 1% Kuroiwa (1967), 1.52% our report (A.T.I.P. – 1995), 10% Richardson (1959). CONCLUSIONS: HBOT continues to prove itself as being the basic therapy for acute CO poisoning, provided we resist the temptation of correcting its moderate acidosis.

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COST-BENEFIT ANALYSIS OF HYPERBARIC OXYGEN THERAPY FOR POST-IRRADIATION INJURIES

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INTRODUCTION: Hyperbaric oxygen therapy (HBOT) is not yet an approved procedure in Slovenia, for any indication. It is therefore necessary to provide information regarding the usefulness and effectiveness of HBOT for a variety of indications. The present study evaluated the cost-effectiveness of HBOT as an adjunct treatment of post-irradiation injuries and osteoradionecrosis.

METHODS: Patients with post-irradiation caries (PIC) were assigned either to a control group (N = 5), or to a group recieving HBOT (N = 5). Similarly, patients with osteoradionecrosis (ORN) were assigned to a control (N = 5) and HBO (N = 7) group. A comparison was conducted between matching groups regarding the final result of the treatment, the time from the beginning of treatment until complete healing (in those patients where healing occurred), the number of hospitalisations, the total number of hospital days, and the total price of the treatments.

RESULTS: Both HBO graphs had significantly ($p < 0.05$) shorter healing times, with significantly better final results (healed v. non-healed) in the ORN HBOT group. The number of hospitalisations did not differ between the PIC groups, whereas it was smaller ($p < 0.05$) in the HBO-ORN group. There was no difference in the total number of hospital days between the control and HBO groups.

CONCLUSIONS: The present study confirms that HBOT enhances both the rate and quality of healing of post-irradiation injuries. An analysis of the costs of treatments revealed that HBO was cost-effective in the treatment of ORN. The cost-effectiveness was not apparent for the PIC group. Cost-effectiveness may be improved, if patients could be treated as out-patients, rather than be accomodated in the hospital during such treatments.

This work was supported by the Ministry of Science and Technology (Slovenia).

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HYPERBARIC OXYGEN THEREAPY OF PSEUDOMONAS DERMATITIS IN THE DOG: A CASE STUDY

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INTRODUCTION: A two year old Dalmatian presented with a non-healting wound due to *Pseudomonas dermatitis* on the metatarsal region of the left hind limb. Conventional therapy, comprising antibiotics, corticosteroids and local chemotherapeutics, was administered at regular intervals over an 8 month period. Treatment with norfioxacin (10mg/kg bw) was initiated subsequent to an antiobiogram. Due to no apparent improvement in the status of the wound and *Pseudomonas dermatitis,* hyperbaric oxygen therapy (HBOT) was intiated as an adjunct to conventional therapy.

METHODS: HBOT comprised 5 treatments per week over a 4 week period. During each treatment the patient was compressed with air to 2.5 ATA in a multiplace chamber for 60 minutes, and inspired pure oxygen via an oro-nasal mask. The wound site was photographed at weekly intervals, for the purpose of determining wound surface area. In addition, a bacteriological examination was conducted of the wound before and after the HBO therapy.

RESULTS: Healing was intiaited after 5 treatments, and a substantial reduction of wound surface area was evidenced as a consequence of HBOT.

CONCLUSIONS: It is concluded that HBOT should be considered as a therapy in Veterinary Medicine, and certainly as an adjunct to conventional therapy in the treatment of non-healing wounds with *Pseudomonas dermatitis.*

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SYDNEY HYPERBARIC CENTRE – RELOCATION

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INTRODUCTION: For over two decades the major hyperbaric medical facility in Sydney was located at the Prince Henry Hospital (Little Bay), but with the advent of change sweeping the public hospital system in the late 1990s, it became necessary to relocate the chamber to the Prince of Wales Hospital (Randwick).

HISTORY: The concept of a Hyperbaric Medical Facility for Sydney was formulated in the early 1960s, with the chamber shell being constructed in August 1964. The Prince Henry Hospital unit closed on October 15, 1995, but during its' period of operation, over 3, 000 patients were treated involving in excess of 13,000 treatments. The Prince of Wales facility opening on March 11th, 1996.

TECHNICAL ASPECTS: The chamber has the following characteristics: Diameter – 3.6 metres, Length – 6.0 metres, Capacity – 14 patients and Depth capability – 3.4 ATA.

PATIENT TREATMENTS: In the first year of operation at the new site, 232 patients were treated involving some 1, 800 patient treatments.

FUTURE EXPANSION: The building was designed to also house a 2.5 metre diameter, 11 ATA treatment chamber and a 1.2 metre diameter research chamber.

CONCLUSION: The relocation of the Sydney hyperbaric facility will provide the population of Sydney and New South Wales with a much improved hyperbaric service well into the foreseeable future.

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ADAPTATION OF THE HYPERBARIC VENTILATOR SECHRIST 500A FOR THE AIR FILLED HYPERBARIC CHAMBERS

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INTRODUCTION: A new hyperbaric chamber, manufactured by the Škoda factory, was installed in the Faculty hospital in Plzen (Czech Republic) in 1996. It is a medium size chamber for compressed air exposures. The ventilator for patients was not the part of the initial delivery.

METHODS: According to the experiences of our colleagues, we used the ventilator SECHRIST 500A. This ventilator consists of two parts: the control unit outside the chamber, which produces the pressure pulses of oxygen, automatically adapted to the pressure conditions in the chamber. A Venturi tube inside the chamber ensured that the pulses produced sufficient breathing volumes for the patient.

RESULTS: The Venturi tube normally creates the breathing volume partially from the oxygen delivered from the control unit and partially from the air in the chamber. Thus, in this operational mode, the ventilator could not deliver pure oxygen to the patient.

CONCLUSIONS: We resolved this by incorporating a specially adapted demand valve as the artificial environment for the Venturi tube of the ventilator. Using this adaptation we achieved regular breathing pressures and volumes without the air from the air filled chamber, and ensured delivery of pure oxygen to the Venturi tube situaed in the air environment of the chamber.

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FIELD EVALUATION OF A PROTOTYPE DIVER THERMAL MONITORING SYSTEM

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INTRODUCTION: A thermal monitoring system was developed to monitor the skin and core temperature of saturation divers, during operational dives to 150 msw.

METHODS: The diver thermal monitoring system comprises a programmable 4-channel logger, a radio pill for monitoring core temperature and a software package for programming the logger and downloading data from the logger to a computer. The logger has 256K of internal memory and 4 input channels: two channels are dedicated to monitoring the surface temperature of the logger, one channel to count the number of pulses emitted by the radio pill, and one channel to monitor the R-R interval. The logger and pill have been successfully pressure tested to 300 msw, both in water and in a helium/oxygen environment. The system was evaluated during several field trials: (i) recreational dives to 5 msw, (ii) simulated operational dives to 6 msw, during which divers conducted underwater welding. In addition to the field trials, exercise and immersion tests were conducted in the laboratory to compare data obtained from the radio pill with that obtained with a rectal thermistor.

RESULTS: There was good agreement between the results obtained with the radio pill and rectal thermistor. The electric field generated during the welding operation interfered with the signal transmission, thus core temperature measurements are not possible when large electromagnetic fields are encountered.

CONCLUSION: The thermal monitoring system is currently being used to monitor the thermal status of divers during operational dives in the North Sea.

This work was supported by the Health & Safety Executive (United Kingdom).

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OXYNET: DEVELOPMENT OF AN INTERNET INFORMATION NETWORK FOR HYPERBARIC OXYGEN THERAPY

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Although Hyperbaric Oxygen Therapy (HBOT) has proven its efficacy in a substantial number of diseases, the lack of appropriate scientific data and well-designed clinical experimental studies in many other fields of hyperbaric medicine, was highlighted during the First ECHM Consensus Conference on Hyperbaric Medicine (Lille, 1994).
A major contributing factor is the lack of an efficient means of communication between HBOT clinicians and researchers, both in HBOT and in other scientific domains.
Modern computer hardware and software should be able to resolve this communication problem. In 1996, we proposed to establish a comprehensive and elaborate Internet site, called OXYNET, designed to provide a solution to three distinct problems:
• a complete and regularly updated directory of all HBOT Centres in Western and part of Eastern Europe,

• a discussion forum to allow fast, wide and accurate responoses to any specific problem,
• a comprehensive searchable database of literature in relation to all aspects of HBOT, with abstracts and references, and English translation of articles having appeared in not readily available or local scientific publications.
The ECHM has adopted the OXYNET project as part of its Research Subcommittee activities, and it should be accessible on the Internet during the second half of 1997.

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"HELIUM IN-HYDROGEN OUT" – A NEW DIVING TECHNIQUE

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INTRODUCTION: The "helium in-hydrogen out" technique separates the underwater working part of the dive on hydrogen, from the heliox phase in the bell and chambers. Inside the saturation chambers onboard the ships, divers breathe the standard helium mixture, but they are supplied with a hydrogen mixture when locking out of the diving bell.

METHODS: The HYDRA 11 onshore dive and HYDRA 12 offshore dive were realized in 1994 and 1996 with this new technique : "He in / H_2 out". A gas reclaim system was tested during these operations. The diver's exhaled gas was reconditioned by purification, re-oxygenation and dehydration. After boosting its pressure, the gas was returned to the diver via bell umbilical.

RESULTS: HYDRA 12 offshore dives at 200/210 msw demonstrated the industrial feasibility of this technique. Four COMEX commercial divers performed four Heliox dives and four Hydreliox dives, each dive lasted from 2 to 6 hours. The divers breathing the hydrogen mixture showed a higher efficiency with regard to task analysis and greater working capacity during sustained efforts. The helium-to-hydrogen and hydrogen-to-helium switches were mastered. The "surface loop" closed circuit breathing system worked perfectly, providing evidence of its total reliability.

CONCLUSIONS: The new "He in/H_2 out" diving technique could be implemented on any DSV, without major changes to the diving equipment. The improvement in diver's capacity, thanks to hydrogen, was evident even at mid-depths.

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SATURATION DECOMPRESSIONS USING TRIMIX WITH NITROGEN CONTENT BETWEEN 16 AND 44%

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INTRODUCTION: The aim of the study was to design an effective decompression system after saturation exposures using physiologically tolerated trimix gas mixtures from any plateau pressures in the medium range of depths.

METHODS: The study was conducted with 15 divers. In every exposure, the trimix applicable for saturation recompression treatment was used (PO_2 = 50 kPa, FN_2 = 16–44%, He balanced). Decompressions were planned according to our model based on experimental data from nitrox and heliox saturation decompressions conducted in our department and were performed with the continuous method (without stops).

RESULTS: Twenty-four man-decompressions were conducted from the plateau pressures between 400 and 800 kPa. Bends and/or other symptoms of decompression stress were not observed in any of the exposures.

CONCLUSIONS: Preliminary results of non-incidental decompressions confirm the correctness of the initial assumptions. Limiting values of helium and nitrogen half-times differed significantly from the proportion 1:2.65 interpreted by Graham's law. The proportion of 1:2 validated in the study does not support the hypothesis of the dominative role of diffusion on the elimination rates of inert gases (helium and nitrogen).

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INNER EAR BAROTRAUMA COMPLICATED WITH COMPRESSIVE MYELOPATHY IN A HYPOTHERMIC DIVER

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INTRODUCTION: Any diver who suffers tinnitus, vertigo or dizziness, and sensorineural hearing loss, following a dive that is unlikely to cause decompression illness, should be considered as a possible case of inner ear barotrauma. Although such a diver is usually counseled to permanently avoid recompression or diving, delayed hyperbaric oxygen maybe an effective and a safe treatment modality.

METHODS: An unusual case of a SCUBA diver with abnormal nasal function is presented. The diver experienced a right side perceptive hearing loss, low frequency tinnitus, fullness in the ear, dizziness and fatigue, shortly after surfacing from a dive within the limits of decompression (15 msw, 40 min bottom time).

RESULTS: During the dive, the diver experienced difficulty equalizing and hypothermia. Thirty-six hours after the dive, there were no otoscopic findings of middle ear barotrauma. Tonal audimetry showed a substantial deficit, and MRI showed protrusion of cervical, thoracic, and lumbar intervertebral disks.

CONCLUSIONS: The occurence of symptoms after surfacing, or shortly after a dive, does not always indicate decompression illness, and the patient should also be examined for evidence of musculoskeletal injury, cerebral thromboembolic disorder, and hypothermia.

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MORPHOLOGICAL (SEMIQUANTITATIVE) ASSESSMENT OF THE CHANGES IN THE LUNGS AFTER EXPERIMENTAL PULMONARY BAROTRAUMA

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INTRODUCTION: The aim of the study was an assessment of the morphological indices of changes in the bronchoalveolar tree and pulmonary vascular bed after pulmonary barotrauma (PB) and of the effect of treatment with air hyperbarism on pulmonary morphological changes caused by PB.

METHODS: PB was produced in a specially constructed high-pressure chamber for small animals, by creating a hyperpressure of about 200kP, which corresponds to a submersion depth of about 20m. Animals (rabbits) were assigned to two experimental

groups: a control group receiving no treatment after PB, and an experimental group receiving decompression treatment. A portion of the animals in the control group were sacrificed immediately after PB (group D), and the remaining animals after three weeks of follow up (group DO). The animals in the experimental group were treated with air hyperbarism (recompression and therapeutic decompression according to therapeutic air table III used in humans with PB, modified by Prof. Doboszynski), immediately after PB. Then, a portion of the animals were sacrificed (group DL), and the remaining animals (group DLO) observed for three weeks. In histological sections prepared by the paraffin method, in which cross-sections of the whole lung were obtained in the frontal plane, semiquantitative examinations were performed.

RESULTS: Blood extravasations were found most frequently within the interalveolar septa of the parahilar region of the lung in group D rabbits, while in the group DL rabbits they occurred in the subpleural region. After PB, independently of the fact whether the treatment with recompression-decompression was instituted or not, the number of distension (non-emphysematous) bullae increased and the bronchoalveolar tree distension increased with time in group DO rabbits. The location of the foci of atelectasis and its intensity were independent of PB.

CONCLUSION: PB causes an increase of a part of the air spaces of the lung, particularly in central and parahilar regions. This disorder, if not treated, intensifies with time of the experiment. Erythrorrhagia in PB belongs to microscopic indices of this trauma, and cleared up during the experimental period (three weeks).

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MACROSCOPIC AND MICROSCOPIC INDICES OF CHANGES IN EXPERIMENTAL PULMONARY BAROTRAUMA

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INTRODUCTION: The aim of the study was an assessment of the macroscopic and microscopic indices after pulmonary barotrauma (PB) .

METHODS: The experiments were carried out in rabbits of either sex, weighing 2240–5250 g. PB was produced in a specially constructed high-pressure chamber for small animals, through creation of hyperpressure of about 200kP which corresponds to a submersion depth of about 20m. The animals were sacrificed directly after PB (group D), and after three weeks of follow up (group DO). In histological sections, routine microscopic examinations were performed.

RESULTS: Postmortem examination revealed gas embolism of the left ventricle of the heart and numerous subpleural extravasations in both lungs in the rabbits. The subpleural extravasations of various intensities were the most frequently observed changes, found on gross examination in this group of animals. They developed in 15 animals i.e. in 78.9% of the total number of rabbits in group D. The second most frequent lesions were subpleural air bullae, which were found in seven rabbits i.e. 36.8%. The most frequently observed morphological changes in Group D rabbits were: acute pulmonary distension or distension bullae (73.68%), blood extravasations (47.37%), and atelectasis (47.37%). It should be stressed that the regions with advanced distension were in the proximity of atelectasis areas (36.84%). Distension bullae were also present (26.31%).

CONCLUSIONS: Extravasations under the pulmonary pleura (78.99%) and bullous distensions of the subpleural tissue, the so called air bullae (36.8%), belong to the most frequently observed gross indices of PB. On the other hand, pneumothoax and mediastinal emphysema are less frequently found.

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COMPUTER TOMOGRAPHY AND AUTOPSY FEATURES OF PULMONARY BAROTRAUMA AND AIR EMBOLIZATION IN A DIVER

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INTRODUCTION & METHODS: With the consent of the authorities, computer tomography (CT) and an autopsy were carried out on a SCUBA diver, who died on emerging after a free ascent from a depth of 20 metres (3 bar).

RESULTS & CONCLUSIONS: The CT showed bilateral pneumothorax, pneumomediastinum, pneumopericardium, pneumoperitonaeum and subcutaneous emphysema in the neck and chest. The autopsy showed that the organs were in an excellent state of conservation without any anatomical artifacts. At a pulmonary level, air could be seen in the wall of the pulmonary vessels and macroscopically confluent haemorrhage-atelectasic areas, similar to pulmunary infarction. This suggests a combination of mechanical trauma (Polak-Adams 1932) and ischaemic damage aggravated by the probable co-existance of acute pulmonary hypertension. A riddled haematic coagulum, due to air bubble entrapment, was found in the right ventricle. This confirms the hypothesis of a heart chamber gas lock (Evans, 1979). At the same time, the presence of air infiltrating the vascular wall of the coronary arteries was noticed (Van Allen, 1929). In general, it appears that the cardiac damage is essentially primary (Leitch-Hallenbeck, 1985). The jugular vein, partially sectionized transversally, permitted the iconographical observation of the air bubbles in the vascular lumen. At the level of the subclavian artery, at the opening of the vessel, a dynamicphoto showed the formation of bubbles from dissolved gas in the blood.

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THE BRITISH HYPERBARIC ASSOCIATION CARBON MONOXIDE DATABASE, 1993–6: DELAY TO DELIVERY TO HYPERBARIC FACILITIES

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INTRODUCTION: The British Hyperbaric Association has conducted a national audit of carbon monoxide (CO) poisoning treated with hyperbaric oxygen, from April 1993 until March 1996. The time taken for delivery to hyperbaric facilities after removal from exposure to CO was documented.

METHODS: A standard dataset was adopted by members of the Association, and copies were returned to Whipps Cross Hospital, where data analysis was conducted by the Department of Clinical Audit. Ethical approval was granted locally, applicable to all members of the Association. Times of rescue, contact with a hyperbaric facility, arrival at the hyperbaric facility and start of treatment were recorded.

RESULTS: Figures were not available for all cases. In the year 1995/6, mean time before contact was 4 hrs 32 mins (n = 126); subsequent mean time to delivery was 4 hrs 46 mins (n = 123); mean time for assessment and preparation in the hyperbaric facility was 1 hr 7 mins (n = 143). For the period 1993–6, mean delay from rescue to delivery was 9 hrs 15 mins (n = 326).

CONCLUSIONS: The delay from rescue to delivery to a hyperbaric facility is multifactorial. A clear national policy on management of these cases is urgently required.

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HYPERBARIC OXYGENATION AND BLOOD FLOW VELOCITY OF VERTEBRAL ARTERY

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INTRODUCTION: The aim of this study was to investigate changes in blood flow velocity (BFV) in the vertebral artery (VA) during hyperbaric oxygenation (HBO).

METHODS: We examined a group of 14 healthy , young volunteers. BFV was measured by transcranial Doppler (TCD) three times: at 1.0 bar (I.); after 10 minutes of air exposure at 2.2 bar (II.), and after 10 minutes HBO (III.).

RESULTS: (I.) Vmax = 68.6±11.2 cm/s; Vmean = 42.2±8.7 cm/s; (II.) Vmax = 62.1±12.9 cm/s; Vmean = 35.9±8.1 cm/s; (III.) Vmax = 54.6±11.1 cm/s; Vmean = 29.8±5.5 cm/s.
Compression to 2.2 bar (II.) did not change Vmax and Vmean significantly. At the end of HBO (III.), Vmax decreased by 20% and Vmean by 30%, compared with baseline (I) values. This difference was highly statistically significant. ($p < 0.01$). The difference in Vmean between II and III was also statistically significant ($p < 0.05$).

CONCLUSION: Despite a 30% decrease in Vmean during HBO, the amount of oxygen dissolved in plasma is 10 times greater than in normobaric conditions (I). This is the main benefit of hyperbaric oxygenation. The BFV in ischemic condition of VA and influence of HBO remains to be investigate in the second part of this study.

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HBO AS AN ADJUNCT THERAPY IN THE TREATMENT OF FROSTBITE: A PROGRESS REPORT

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INTRODUCTION: Following initial treatment of frostbite of an extremity by rewarming, to prevent direct injury from intracellular ice formation and protein denaturation, medical treatment is directed toward prevention of additional injury and abrogation of affected ischemic tissue due to microvascular damage. Though several case studies have been reported, whereby HBO was successfully applied in the treatment of frostbite injury, it is not normally included as an adjunct to conventional treatment. To date, we have been requested to provide HBO therapy in a total four frostbite cases.

METHODS: A total of four patients with frostbite injury have been referred to our laboratory for HBO therapy. With the exception of one patient, all recieved treatment within several days of the injury. One patient recieved the injury in the Himalayas, and there was a several week delay between injury and the first treatment. The patients were treated at 2.5 ATA for 90 minutes, some receveing two treatments daily and others only one treatment daily. The number of treatments varied among patients, from 14 to 30.

RESULTS: In patients recieving HBO therapy within days of injury, the injury healed.

CONCLUSIONS: It is concluded that HBO therapy should be considered as an adjunct therapy in the treatment of frostbite.

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DYNAMIC MODELLING OF TRANSCUTANEOUS OXIMETRY

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INTRODUCTION: Ischaemic tissue damage can be evaluated by measuring the tissue oxygen partial pressure (PO_2) with a transcutaneous PO_2 probe (Tc PO_2). A new method is proposed for dynamic monitoring of Tc PO_2 based on the response to increased oxygen delivery.

METHODS: Increased oxygen delivery is achieved by hyperbaric oxygen therapy. The amount of oxygen delivered is determined from the absolute pressure in the chamber. The evaluation of measured data is solved by the construction of dynamic regresion models derived from pathophysiological laws, such as Kroghs model of oxygen tissue distribution. A different dynamic model was tested from the simple non-dynamic differential model with time delay.

RESULTS AND CONCLUSION: Normal tissue can be represented by a linear dynamic model without time delay. Conversely, ischaemic tissue can be represented by a linear dynamic model with delay. This enables the determination of the stage of ischaemic tissue damage.

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INVITED LECTURE: HYPERBARIC OXYGEN POTENTIATES WOUND HEALING

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INTRODUCTION: A patient or laboratory animal under 2.5 ATA with 100% oxygen increases the tissue PO_2 about 10 times and percent oxygen dissolved in the plasma about twenty fold. This effect has been proven to be beneficial in wounds, especially in angiogenesis, the formation of new blood vessels.
In normal wounds, the first capillary buds can be seen at the wound edge as early as 48 hours after wounding. Capillaries grow into the wound space and provide a supply system for the synthesis and deposition of wound connective tissue. Collagen, synthesized and deposited by fibroblasts, and angiogenesis, growth of endothelial cells are two of the most important aspects of normal wound healing, and neither can occur without oxygen.
Preliminary data suggests that both low and high oxygen environments stimulate macrophages to release growth factor, which in

turn stimulates angiogenesis. The growth factor we studied, vascular endothelial growth factor or VEGF, is thought to be a major stimulator of neurovascularization in wounds and many tumours. Interestingly, it has been previously and often demonstrated that hypoxia stimulates VEGF, production from a variety of cells including many found in the wound environment (Shweiki *et al.*, 1992). The study to be discussed in this paper examines the paradox of both hyperoxia and hypoxia promoting similar effects.

The typical wound environment is hyperlactated and hypoxic, and stimulates macrophages to synthesize and release growth factors. However, clinically patients with poor perfusion heal more slowly than those who have good perfusion and oxygenation. Herein lies the paradox. How does hypoxia, which stimulates macrophages to release growth factors, co-exist with the clinically observed beneficial effects of hyperoxia? This study attempts to explain this paradox by studying endothelial cell response to VEGF in varying oxygen tensions in the Matrigel angiogenesis model. We hypothesized that tissue hyperoxia, contrary to established thought, would enhance angiogenesis.

METHODS: We studied angiogenic response to standardized stimuli under increasing oxygen environments using the murine Matrigel angiogenesis model (Passaiti *et al.*, 1992). We chose the murine matrigel angiogenesis assay because of its technical feasibility, its *in vivo* design, its ideal properties as a substrate for endothelial cell migration and growth, and its capability of PO_2 measurement. Matrigel is a basement membrane complex containing primarily laminin and type IV collagen. It contains minute amounts of growth factors, including transforming growth factor beta (TGF-B), epidermal growth factor (EGF) and platelet derived growth factor (PDGF), but does not stimulate angiogenesis when this assay is used under normal circumstances. At 4°C Matrigel is a liquid, but after injection subcutaneously into mice, it reconstitutes as a gel between 22–35°C.

Two 1 milliliter injections of Matrigel were placed subcutaneously into the dorsum of 5 month old retired breeders, female Swiss-Webster mice. The control group I consisted of Matrigel alone (1 ml), while VEGF (100 ng) *or* anti-VEGF antibody (1 µg) were separately added to the Matrigel prior ro injection for groups II and III. Each group was divided into four sub-groups and exposed to varying oxygen environments: (1) continuous room air; (2) 100% oxygen at 1 atmosphere (1 ATA); (3) 100% oxygen at 2 atmospheres; and (4) 100% oxygen at 2.5–3.0 atmospheres, with subcutaneous oxygen tension measurements via Clark electrode in all sub-groups. Each test group was treated for 90 minutes twice daily. At 7 days, the gel plugs were harvested and sections were graded, in a double blind fashion, for the extent of neovascular formation. Grading: 0 = no vessels; 0.5 = scattered vessels; and 1 = maximal vessels in all quandrants. Results were calculated as a mean angiogenesis score + standard error. All data were repeated to reconfirm its validity and this subsequent data is combined with the original pilot data.

RESULTS: Matrigel alone stimulated no angiogenic activity in the control (room air, 21% oxygen) group. This result is consistent with previous studies in other laboratories and our own. However, at higher oxygen tensions, as measured with a tissue oximeter, significant increases in angiogenesis were seen in all hyperoxic conditions when compared to controls. Our data showed that given this dosage schedule, a subcutaneous PO_2 of approximately 120 mmHg is needed to significantly effect angiogenesis. The peak effect seemed to occur at a subcutaneous PO_2 of 200–300 mmHg. Oxygen toxicity with pulmonary edema was seen in pilot studies in a 3 atmosphere group, with measured subcutaneous PO_2 of 450 mmHg. This may account for the tailing off of the angiogenesis score we saw in the 3.0 ATA 100% oxygen group.

VEGF supplemented matrigel plugs showed significantly higher angiogenesis score at 2.5 ATA when compared to controls. The amount of angiogenesis seen in the control group is consistent with our previous experience with VEGF supplemented matrigel. The 2.5 ATA group, however, shows the highest angiogenesis score we have seen using the murine matrigel angiogenesis assay and may have expressed the upper limits of this assay.

Importantly the anti-VEGF neutralizing antibody quenched the angiogenic potentiating effect(s) of hyperbaric oxygen. This effect adds foundation to the belief that increasing PO_2 potentiates the release and/or effect of VEGF within the wound.

DISCUSSION: The healing wound is thought by many to be a two compartment model comprised of the wound space and the vascularized connective tissue growing from the wound edge, which eventually replaces the wound space. The central wound space compartment is the regulatory compartment and the vascularized connective tissue is the responder compartment. Oxygen plays a pivotal role in both of these compartments. In the wound space, lactate and oxygen levels not only stimulate collagen synthesis, but also stimulate release of growth factors from macrophages and possibly other cells as well. In the responder compartment, oxygen is absolutely required for collagen synthesis and possibly helps endothelial cells to respond more effectively to growth factors, such as VEGF. Collagen synthesis is proportional to PO_2 over a range of 0 to about 250 mmHg. Angiogenesis in this study seems to be PO_2 dependent over about the same range.

The mechanism by which hyperbaric oxygen achieves angiogenesis is thought to be a stimulation by an oxygen-gradient phenomenon between these two compartments that Hunt, Knighton and Silver have found to be central in angiogenesis of normal wound healing (Knighton *et al.*, 1981, 1983; Silver, 1984). In normal wounds, the wound space is hypoxic compared to the neovascularized tissue. This phenomenon sets up a steep oxygen gradient across a short distance. This gradient attracts macrophages (Knighton *et al.*, 1984; Silver, 1984) and may stimulate them to produce VEGF, which in turn stimulates the endothelial cells in the high end of the gradient to grow. However, the lactate concentration is not diminished in hyperoxia, becauseleukocytes release lactate whether they have oxygen or not.

Clearly, the oxygen-macrophage-VEGF-endothelial cell interaction is a main component of angiogenesis. We have previously demonstrated that lactate and hypoxia stimulate the macrophage to produce VEGF with resultant angiogenesis. These cells may then, when exposed to normoxia or hyperoxia, grow at a faster rate. The data presented in this paper clearly shows that oxygen must impact the macrophage-VEGF-endothelial cell pathway, acting at several possible points: macrophages, VEGF itself, or possibly endothelial cells response to VEGF.

The clinical use of hyperbaric oxygen therapy is limited to a maximal partial pressure of 2.0 to 2.8 ATA oxygen (Hammarlund, 1994) with a relative tissue PO_2, in this study of 200 to 300 mmHg. Exceeding this pressure, on this exposure schedule, adds no advantages and increases the toxic effect of oxygen (Hammarlund, 1994). We were able to show that the angiogenic response to a standardized stimulus is proportional to ambient PO_2 over a wide range. Anti-VEGF antibody inhibits the response to increased oxygen tension to below that seen in nonsupplemented matrigel. The paradox between low and high oxygen having similar effects, may be in part explained by the fact that endothelial cell response to VEGF may require oxygen and is upregulated in hyperoxia, while hypoxic areas of the wound stimulate cytokine and growth factor release from many cells. In addition, macrophages release VEGF at low PO_2 and, due to a separate mechanism, also release VEGF at very high PO_2. we postulate that VEGF released by macrophages may be diphasic and is a focus of some future research. This data helps explain some of the beneficial effects of hyperbaric oxygen on wound healing and more specifically upon angiogenesis.

REFERENCES:

1. Shweiki D. *et al.* (1992). Vascular endothelial growth factor induced by hypoxia may mediate hypoxia-initiated angiogenesis. Nature 359: 843–845.

2. Passaniti A. *et al.* (1992). A simple, quantitative method for assessing angiogenesis and antiangiogenic agents using reconstituted basement membrane, heparin, and fibroblast growth factor. Lab. Invest. 67: 519–528.
3. Knighton D. *et al.* (1983). Oxygen tension regulates the expression of angiogenesis factor by macrophages. Science 221: 1283–1289.
4. Knighton D. et al. (1981). Regulation of wound healing angiogenesis: Effect of oxygen gradients and inspired oxygen concentration. Surgery 90: 262–270.
5. Silver I. (1984). Cellular microenvironment in healing and non-healing wounds. In: Soft and Hard Tissue Repair. T.K. Hunt et al. (Eds.) New York: Praeger, pp. 50–66.
6. Knighton D. et al. (1984). Regulation of repair: Hypoxic control of macrophage mediated angiogenesis. In: Soft and Hard Tissue Repair. T.K. Hunt et al. (Eds.) New York: Praeger, pp. 41–49.
7. Hammarlund C. (1994). The physiologic effect of hyperbaric oxygen. In: Hyperbaric Medicine Practice. E.P. Kindwall (Ed.) Flagstaff, Arizona: Best Publishing Co., pp. 17–32.

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HYPERBARIC OXYGEN THERAPY IN THE MANAGEMENT OF CLOSTRIDIAL GAS GANGRENE

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INTRODUCTION: In the past, advances in the treatment of clostridial myonecrosis were limited to the method and extent of surgical debridement or to variations of antibiotic therapy. The results of the addition of hyperbaric oxygen therapy (HBO) to the treatment of clostridial gas gangrene have been reported to be dramatic, in terms of both decreased mortality and saving of viable tissue and functional limbs.

METHODS: Fifty-two cases with clostridial gas gangrene were treated in the Turku University Hyperbaric Centre. The presumptive diagnosis was made on the basis of the clinical picture and the presence of gram-positive rods on smear. Each patient underwent surgical debridement, antibiotic treatment and HBO therapy.

RESULTS: In the clinical material, 22 cases had diffuse spreading myonecrosis, 14 of whom survived. Thirty patients developed clostridial cellulitis with toxicity, 26 survived. The overall mortality was 23%. All 12 patients who died had been transferred from other hospitals of the country and were already moribund on arrival.

CONCLUSIONS: The addition of HBO to the treatment protocol of gas gangrene has improved the overall results. Hyperharic oxygenation in gas gangrene is life-, limb- and tissue saving, it clarifies demarcation, inhibits toxin production and augments tissue repair. Early diagnosis remains essential for final outcome. Patient survival can be achieved if the disease is recognized early and appropriate therapy applied promptly.

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PYODERMA GARGRENOSUM AND HYPERBARIC OXYGEN THERAPY: A CASE REPORT

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INTRODUCTION: Pyoderma Gangrenosum (PG) is characterized by exacerbations and remissions of morphologically unique skin ulcers. It is frequently thought to be the cutaneous manifestation of an underlying systemic disease. The efficacy of HBO in this disease has been reported by several investigators.

METHODS: A 56 years old woman, allergic to corticosteroids, with arm ulcers characteristic of PG was treated with HBO (2.5 ATA for 60 min. daily). She had associated Crohn's disease. RESULTS: The ulcers were observed to heal with HBO. Newly formed epithelium was evident growing inwards from the margins. The abundant formation of granulation tissue and the ability of the HBO to arrest further extension of the ulceration was observed. The pain disappeared after the first day of therapy.

CONCLUSIONS: HBO might become the treatment of choice for all ulcers of PG type.

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MORTALITY RISK FACTORS AND PREDICTIVE PROGNOSTIC EVALUATION BASED ON STRATIFICATION ON SEVERITY LEVELS (PHASE 1, 2, 3, 4) IN PROGRESSIVE NECROTIZING INFECTIONS OF SOFT TISSUE

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INTRODUCTION: The purpose of the study was to identify elementary clinical parameters obtainable at the patient's bedside, for clinical decision making.

METHOD: The authors have identified 7 variables taken from anamnestic data and clinical symptoms observable on examination. The evolution of each of these seven variables was evaluated in the subsequent phases and in relation to mortality/survival.

RESULTS: Of 94 cases admitted in the period 1991 to 1995, there were 68 males and 26 females (ranging in age from 17 to 87). Mortality = 17.2% (16), survivors 82.98% (78). Age-related mortality = 6.67% (under 49), 26.5% (over 49). Fisher's exact test: $Chi^2 = 6.55$; $p = 0.01$. Mortality in acute associated pathologies was 33.33%, and in cases without other acute pathologies, 10.45% ($Chi^2 = 7.14$, $p = 0.01$). The combination of diabetes, peripheral vasculopathy and obesity in patients over 49, increased mortality to 30.30%, compared with mortality = 0 in patients under 49 without the these pathologies ($Chi^2 = 4.68$; $p = 0.04$). Slow evolution mortality = 29.63%; rapid evolution = 5.45%; fulminant evolution = 41.67% ($Chi^2 = 13.41$; $p < 0.01$). Evolution-related mortality at outbreak was evaluated in cases treated with promptitude and three-therapy. Symptoms-related mortality = 3.3% for *phase 1,* 24.15% for *phase 2,* 100% for *phase 4;* mortality = 0 for *phase 3* with two patients surviving (Chi^2 (3) = 11.94; $p = 0.01$).

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HBO RATIONALE IN SURGICAL RECONSTRUCTION OF PHARYNGOSTOMA

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INTRODUCTION: The surgical reconstruction of pharyngostoma after hemipharyngo-laryngectomy, or pharyngotomy, often fails and surgery must be repeated. Pharyngostomes may be classified as simple and complicated. The former having small slits in the epipharynx and requiring only residual mucosa for closure, and

the latter having large ruptures in the pharynx or esophagus, thus requiring more tissue and muscle-cutaneous flaps.

METHOD: We had nine cases of complicated pharyngostoma, all occurring after plastic surgery. The patients, males ranging in age from 53 to 80 years, were affected by pharyngo-laryngeal carcinoma. In eight cases, we utilised the muscle-cutaneous flap of the large pectoral muscle for the reconstruction of the pharyngostoma; in only one case, we utilised the right sterno-cleido muscle. Every patient received HBO therapy before and after the operation. The treatments were conducted at 2.5 ATA and comprised 3 cycles of 20 min. 100% oxygen breathing followed by a 5 min. air break.The four cases which will be discussed were: (1) Patient AR (aged 79): laryngeal carcinoma. The patient received 37 HBO treatments. (2) Patient AL (aged 60): laryngeal adenocarcinoma. The patient recieved 30 HBO treatments. (3) Patient TP (aged 53): pharyngo-laringeal adenocarcinoma. The patient recieved 24 HBO treatments. (4) Patient CS (aged 68): epidermoidal carcinoma of left emilarynge. The patient received 11 HBO treatments.

RESULTS: Hyperbaric oxygen treatment (HBOT) in the pre-operation stage eliminates the inflammation and improves the vitality of tissues near the stoma. HBOT applied post-operatively improves the cicatrization and sprouting of muscle-cutaneous lembs. HBOT produces spontaneous cicatrization only for small pharyngostoma. In fact, HBOT produces effects that allow the growth of muscle-cutaneous flaps. The surgical reconstruction of pharyngostomes is indispensable for neoplastic patients who underwent destroying operations.

CONCLUSION: We did not observe any recurrences, fistulas or esophageal stenoses within one year after the operation, for this reason we maintain that HBO therapy, applied pre- and post-operatively, is indispensable for all pharyngostomes, particularly for complicated or recurrent pharyngostomes.

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INDICATION ABOUT HYPERBARIC TREATMENT OF ASEPTIC NECROSIS OF THE FEMORAL HEAD (NATF)

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INTRODUCTION: The aseptic necrosis of the femoral head is a pathology, which is exponentially increasing in the world population; this is due to the use of more efficacious diagnostic imaging and to the modifications in characteristics and quality of life. We analyzed 109 cases of NATF, evaluated according to Ficat's classification, together with NMR images for diagnosis, both before and after the treatment.

METHODS: Patients received 20 to 60 hyperbaric oxygen treatments at 2.2 ATA for 90 minutes (100% O_2 breathing).
RESULTS: 96% of hips classified in Ficat >2 faced a prosthetic joint replacement (28 cases), and 94% of hips classified in Ficat < 2 recovered from the necrosis completely.

CONCLUSIONS: Precocius diagnosis and the timeliness in hyperbaric treatment allows almost complete recovery of femoral head necrosis classified at < 2 Ficat's stage; on the contrary we do not see any necessity of hyperbaric treatment in cases classified Ficat >2.

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THE ROLE OF HBO IN TREATMENT OF ANORECTAL AND COLIC DISEASES DETERMINED BY CLOSTRIDIUM DIFFICILE

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INTRODUCTION: Clostridium difficile is the main agent of colorectal diseases in adult patients. It is very important to determine the prevalence of clostridium in the stool samples. This study was designed to evaluate the therapeutic effect of HBO on anorectal, and colic diseases determined by clostridium difficile.

METHODS: Diagnosis of clostridium difficile disease requires the following: (1) Initial abdominal pain with diarrhoea; (2) semiformed and greenish stools with blood; (3) days of hospitalisation; (4) beginning of symptomatology after one or more weeks of antibiotic administration; (5) leukocytes in stools; (6) therapeutic administration of cephalosporins;(7) the endoscopic examination reveals a hypertrophic, green and sparsely haemorrhagic mucosa. These signs are often combined with positivity for clostridium difficile toxin revealed by immunoenzymatic system (EIA) in 37 vs. 45 of our patients, and in 3 by examination of tissue culture. In 33 patients (of 37 with positivity for toxin of clostridium difficile) we had positive results in the first sample of stools; 2 in the second sample and 2 in the third. On the whole, the predictive negative value of the first sample of stools was 98% and, in all patients with two or more clinical or laboratory predictive signs, we made diagnosis of infectious disease by clostridium difficile when the first or second sample of stools was positive for specific toxin by immunoenzymatic system.

RESULTS: On the basis of our experience in treating anorectal-colic disease, we consider the following regimens of hyperbaric oxygen therapy efficacious: the first cycle of treatments is conducted at 2.5–2.8 ATA for 90 min (20 min on 100% O_2 and 5 min on air, repeated for 90 min.) for obtaining the antioedemogenic and antibacterial effects. This protocol is repeated twice daily for 10–15 days; the second cycle of treatments is conducted at 2.2–2.5 ATA, one treatment daily for 15–20 days with the same intervals for breathing air, and enhances the repairing process.

CONCLUSION: Hyperbaric oxygen in the treatment of clostridial infection is beneficial because: (a) it increase the interstitial PO_2, even in conditions of reduced capillary blood flow; (b) it reduces the interstitial oedema, improving the perfusion of the damaged area, improving the aerobic metabolism of cells and reducing the release of oxygen free radicals or stimulating the enzymatic production of scavengers, resulting in a reduction of xanthine-oxidase; (c) it reduces the release of prostaglandins, leukotrienes, serotonine, and bradykinine, enhancing neutrophil activation that opposes growth of clostridium difficile. Finally, it is very important to combine HBOT with an alkaline diet to solve critical clinical conditions. HBOT should be applied immediately after microscopic examination of stools with lactoferrine indicates positivity for toxin of clostridium difficile by immunoenzymatic assay.

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SUDDEN DEATH AFTER HYPERBARIC OXYGEN THERAPY – A CASE REPORT

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INTRODUCTION: We report the case of a patient referred for hyperbaric oxygen following parasuicidal carbon monoxide (CO) poisoning, who died fifteen minutes after the end of treatment.

CASE REPORT: A man of 75 years experienced chest pain at 07.30. He tried to avoid hospital admission by killing himself with car exhaust. At 08.30, he was discovered unconscious in the garage. ECG showed atrial fibrillation, and a chest X-ray was said to be normal. Breathing 60% oxygen, he was transferred by helicopter to the nearest hyperbaric unit (60 miles away) arriving at 16.00. He received the US Air Force CO table. He sustained a tonic/clonic convulsion five minutes after the treatment ended, and died in electromechanical dissociation less than ten minutes later. Post mortem, cardiac tamponade from haemopericardium due to a ruptured thoracic aortic aneurysm was found. The chest X-ray from the referring hospital was later reported as abnormal. There was no myocardial infarction.

CONCLUSIONS: The cause of the convulsion is debatable, but may have involved the 'off oxygen' effect. Death was probably inevitable. The responsibility for diagnosis should rest with the referring hospital.

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SUDDEN SENSORINEURAL DEAFNESS: TREATMENT WITH HYPERBARIC OXYGEN THERAPY AFTER FAILURE OF A TEN DAY COURSE OF "CLASSICAL" DRUG THERAPY

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INTRODUCTION: The optimal treatment of Idiopathic Sudden Sensorineural Deafness (ISSD) is not well defined. This is partly due to the fact that there can be no causal therapy for a disease of which the cause is not known. The therapeutic outcome of several proposed drug treatment regimes is in the same range as the spontaneous recovery rate, which can be as high as 65%.

METHODS: During the last two years, 26 patients have been treated with Hyperbaric Oxygen Therapy (HBOT) following a strict stepwise therapeutic protocol. All patients were treated initially with high-dose intravenous steroids, associated with hypervolemic haemodilution, if indicated. Only upon failure of this treatment after 10 treatment days, were patients additionally treated with HBOT (daily sessions at 2.5 ATA for 90 minutes).

RESULTS AND CONCLUSIONS: After a mean of 11 HBOT sessions (9–30), we observed an average hearing gain of 43% (±23%), that persisted up to a 3-month follow-up. This compares favourably with reports in the literature, and is consistent with a previous study by one of us (Desloovere, 1988). Because of the lack of randomised prospective studies, this preliminary uncontrolled study will now be extended and randomised versus placebo, to include a valid control group.

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HOW MANY HBO TREATMENTS ARE NECCESSARY FOR THE THERAPY OF SUDDEN DEAFNESS AND ACUTE TINNITUS?

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INTRODUCTION: Since the 1st ECHM conference (1994) sudden deafness is an accepted HBO indication. The aim of this study was to evaluate HBO effectiveness in sudden deafness/acute tinnitus according to number of treatments (10/15).

METHODS: Patients with sudden deafness and acute tinnitus were treated with HBO after standard treatment (i.v. infusions, rheological drugs) without sufficient improvement. Prior to HBO therapy, after 10 and 15 treatments, and at least 3 months later, we took a tone audiogram and/or a questionaire with a visual analogue scale (VAS) according to recommendations of the 4th International Tinnitus Seminar, Bordeaux ('91) to determine tinnitus loudness. In the tone audiogram, a threshold recovery in 2 frequencies of over 10 dB and up to 20 dB was regarded as improvement, and over 20 dB as good improvement. In VAS we regarded 50% or less of initial loudness as improvement. Patients were treated 15 times on six days/week, breathing 100% oxygen for 60 min. at 250 kPa.

RESULTS: From January to June 1996 we treated 129 patients. Mean delay after onset of symptoms was 6 weeks. In patients with sudden deafness (n = 43) improvement in hearing was achieved in 11 patients (25.6%) after the 10th treatment and 14 patients (32.6%) after the 15th HBO session. Follow up at ≥3 months after HBO showed similar results (13 patients). Acute tinnitus loudness was found to decrease by ≤ 50% in 10.9% of the patients after 10 treatments, and in 45.0% of the patients after 15 treatments (n = 129). In the follow up, these results were kept within 39.8% (n = 123).

CONCLUSIONS: In sudden deafness and tinnitus 15 HBO-treatments show better results than 10 treatments. These results are confirmed by a follow up 3 months after HBO.

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TREATMENT OF PSORIASIS BY HYPERBARIC OXYGENATION COMBINED WITH PSORALEN+ULTRAVIOLET LIGHT (PUVA) THERAPY

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INTRODUCTION: The study was based on three outcomes in pathophysiologic process in psoriasis: local hypoxia in psoriatic plaques, increased intensity of local peroxidative activity and oxygen dependent reaction in Psoralen-Tymin base conjunction.

METHODS: 13 subjects with clinical manifestations of psoriasis. Eight subjects were treated with PUVA therapy over a period of 10 years. Recidivism was frequent and remissions poor. Subjects were divided in two groups and all underwent HBO therapy. Group A (8 subjects: 5 males & 3 females) continued previous PUVA therapy with simultaneous HBO treatment of 10 sessions. Group B (5 subjects: 2 males & 3 females) underwent only HBO treatment (20 sessions).

RESULTS: In group A, the remission period was on average 9.5 months. In group B remission was on average 4.8 months.

CONLUSION: HBO therapy evidently improves results of PUVA therapy in treatment of psoriasis.

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INVITED LECTURE: SYNAPSES UNDER PRESSURE: THE Ca^{2+} CHANNELS ENIGMA

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Pressure, like temperature, is one of the fundamental physical variables, which constrain living entities. The study of pressure effects on biological systems is motivated by biophysical, environmental, evolutionary and diving medical reasoning. Synaptic transmission is the most pressure-sensitive event in nerve cells function. Previous studies at a single release site in crustacean neuromuscular synapses, using intracellular synaptic potentials (EPSPs, IPSPs) and extracellular synaptic currents (EPSCs) measurements revealed important aspects of the cellular mechanisms underlying pressure (helium 0.1–10.1 MP) effects. High pressure depressed (60%) single excitatory (glutamate-mediated) synaptic responses and slowed their release kinetics. However, frequency dependent dynamic responses such as facilitation and potentiation were enhanced. Postsynaptic- as well as presynaptic inhibitory (GABA-mediated) responses were similarly affected. Pressure increased the frequency of the spontaneous miniature EPSCs (mEPSCs), observed usually in low yield (LY) synapses, but had little effect on their amplitude histogram. Statistical quantal analysis revealed that pressure decreased the mean number of quanta released per single EPSCs (quantal content, m) without changing the quantum current (q), greatly decreased the number of available active zones (n), but the effect on the probability of release (p) was different for various types of synapses, and that "giant" mEPSCs (size of 2–5 q) coexisted with depressed evoked EPSCs. High $[Ca^{2+}]o$ could antagonize, whereas low $[Ca^{2+}]_0$ mimicked most of the pressure effects on the evoked responses. Analysis of theoretical models of synaptic release in crustacea suggested that pressure depresses the maximal entry of Ca^{2+} into the presynaptic terminals. Further experiments in frog peripheral nerve have demonstrated, that pressure moderately decreases presynaptic action potential Na+ current, and greatly diminishes the amplitude, depresses the maximum, and possibly shifts the voltage dependence of Ca^{2+} current through N-like (ω-CgTx sensitive), less so in L-like (dihydropiridines sensitive), voltage-gated Ca^{2+} channels that are associated with transmitter release. Heinemann et al. (1987) have noticed that L-type Ca^{2+} current was not sensitive to high pressure in chromaffin cells. Other evidence suggested that N-type Ca^{2+} channels are more sensitive to various biochemical and physical perturbations. The question that arises, is how CNS synapses react to increase in pressure in view of all these findings?

Fagni and his colleagues have demonstrated in brain slices, that pressure depressed both population EPSPs (pEPSP) and the resultant population spikes (PS) in Schaffer collaterals- pyramidal cells excitatory synapse in CA1 hippocampus region. Nevertheless, a general hyperexcitability of the cells was attributed to decrease in GABA transmission and enhanced excitation mediated by NMDA receptors. Similar 45% reduction in pEPSP, but with little effect on the PS, was observed in the perforant path-granular cells excitatory synapse in the dentate gyrus. This was associated with increased facilitation in a normally depressing synapse, increased frequency response, and hyperexcitability. However, presynaptic mechanisms were postulated. In both synapses, N-type Ca^{2+} channels are responsible for about 50% of the release, whereas P-Q-type channels (ω-AGA-IVA sensitive) may be responsible for 60–70% of the release. In the cerebellum, the parallel fibers (PF) synapse onto Purkinje cells responded to high pressure almost identical to crustacean synapses, whereas the robust climbing fibers (CF) excitatory input on the same cells was almost resistant to pressure (less than 10% reduction in EPSP). The relative composition of Ca^{2+} channels in the PF synapses is N-type 30%, P-type (no Q-type) 50%, and unknown 20%, whereas in CF synapses it is not clear. In rat spinal cord, pressure eliminates all glycinergic inhibition and about 80% of the GABAergic inhibition of the monosynaptic reflex. N-type Ca^{2+} channels are responsible for 52%, and P-Q type for 90% of the glycinergic response.

In conclusion, high pressure reduces presynaptic Ca^{2+} inflow and depresses evoked synaptic transmission mainly by modulating the presynaptic quantal release parameters. However, the severity of the effects seems to be correlated with the proportion of the pressure sensitive N-type Ca^{2+} channels present in each presynaptic terminal. The increasing knowledge about the coexistence of a variety of Ca^{2+} channels in CNS synapses suggest that quantitative pressure effects would be synapse specific, thus the final response would be circuit specific.

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THE INTRACEREBRAL MICRODIALYSIS TECHNIQUE USED FOR IN VIVO RECEPTOLOGICAL STUDIES IN THE HYPERBARIC FIELD

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INTRODUCTION: Pressure and inert gases act at the phospholipid membrane level. Usually, binding experiments are conducted on isolated receptors. Intracerebral microdialysis is a new technique allowing direct receptological experiments on *in vivo* diving animals.

METHODS: Direct binding experiments have been performed, *in vivo* and under hyperbaric conditions, by perfusion, in the dialysis probe, of radioactive H^3-Spiperone solutions. Competition experiments between the initiated antagonist and cold ligands permitted direct studies of the D_2 dopaminergic receptors, when the dialysis probe was inserted in the striatum. These studies have been done under 5 MPa Heliox, 1.7 MPa Nitrox and 70% normobaric normoxic Nitrous Oxide environments.

RESULTS: While the animal is kept under hyperbaric conditions, direct (on line) measurement of the radioactive dialysates, demonstrated significant differences between HPNS and narcotic conditions: D_2 receptor being inhibited under pressure when an induction or an arousal of their affinity have been noticed under narcotic atmospheres.

CONCLUSIONS: Differences in D_2 receptor variations under narcosis or under high pressure allowed us to explain the respective decrease or increase in dopamine extracellular levels under the same conditions.

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HIGH PRESSURE OF HELIOX INDUCED STRIATAL GLUTAMATERGIC HYPERACTIVITY: A MICRODIALYSIS AND BEHAVIORAL STUDY

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INTRODUCTION: Previous studies have suggested that HPNS could be linked toglutamatergic neurotransmission changes at the central level. Moreover, neurochemical studies have demonstrated that the striatum, a structure which receives glutamatergic projections from cortical area, has a share in the hyperbaric locomotor and motor hyperactivity (LMA) development. In this work, we used microdialysis to monitor the extracellular level of glutamate at the striatal level in a rat submitted to 8 MPa of helium oxygen mixture and study the effects of intrastriatal injection of 2-APH, and NMDA antagonist, on some behavioral disorders.

METHODS: In free moving rats, we used the microdialysis technique associated with an actimetric device as previously described. A canula was stereotaxically implanted in the striatum. Amino acid contents of microdialysates were analysed using HPLC-FD. In behavioral studies, rats were pretreated by 20nmol of 2-APH locally administered in the striatum before pressure exposure. Hyperbaric conditions consisted of a compression rate of 1 bar/min to 8 MPa and a 3 h stage under pressure.

RESULTS AND CONCLUSIONS: Neurochemical studies showed that pressure induced both glutamate and glutamine increase ($P < 0.01$) in the striatum at the extracellular level. These results confirm the previous hypothesis of Chapman et al. (1986) and suggest that pressure could enhance the glutamatergic synaptic activity. The pharmacological study has shown that 2-APH striatal injection decreases the LMA. Thus, we suggest that pressure induces hyperactivity of striatal NMDA receptors, which has a share in the LMA, and that the striatal glutamate increase could participate in the NMDA receptors mediation enhancement.

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HPNS INUCED MORPHOLOGICAL CHANGES IN RAT BRAIN

J. Wenzel, H. D. Mennel and G. Stumm.

Abstract not received. Full paper available in the Proceedings of the meeting.

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LATENCY TO CNS OXYGEN TOXICITY IN RATS AS A FUNCTION OF CO_2 PRODUCTION AND PO_2

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INTRODUCTION: CNS oxygen toxicity can occur as convulsions and loss of consciousness, without any warning symptoms . We made a quantitative study of the effectof metabolic rate on sensitivity to oxygen toxicity in the rat.

METHODS: Nineteen rats were exposed (126 exposures) to twelve combinations of four pressures (456, 507, 608 and 709 kPa) and three ambient temperatures (15, 23 and 29°C) until the appearance of the first electrical discharge (FED) preceding the clinical convulsions. Carbon dioxide production (VCO_2) was also measured.

RESULTS: A thermoneutral zone (VCO_2 = 0.87 ml/g.h) exists between the temperatures of 24 and 29°C; at temperatures lower than this, the metabolic rate increased by 1.2 to 4 times the resting level. Latency to the FED decreased linearly with the increase in VCO_2, at all four oxygen pressures. The slopes (absolute value) and intercepts decreased linearly with the increase in oxygen pressure.

CONCLUSIONS: We derived two alternative equations which describe latency to the FED as a function of both oxygen pressure and metabolic rate. Various environmental and otherphysiological factors said to influence sensitivity to CNS oxygen toxicity can be explained by their effect on metabolic rate. In situations where there is a risk of CNS oxygen toxicity, that risk would be reduced by a low metabolic rate.

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COMPARISON BETWEEN NITROGEN NARCOSIS AND NORMOBARIC NITROUS OXIDE NARCOSIS. NEUROCHEMICAL AND BEHAVIOURAL ASPECTS

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INTRODUCTION: In order to use normobaric Nitrous Oxide breathing mixtures as models of pure narcosis, independently of the hydrostatic pressure effects, it is necessary to verify that the neurochemical and behavioural variations produced respectively by Nitrox and N_2O are similar.

METHODS: Neurochemical studies using intracerebral microdialysis were performed under 20, 40, 60 and 80% of N_2O normobaric mixture and under 0.9 and 1.7 MPa of Nitrox. Analysis concerned essentially the dopaminergic striatal pathways. Behavioural Fixed Ratio 15 experiments have been performed in the same conditions.

RESULTS: Neurochemical studies show a significant 70% decrease in extracellular dopamine concentration at once under 60 % N_2O and under 0.9 MPa Nitrox. There is also a behavioural correlation between the two breathing mixtures expressed by the decrease of the lever press number in the Fixed Ratio test.

CONCLUSION: A scale of narcosis bas been established for the first time, concerningneurochemical and behavioural results, under N_2O and Nitrox. Correlations exist between the two narcotic mixtures, but some differences still remain, especially concerning DOPAC.

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NEUROCHEMICAL AND BEHAVIOURAL STUDIES OF AN EVENTUAL ADAPTATION TO NARCOSIS

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INTRODUCTION: Inert gas narcosis is the major factor decreasing a diver's capacity in the range of 0–100 m. The aim of this study was to verify the existence of an adaptation to narcosis, by conducting neurochemical and behavioural experiments, re-

spectively, before and after repeated exposures to a narcotic Nitrous Oxide breathing mixture.

METHODS: The neurochemical studies consisted of a double stereotaxic implantation of microdialysis probes in the left and right striatum. The first measurement was performed on one side during a 2 hour exposure to 60% N_2O, while the second was performed on the other side after 8 successive exposures of 120 min. each to 60 % Nitrous Oxide. The analysis focussed on dopamine and its metabolites. An identical protocol was established, concerning behavioural studies, with a visual detection test, in which rats were required to respond to a slight luminous increment of the houselight (from 3 to 11 lux).

RESULTS: The neurochemical study demonstrated a marked difference in the variation of dopamine before (70% decrease) and after (40% increase) the repetitive exposures to narcotic conditions, but the behavioural responses were not significantly altered by the 8 successive exposures to 60% normoxic Nitrous Oxide.

CONCLUSIONS: The differences between neurochemical and behavioural responses will be discussed. Experiments should be conducted on man in order to check, if repetitive exposures of professional divers to normobaric narcotic conditions may lead to an increase of their capacities during an operational dive, under Nitrox, in the range of 0–80 m.

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TRINATIONAL (SWISS-AUSTRIAN-SLOVENE) SATELLITE MEETING ON DIVING AND HYPERBARIC MEDICINE

Bled, Slovenia
September 20, 1997

INTRODUCTION

TRIALS AND TRIBULATIONS OF DIVING AND HYPERBARIC MEDICINE IN SLOVENIA

Igor B. Mekjavić[1, 2] and Branko Brodnik[3]

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Diving and hyperbaric medicine are in their infancy in Slovenia. Until recently, patients requiring hyperbaric oxygen therapy were regularly forwarded to Hyperbaric facilities in neighbouring countries. At the instigation of the Department of Automatics, Biocybernetics & Robotics (Jozef Stefan Institute, Ljubljana) and with the generous support of the Ministry of Science and Technology (Slovenia), the author established a Baromedical Laboratory in the Institute of Physiology (School of Medicine, Ljubljana), with the aim of introducing this new branch of Medicine in Slovenia. Since the laboratory's official opening in 1995, the main focus has been research and training of medical personnel. Despite the fact that hyperbaric oxygen therapy has gained wide acceptance among physicians in Slovenia, the use of hyperbaric oxygen is not an approved procedure, even for diving accidents. An application for approval of the use of hyperbaric oxygen for indications specified by the European Committee on Hyperbaric Medicine and the Undersea Hyperbaric Medical Society, submitted in 1995, is currently being reviewed by the Slovene Medical Council (Ministry of Health, Slovenia). In the interim, hyperbaric oxygen therapy is performed on a regular basis, but only as an experimental procedure. Physicians wishing to provide their patients with hyperbaric oxygen therapy are required to submit an application to the Ethics Review Committee, and to inform their patients that the procedure is experimental and not approved by the Ministry of Health. Consequently, the laboratory is not reimbursed for these treatments, and the treatments are conducted on a volunteer basis by the physicians and staff of the Baromedical Laboratory. To enhance the safety of recreational divers, who are not medically covered in case of diving accidents in Slovenia, the author established DAN-Europe/Slovenia. The XXIII Annual Scientific Meeting of the European Underwater and Baromedical Society and the Trinational (CH-A-SLO) Satellite Meeting on Diving and Hyperbaric Medicine, being held in Bled this year, are a form of recognition by our European colleagues of the efforts of all scientists, physicians and students that have assisted in the development of Diving and Hyperbaric Medicine in Slovenia. For this, and the honour of hosting these meetings we are extremely grateful.

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DEVELOPMENT OF DIVING MEDICINE AND HYPERBARIC OXYGEN THERAPY IN AUSTRIA

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Much credit for the development of diving in Europe must be attributed to Dr. Hans Hass from Vienna. His books and lectures inspired a generation of underwater explorers and scientists, among them Dr. Friehs who established the foundation of diving medicine and hyperbaric oxygen therapy in Austria. From 1964 to 1968, Dr. Friehs established contacts with Dr. Boerema in Amsterdam and Dr. Bernhard in Boston, and visited all existing hyperbaric facilities in Europe. During his one year fellowship in the hyperbaric facility at Childrens Hospital (Harvard Medical School, Boston, USA), he also visited all the hyperbaric facilities on the East Coast of U.S.A. With the commencement of the construction of the new Surgery Department in Graz, Dr. Friehs assisted with the planning and design of a Hyperbaric Chamber, which was subsequently constructed by Wagner-Biro Comp. (Graz). The hyperbaric facility in Graz was completed in 1971, and was the largest chamber in Central Europe at the time. Having introduced experimental neonatal heart surgery under 3 ATA HBO and short circulatory arrest in 1969, Dr. Friehs and his colleagues commenced with HBO treatments for a variety of indications. In 1974, personnel of the Graz hyperbaric facility collaborated with the Fire Fighting School of Styria to develop a SCUBA diving training programme. During the construction of the Vienna Underground in 1980, supervised by the Arbeiter-Samariter Bund, the Graz hyperbaric facility was responsible for treatment of decompression accidents. In 1990, Dr. Mader commenced HBO treatments in Vienna, using a Haux Chamber. Finally, in 1994 the Austrian Society for Diving and Hyeperbaric Medicine was established. The latest development in the Graz hyperbaric chamber has been the introduction in 1995 of combined 630nm KTP-DYE-LASER + 2 ATA Hyperbaric Oxygenation in PHOTOSAN-3 Photodynamic Therapy + 450 local Hyperthermia, as an adjuvant following tumor surgery inside the chest; or endoscopic desobliteration of stenotic and otherwise inoperable cancer of the tracheobronchial tree and esophagus.

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DIVING AND HYPERBARIC MEDICINE IN SWITZERLAND

P. Knessl

Despite its long stretched lake shores, Switzerland can hardly be described as a maritime nation. Therefore, no naval medicine could foster the development of civilian diving and hyperbaric medicine, as in most of the surrounding countries. The tiny Swiss

civilian diving sector could not support any progress in this field. Such unfavourable conditions were, from time to time, compensated by personal courage and scientific interest of a few. Since the introduction of diving computers into the general diving scene, the knowledge of the "Swiss table" has become widespread. The credit for the development of the Swiss Dive Tables must be attributed to the late Prof. A.A. Bühlmann of the Department of Medicine at Zurich University, and to his coworkers in the medical and diving field. The first small hyperbaric chamber in Zurich became operational in 1959. The next large unit, designed for mixed gas deep diving experiments, served during the sixties and seventies not only for basic research, but also as an emergency treatment centre. The slowdown in the expansion of the offshore oil industry and partial replacement of manned deep sea diving operations by robotic devices seriously affected the research activity in Zurich too.

Nowadays, the size of the Swiss diving population is quite large. History of organized sport diving in Switzerland dates back to the year 1957. Physicians interested in diving have been officially involved since the creation of the medical commission of the Swiss Underwater Sports Federation in 1959. In the early eighties a need was felt for an independent medical society. Efforts, mainly by our French speaking colleagues and namely of Dr. Gloor, led in 1985 to the foundation of the Swiss Underwater and Hyperbaric Medical Society SUHMS. From the very beginning, the Society accommodated mainly physicians interested in diving medicine and actively diving physicians as ordinary members, but offered an extraordinary membership to the non-medical public as well. A number of members are actively involved in the practice of hyperbaric medicine and in many international committees and societies. Physicians responsible for the University Hospital-based hyperbaric units form a working party within the Society.

The activity during the past 12 years has focused mainly on enhancing public awareness and diving accident prevention. Several symposia have been organised in the past, including a satellite to the annual meeting of the Swiss Society of Intensive Medicine in Lausanne. In addition, the diver's emergency tag was created and editions of the "Manual: Fitness to Dive" punlised in German and French. From 1986 to 1992, three Symposia on HBO, the last one combined with the XVIIIth Annual Meeting of the EUBS, were organized in Basel by the present Society president Dr. Schmutz. Diving and Hyperbaric Medicine is not yet recognised as a specialty, and presently has a marginal role in the realm of Swiss medicine. Regardless, SUHMS is a regular member and an official partner of the Swiss Medical Federation. It provides consultation to the insurance companies and to sport diving organizations.

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HYPERBARIC OXYGEN

CLINICAL APPLICATION OF HYPERBARIC MEDICINE IN SWITZERLAND

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There are 5 medical faculties in Switzerland. All are provided with a hyperbaric chamber, one of them being located outside of the hospital walls. Another is located in a major non-universitary hospital, two are in private clinics and one is free standing. The most busy chambers are those of Basel, Lucerne and Zürich. This report will deal with the general situation of HBO in Switzerland and on some of the activities of these centers with special reference to acute and elective surgery in maxillo-facial problems (Kantonsspital Zürich), acute accoustic trauma (Kantonsspital Luzern) and reperfusion problems of the skin in elective and reconstructive surgery of the knee and the ankle (Kantonsspital Bruderholz).

Retrospective data with case studies will be presented and discussed.

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CO INTOXICATION AND HBO

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INTRODUCTION: Carbon monoxide (CO) poisoning is the most frequent occupational intoxication in Western civilised countries. Inhalation of CO results in tissue hypoxia not only by binding to haemoglobin and myoglobin, but also by affecting cytochrome P-450 and by inhibition of cytochrome a3 oxidase. Recent studies have demonstrated that the actual CO-Hb and the clinical symptoms of intoxication may be strikingly incongruous. Low levels (10–20%) of CO-Hb cause minor symptoms, suh as drowsiness, headache and nausea; higher levels (>20–50%) result in precoma, coma and myocardial disturbances. Death occurs at 60–70 %CO-Hb. Myofibril degeneration and even late neurological sequelae have also been reported afer CO exposure.

INDICATIONS: As a therapeutic intervention, hyperbaric oxygen (HBO) is not only recommended in acutely intoxicated patients (early indication), but additionally in patients with neurological or cardiac dysfunction. Furthermore, a history of unconsciousness is an indication for HBO, even if the actual blood CO content has already returned to normal values.

METHODS: In our centre, hyperbaric oxygen therapy is routinely carried out on every patient after CO exposure and usually consists of three sessions at 3 ATA for 60 minutes each, or adapted to the atual CO-Hb level and clinical signs.

RESULTS: Reviewing the data of 238 patients over a period of 20 years, the indication for HBO treatment is: (1) comatose patients (33%; CO-Hb = 1.8–68%), (2) patients displaying symptoms like nausea and vomitting (45%; CO-Hb = 0.8–48%), and (3) patients without symptoms (22%; CO-Hb > 15%). With the exception of four patients, all recovered completely. Two patients died from their severe burn injury, two patients never emerged from their deep coma.

CONCLUSIONS: Our data suggests that a routine HBO treatment may contribute to a satisfactory outcome in patients with CO intoxication.

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TREATMENT OF FROSTBITE WITH HBO

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Studies concerning tissue injury associated with burns have demonstrated that by preserving tissue oxygenation, cells within the zone of stasis can be saved and the extent of injury decreased. Hyperbaric oxygen (HBO) provides better tissue oxygenation, and is recognised as being beneficial in the treatment of burns. Progressive ischemia produced by thermal injury is similar to that of frostbite. Consequently, if HBO reverses progressive ischemia

in burns, we postulate that it may also be effective in the treatment of frostbite. Several case reports will be presented, which suggest that HBO therapy should be considered as an adjunct to conventional treatment of frostbite. We also propose that a multicenter study be initiated in collaboration with colleagues having the opportunity to treat frostbite cases.

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DIVING WITH DIABETES

E. Schenk

Vienna, Austria

Diabetes mellitus is an endocrine disease characterised by metabolic abnormalities and by long term complications involving the eyes, kidneys, nerves and blood vessels. Insulin dependent (IDDM) and non-insulin dependent (NIDDM) diabetic patients who wish to SCUBA dive should be able to control their blood glucose levels, and their Hb Alc values should not be less than 6.5%. They should also not have had any acute metabolic complications, such as diabetic ketoacidosis, hyperosmolar coma or hypoglycemia in the preceding 12 months. Diabetice divers should measure their blood glucose before and after each dive. The blood glucose before the dive should be > 150 mg%, and after the dive > 120 mg%. In general, it is advisable to increase the carbohydrate intake when diving. Alcohol should not be consumed 24 hours before diving. A diabetic diver should dive with a companion who understands the specific acute problems of this illness. Regarding long term complications, divers with diabetes need to carefully monitor their urine (microproteinuria) and blood pressure.

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CARDIOLOGICAL PROBLEMS

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SCUBA diving requires physiological adaptation as a consequence of the increased ambient pressure, changes in partial pressure of oxygen, breathing resistance and water temperature. Cardiac arrhythmias, bradyarrhythmias (sinus node dysfunction, AV conduction disturbances) or tachyarrhythmias (with or without premature complexes) may occur during SCUBA diving. Patients with arrhythmias Lowe III/IV using a bicycle ergometer, second degree AV block (Wenckebach) or third degree AV block, bifascicular block and syncope, must not SCUBA dive. Also, patients with ischaemic heart disease. Recently, myocardial infarction during SCUBA diving was attributed as the cause of death in a 27 year old diver, with undiagnosed severe endomyocardial fibrosis and arrhythmia.
Patients with systolic and diastolic murmur must have a Doppler echocardiogarphy and a Doppler flow echocardiogarphy before being allowed to dive. Valve regurgitation without hemodynamic importance during exercise requires regular echocardiography. Most patients with mitral valve problems are asymptomatic, but some might be prone to paroxysmal supraventricular or ventricular tachycardia.

CONCLUSIONS: In many cases, complete medical history, conscientious inspection and examination; electrocardiogram and roentgenogram should provide evidence of any cardiological problems. Occasionally, other methods such as echocardiography will be necessary.

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STANDARDS FOR FITNESS TO DIVE PROCEDURES

Jürg Wending

Bienne, Switzerland

There is an increasing consensus about the fitness to dive criteria for professional divers between the various European countries. This is mainly due to the excellent workshops organised by the EDTC. While the French have edited their regulations already in 1992, the German revision of the G31 regulations were edited in 1993, the most complex and modern approach are HSE (Health & Safety Executive) proposals of the British government. These regulations, presented in Newcastle 3/97, will be discussed. Points of special interest are the contraindications due to diabetes, asthma, AIDS, malaria drugs, coagulation disorders (factor V Leiden).
In contrast to professional divers, fitness to dive assessment for recreational divers is very variable. As there is no obligation for the divers to be checked, the compromise is to find the correct amount of investigations that fulfils our criteria for a validation procedure, but still not being too expensive and thus keeping away divers from being examined.
What about the qualification of the examining doctor of divers? This point is being studied by the subcommittee of the European Diving Technology Committee (EDTC) and the European Committee on Hyperbaric Medicine (ECHM). The proposals will be that the examining doctor should have a special training and certification, whereas initial and difficult assessments should be performed by diving medicine specialists with a more comprehensive examination.

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DEHYDRATION CAUSES DECOMPRESSION SICKNESS: REPORT OF TWO DIFFERENT CASES

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Strict adherence to decompression rules does eliminate the creation of asymptomatic microbubbles. Repetitive diving, increasing depths and bottom times augment the amount of microbubbles in the bloodstream that may cause typical symptoms of decompression sickness. This is a report of two experienced divers who had serious spinal cord symptoms after borderline decompression dives. Both were equipped with a diving computer for calculating decompression and were not aware of any mistakes when ascending to the surface. They both experienced severe spinal cord symptoms with motor insuffiency, a loss or irritation of sensibility, paresthesia and hyperreflexia.
One of the divers, a 42 year old Austrian diving instructor in very good physical condition, had lost a lot of fluid because of training for a competition (10 km jogging in warm climate) without drinking enough. Two hours later he went diving. Ten minutes after diving (40 min, max. depth 42 m) he had hemiplegia from TH 10 spinal segment, thoracic pain and respiratory insuffiency. After emergency treatment with 100% oxygen he was brought to a local hospital. There he received infusions, steroids, analgetics and further normobaric oxygen. A hyberbaric oxygen treatment was organized within three hours. After stabilization and clinical improvement he was transported back to Austria with an ambulance jet. In the chamber of the Department of Thoracic and Hyperbaric Surgery, University of Graz, he had 40 sessions of hyperbaric oxygen therapy.

At the beginning, he had to use a wheel chair, after daily improvements he was able to leave the chamber without help. One year after his accident he can walk a distance of about 3 kilometers without problems, but has a persisting loss of sensibility in the left leg and slight hyperreflexia. He is now fully reintegrated in his job. The other diver, a 28 old German PADI – Diving Instructor, did not ingest fluids after drinking huge amounts of alcohol and had little sleep the night before diving. Directly after diving (38 min, max. depth 44 m) he had motor insuffiency with weakness in both lower extremeties. After breathing normobaric oxygenand drinking 2 liters of water he improved, but 6 hours later the symptoms worsened again so that he had to be treated in a local hyperbaric chamber. After three sessions of HBO he was transported back to Germany by plane. There he had 30 HBO treatments (90 min; 2,5 ATA) and daily physical rehabilitation in Druckkammer – Centrum 1, Stuttgart. Before therapy, he was unable to stand on the right leg and had hyperaesthesia in the right and hyperreflexia in both legs. After the therapy he had no motor insuffiency, a slight hyperaesthesia in the right foot and reduced hyperreflexia.
We postulate that both divers were dehydrated, because of loss of fluid due to sports in warm climate and the hydrostatic differences with increased diuresis through diving. We conclude that dehydration due to the lack of fluid intake and excessive fluid loss after sports, were responsible for the developement of severe decompression sickness in these cases. In a state of dehydration, hemorheological unbalances favour otherwise asymptomatic microbubbles in blood to create decompression sickness.

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EVALUATION OF DECOMPRESSION STRESS WITH TEAR FILM BUBBLES

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INTRODUCTION: In the process of evaluating the advantages and disadvantages of hard, soft and hybrid contact lenses for diving, Mekjavić and colleagues (1991, 1992, 1993 and 1994) noted the development of bubbles in the tear film following decompression. These bubbles appeared as a consequence of decompression from depth and to altitude. We conducted further studies to: (i) assess the possibility of using tear film bubble formation as an index of decompression severity, (ii) compare the method of counting tear film bubbles with the Doppler ultrasound method of determining venous gas emboli, (iii) determine whether a dose-response relation existed between tear film bubble formation, dive depth and bottom time, (iv) assess whether the method could be used to evaluate dive decompression tables.

METHODS: Subjects paricipating in the studies had an ocular tear film examination prior to, and immediately following each hyperbaric exposure. Presence of tear film bubbles was determined with a slit-lamp microscope. In addition, we also conducted ultrasonicsurveillance of the precordial region and rated the bubbles according to the Kisman-Masurel scheme. Tear film bubble formation was evaluated: (i) following dives to a given depth, but with different bottom times, (ii) following dives to different depths, with maximal allowable bottom times for a no-decompression stop dive (according to the PADI tables), and (iii) following 60 minute exposure to 2.5 ATA, either inspiring air or 100% oxygen.
RESULTS: There was a significant dose-response relation between tear film bubble count, dive depth and bottom time. Regardless of the depth of the dive, there was no significant difference between the tear film bubble counts observed following all the no-stop decompression dives investigated. Oxygen breathing prevented a significant increase in tear film bubble count following decompression. Finally, for the dives conducted, Doppler did not reveal any bubbles present.

CONCLUSIONS: We conclude that tear film bubbles reflect the severity of decompression stress. The technique appears to be more sensitive than the method of Doppler ultrasonic surveillance of the precordial region. As such, the method may be used to evaluate the suitability of dive decompression tables.

REFERENCES:
1. Mekjavić I.B., R.A. Strath and G.I. Morariu (1993). Undersea and Hyperbaric Medcine 20 (Suppl.): 83.
2. Strath R.A. and I.B. Mekjavić (1991). Optometry and Vision Science 68 (Suppl.): 111.
3. Strath R.A., G.I. Morariu and I.B. Mekjavić (1992). Optometry and Vision Science 69: 973–975.
4. Strath R.A ., G.I. Morariu and I.B. Mekjavić (1994). Proc. XXth Ann. EUBS Meeting, Istanbul, Turkey.

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PULMONARY EDEMA IN DIVERS AND SWIMMERS

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INTRODUCTION AND METHODS: Pulmonary edema (PE) occurring during SCUBA diving or swimming in healthy persons has been reported for the first time in 1981. Most individuals developed dyspnea, cough and expectoration of frothy, bloodstained sputum after otherwise uneventful diving or swimming in cold water. Symptoms resolved, either spontaneously within hours and up to four days, or after standard medical treatment for PE. A review of the literature published until June 30, 1997 and our own experiences with six divers and swimmers (one female) are presented.

RESULTS: Worldwide, 53 episodes of PE in 23 divers (eight females) and 14 swimmers (two females) have been published by four different groups to date. To gain additional information about the incidence of PE, a survey among 1250 Swiss sport divers was conducted in 1994. Furthermore, a few isolated, nonpublished cases were retrieved from experts in diving medicine. Two studies trying to elucidate possible predisposing factors and underlying mechanisms showed inconclusive results.

CONCLUSIONS: PE occurring during scuba diving or swimming is a well documented, however extremely rare, even in healthy individuals. Since the first reported episodes occurred in cold water, the name "cold-induced pulmonary edem" was coined. Based on the observation of PE occurring in warmer regions of the world as well, low temperature can no longer be considered as the main predisposing factor. It is likely that PE in divers and swimmers occurs more often than has been reported in the medical literature. Pathogenetically, the combination of factors such as vasoconstriction (increased afterload), immersion (increased preload) and exercise (increased cardiac output) are postulated. However, the responsible mechanisms remain unclear and speculative.

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NITROGEN NARCOSIS POTENTIATES HYPOTHERMIA

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INTRODUCTION: Per- and post-operative hypothermia is a well known phenomenon, and is partly attributed to the anesthetics administered during surgery. A series of studies have been completed to assess whether the narcosis induced by elevated levels of partial pressure of nitrogen during diving may inhibit temperature regulation and contribute to the etiology of hypothermia in divers.

METHODS: To assess the influence of narcosis *per se* on human temperature regulation, experiments were conducted under normobaric conditions, in which subjects were rendered hypothermic by immersion in 15 and 28°C water, while inspiring either air, or a normoxic mixture containing 30% N_2O. The effect of nitrogen narcosis was evaluated by examining thermoregulatory responses of subjects head-out immersed in 15°C water, breathing air at either 1 ATA or 6 ATA.

RESULTS: N_2O inhibits the magnitude of shivering and displaces the threshold core temperature for onset of shivering to lower temperatures. Studies comparing the shivering response in normobaric conitions to that in hyperbaric conditions demonstrated that a partial pressure of nitrogen of 4.0 ATA, exerted an inhibitory effect on shivering and consequently increased the rate of cooling of core temperature. During these studies, subjects were requested to also provide a rating of their peception of thermal comfort. Mild narcosis, whether induced by N_2O or hyperbaric nitrogen altered the perception of thermal comfort. Subjects perceived the immersions conducted with N_2O and in hyperbaric conditions as less thermally uncomfortable, as those that were conducted while inspiring air at 1 ATA.

CONCLUSIONS: To date, hypothermia prevalent among divers has been attributed primarily to physical factors, namely increased mass heat transfer. These studies demonstrate that, in part, hypothermia among divers may also be attributed to the inhibitory effect of narcosis on the thermoregulatory system. Shivering, an autonomic response for enhanced heat production, is inhibited. Furthermore, the first defence mechanism against cooling, namely perception of discomfort, is also altered. Thus, divers exposed to mild narcosis are unlikely to initiate adequate behavioural responses to prevent further core cooling.

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DIVING FOR THE HANDICAPPED

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Within the last years an increasing number of programs for persons with physical disabilities have made diving accessible for this community. These programs accommodate the special needs of the diver and are quite successful. Additionally, sophisticated SCUBA equipment enables many individuals with physical handicaps to increase their activities under water and let them feel equal to nondisabled fellow divers. Most SCUBA instructors have little experience teaching disabled students to dive and have to experiment with various techniques to find what works best for the individual student. Nearly all diving agencies' standards are developed for nondisabled divers and contain requirements that are inappropriate for disabled divers. Instructors are obligated to certify divers who can master the given skills only, regardless of the fact that a lot of divers can cope with their handicap very well when diving together with an experienced nondisabled buddy. The physical examination has to take into account the individual impairment and the diving medical test should cover a clear separation between "unrestricted" diving and therapeutic diving training, depending on the type of disability. Problems concerning fitness to dive with different disabilities and a special certification specifying the disability, the training and the conditions of dives that can be performed, have to be discussed by diving medical societies and diving associations to develop specific guidelines.

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SHOULD CHILDREN DIVE?

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INTRODUCTION: There is an increasing tendency to introduce children to SCUBA diving. Some facts give an idea about the risks and limitations of children diving.

FACTS: *Respiratory system:* Alveolar growth is terminated at the age of 8 years. Elastic tissue has the definitive stability with 18 years. Risks: respiratory exhaustion, hypoxaemia, local or general barotrauma. *Cardiovascular System:* Certain turbulances in the Vena cava inferior are normal, but support the development of intravascular bubbles. Up to 40% of children under the age of 8 years have an open foramen ovale. Risks: Chokes and paradoxical embolism of bubbles. *Ears:* Children do not know how to voluntarily open the tuba Eustachii. Barotrauma of the middle ear and infections may cause hearing defects. *Bones:* Saturation and desatturation is not known in children. Microbubbles and heavy diving gear could alter bones growing. *Fitness:* Low performance is ascociated with higher mortality. Minimal fitness is mandatory. *Thermobiology:* Low body surface area per weight, and low subcutanous fat can lead to hypothermia. *Psychology:* Minimal intellectual preformance is neccessary for the theoretical background. Normal neurovegetative instability, emotional lability of children and the motivation to dive could be a risk factor. *Studies: Pouliquen, Haiti:* No fatal diving incident in 12, 000 dives with children betwen the ages of 4 and 12 years. *McAniff,* USA: 1976–86 ≤ 3 fatal diving incidents in children younger than 16 years. Gilchrist, USA: Increasing mortality only in the group of adolescents.

CONCLUSIONS: Regular extensive medical checks for fitness to dive and psychological assessment. Minimal performance of physical fitness. Adapted equipment. Special education of the instructor. *What we cannot conclude:* Depth Limitation. Diving tables. Security guide lines. Tables for the treatment in case of accident. *Proposal:* Prudence!! Body hight ≥ 150 cm, body wight ≥ 45 kg. Age ≥ 8 years.

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DIVING EMERGENCIES IN REMOTE AREAS

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Diving emergencies are generally managed by checklists as for example the DAN Diving Accident Flow Chart. While for field first aid measures, there is an almost worldwide consensus (flat position, rehydration, normobaric oxygenation, HBO), but further steps can vary widely according to the situation. In usual recreational

diving sites the next step would be to call a diving emergency hotline, organise the appropriate transport medium to the next hyperbaric chamber. Reality, however, is often much different, because in remote areas some or all of these services are not easily available.

In remote areas risk assessment and safety planning is therefore extremely important. The codes of practice for English professional divers prescribes that an HBO chamber has to be immediately available for important decompression times or within two hours for lesser decompression. For no stop dives, a chamber must be within 6 hours travelling distance. The same conditions should apply for recreational divers. Thus, remote areas are not only distant islands, but also major parts of the European coastline. Three approaches are possible, to achieve satisfactory diving safety: 1) Reduce decompression stress and prepare HBO equipment which will suffice for a several hour transport time. 2) Provide a transportable HBO chamber and doctor. 3) Provide O_2 regulator for inwater therapy and oxygen for >4 hours and medical back-up on call. Advantages and disadvantages and technical standards of the three safety measures will be discussed.

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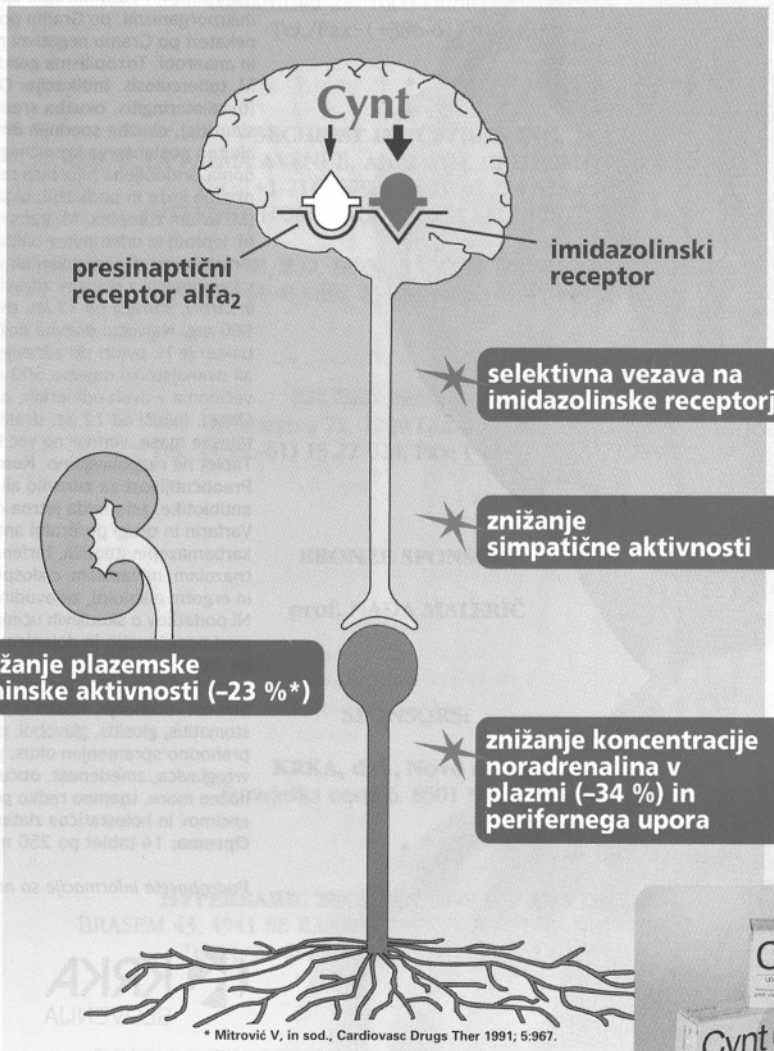

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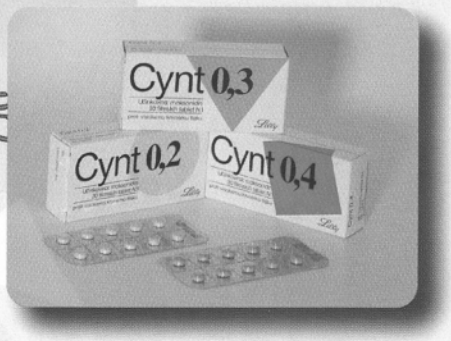

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Splošna načela

ZV objavlja le izvirna, še ne objavljena dela. Avtor je odgovoren za vse trditve, ki jih v prispevku navaja. Če je članek pisalo več soavtorjev, je treba navesti natančen naslov (s telefonsko številko) tistega avtorja, s katerim bo uredništvo sodelovalo pri urejanju teksta za objavo ter mu pošiljalo prošnje za odtis.

Če prispevek obravnava raziskave na ljudeh, mora biti iz besedila razvidno, da so bile raziskave opravljene skladno z načeli Kodeksa medicinske deontologije in Deklaracije iz Helsinkov/Tokija.

Če delo obravnava poizkuse na živalih, mora biti razvidno, da je bilo opravljeno skladno z etičnimi načeli.

Prispevki bodo razvrščeni v eno od naslednjih rubrik: uvodnik, raziskovalni prispevek, strokovni prispevek, pregledni članek, kakovost v zdravstvu, pisma uredništvu in razgledi.

Raziskovalna poročila morajo biti napisana v angleščini. Dolga naj bodo do 8 tipkanih strani. Slovenski izvleček mora biti razširjen in naj bo dolg do tri tipkane strani. Angleški ne sme biti daljši od 250 besed.

Če besedilo zahteva aktivnejše posege angleškega lektorja, nosi stroške avtor.

Ostali prispevki za objavo morajo biti napisani v slovenščini jedrnato ter strokovno in slogovno neoporečno. Pri raziskovalnih in strokovnih prispevkih morajo biti naslov, izvleček, ključne besede, tabele in podpisi k tabelam in slikam prevedeni v angleščino.

Članki so lahko dolgi največ 12 tipkanih strani (po 30 vrstic) s tabelami in literaturo vred.

V besedilu se uporabljajo le enote SI in tiste, ki jih dovoljuje Zakon o merskih enotah in merilih.

Spremni dopis

Spremno pismo mora vsebovati: 1. izjavo, da poslano besedilo ali katerikoli del besedila (razen abstrakta) ni bilo poslano v objavo nikomur drugemu; 2. da so vsi soavtorji besedilo prebrali in se strinjajo z njegovo vsebino in navedbami; 3. kdaj je raziskavo odobrila Etična komisija; 4. da so preiskovanci dali pisno soglasje k sodelovanju pri raziskavi; 5. pisno dovoljenje za objavo slik, na katerih bi se morebiti lahko prepoznala identiteta pacienta; 6. pisno dovoljenje založbe, ki ima avtorske pravice, za ponatis slik, shem ali tabel.

Tipkopis

Prispevki morajo biti poslani v trojniku, tipkani na eni strani boljšega belega pisarniškega papirja formata A4. Med vrsticami mora biti dvojni razmik (po 30 vrstic na stran), na vseh straneh pa mora biti rob širok najmanj 30 mm. Avtorji, ki pišejo besedila s pomočjo PC kompatibilnega računalnika, jih lahko pošljejo uredništvu v enem izpisu in na 5.25 ali 3.5 inčni disketi, formatirani na 360 KB ali 1,2 MB, kar bo olajšalo uredniški postopek. Ko je le-ta končan, uredništvo disketo vrne. Besedila naj bodo napisana z urejevalnikom Word for Windows ali z drugim besedilnikom, ki hrani zapise v ASCII kodi.

V besedilu so dovoljene kratice, ki pa jih je treba pri prvi navedbi razložiti. Že uveljavljenih okrajšav ni treba razlagati (npr. L za liter, mg za miligram itd.).

Naslovna stran članka naj vsebuje slovenski naslov dela, angleški naslov dela, ime in priimek avtorja z natančnim strokovnim in akademskim naslovom, popoln naslov ustanove, kjer je bilo delo opravljeno (če je delo skupinsko, naj bodo navedeni ustrezni podatki za soavtorje). Naslov dela naj jedrnato zajame bistvo vsebine članka. Če je naslov z avtorjevim imenom in priimkom daljši od 90 znakov, je potrebno navesti še skrajšano verzijo naslova za tekoči naslov. Na naslovni strani naj bo navedenih tudi po pet ključnih besed (uporabljene naj bodo besede, ki natančneje opredeljujejo vsebino prispevka in ne nastopajo v naslovu; v slovenščini in angleščini) ter ev. financerji raziskave (s številko pogodbe).

Druga stran naj vsebuje slovenski izvleček, ki mora biti strukturiran in naj vsebuje naslednje razdelke in podatke:

Izhodišča (Background): Navesti je treba glavni problem in namen raziskave in glavno hipotezo, ki se preverja.

Metode (Methods): Opisati je treba glavne značilnosti izvedbe raziskave, opisati vzorec, ki se preučuje (npr. randomizacija, dvojno slepi poizkus, navzkrižno testiranje, testiranje s placebom itd.), standardne vrednosti za teste, časovni odnos (prospektivna, retrospektivna študija).

Navesti je treba način izbora preiskovancev, kriterije vključitve, kriterije izključitve, število preiskovancev, vključenih v raziskavo in koliko jih je vključenih v analizo. Opisati je treba posege, metode, trajanje jemanja posameznega zdravila, kateri preparati se med seboj primerjajo (navesti je treba generično ime preparata in ne tovarniško) itd.

Rezultati (Results): Opisati je treba glavne rezultate študije. Pomembne meritve, ki niso vključene v rezultate študije, je treba omeniti. Pri navedbi rezultatov je treba vedno navesti interval zaupanja in natančno raven statistične značilnosti. Pri primerjalnih študijah se mora interval zaupanja nanašati na razlike med skupinami. Navedene morajo biti absolutne številke.

Zaključki (Conclusions): Navesti je treba le tiste zaključke, ki izhajajo iz podatkov, dobljenih pri raziskavi; treba je navesti ev. klinično uporabnost ugotovitkov. Navesti je treba, kakšne dodatne študije so še potrebne, preden bi se zaključki raziskave klinično uporabili. Enakovredno je treba navesti tako pozitivne kot negativne ugotovitke.

Ker nekateri prispevki (npr. pregledni članki) nimajo niti običajne strukture članka, naj bo pri teh strukturiranost izvlečka ustrezno prilagojena. Dolg naj bo od 50 do 200 besed; na tretji strani naj bodo: angleški naslov članka, ključne besede v angleščini in angleški prevod izvlečka.

Na naslednjih straneh naj sledi besedilo članka, ki naj bo smiselno razdeljeno v poglavja in podpoglavja, kar naj bo razvidno iz načina podčrtavanja naslova oz. podnaslova, morebitna zahvala in literatura. Odstavki morajo biti označeni s spuščeno vrstico. Tabele, podpisi k slikam in razlaga v tekstu uporabljenih kratic morajo biti napisani na posebnih listih.

Tabele

Natipkane naj bodo na posebnem listu. Vsaka tabela mora biti oštevilčena z zaporedno številko. Tabela mora imeti najmanj dva stolpca. Vsebovati mora: naslov (biti mora dovolj poveden, da razloži, kaj tabela prikazuje, ne da bi bilo treba brati članek; če so v tabeli podatki v odstotkih, je treba v naslovu navesti bazo za računanje odstotka; navesti je treba od kod so podatki iz tabele, ev. mere, če veljajo za celotno tabelo, razložiti podrobnosti glede vsebine v glavi ali čelu tabele), čelo, glavo, morebitni zbirni stolpec in zbirno vrstico ter opombe ali pa legendo uporabljenih kratic v tabeli. Vsa polja tabele morajo biti izpolnjena in mora biti jasno označeno, če morebiti podatki manjkajo.

V besedilu prispevka je treba označiti, kam spada posamična tabela.

Slike

Risbe morajo biti risane s črnim tušem na bel trd papir. Pri velikosti je treba upoštevati, da bodo v ZV pomanjšane na širino stolpca (81 mm) ali kvečjemu na dva stolpca (168 mm). Morebitno besedilo na sliki mora biti izpisano z laserskim tiskalnikom. Pri velikosti črk je treba upoštevati, da pri pomanjšanju slike za tisk velikost črke ne sme biti manjša od 2 mm. Grafikoni, diagrami in sheme naj bodo uokvirjeni.

Na hrbtni strani vsake slike naj bo s svinčnikom napisano ime in priimek avtorja, naslov članka in zaporedna številka slike. Če je treba, naj bo označeno kaj je zgoraj in kaj spodaj.

V besedilu prispevka je treba označiti, kam spada posamična slika.

Literatura

Vsako trditev, dognanje ali misel drugih je treba potrditi z referenco. Neobjavljeni podatki ali osebno sporočilo ne spada v seznam literature. Navedke v besedilu je treba oštevilčiti po vrstnem redu, v katerem se prvič pojavijo, z arabskimi številkami v oklepaju. Če se pozneje v besedilu znova sklicujemo na že uporabljeni navedek, navedemo številko, ki jo je navedek dobil pri prvi omembi. Navedki, uporabljeni v tabelah in slikah, naj bodo oštevilčeni po vrstnem redu, kakor sodijo tabele in slike v besedilo. Pri citiranju več del istega avtorja dobi vsak navedek svojo številko, starejša dela je treba navesti prej. Vsi navedki iz besedila morajo biti vsebovani v seznamu literature.

Literatura naj bo zbrana na koncu članka po zaporednih številkah navedkov. Če je citirani članek napisalo 6 avtorjev ali manj, jih navedite vse; pri 7 ali več je treba navesti prve tri in dodati et al. Če pisec prispevka v originalni objavi ni imenovan, se namesto njega napiše Anon. Naslove revij, iz katerih je navedek, je treba krajšati kot določa Index Medicus.

Primeri citiranja

– primer za knjigo:

1. Bohinjec J. Temelji klinične hematologije. Ljubljana: Dopisna delavska univerza Univerzum, 1983: 182–3.

– primer za poglavje iz knjige:

2. Garnick MB, Brenner BM. Tumors of the urinary tract. In: Braunwald E, Isselbacher KJ, Petersdorf RG, Wilson JD, Fauci AS eds. Harrison's principles of internal medicine. 11th ed. Vol 2. New York: McGraw Hill, 1987: 1218–21.

– primer za članek v reviji:

3. Šmid L, Žargi M. Konikotomija – zakaj ne. Med Razgl 1989; 28: 255–61.

– primer za članek iz revije, kjer avtor ni znan:

4. Anon. An enlarging neck mass in a 71-year-old woman. Am J Med 1989; 86: 459–64.

– primer za članek iz revije, kjer je avtor organizacija:

5. American College of Physicians. Clinical ecology. Ann Int Med 1989; 111: 168–78.

– primer za članek iz suplementa revije:

6. Miller GJ. Antithrombotic therapy in the primary prevention of acute myocardial infarction. Am J Cardiol 1989; 64: Suppl 4: 29B–32B.

– primer za članek iz zbornika referatov:

7. Schneider W. Platelet metabolism and membrane function. In: Ulutin ON, Vinazzer H eds. Proceeding of 4th international meeting of Danubian league against thrombosis and haemorrhagic diseases. Istanbul: Goezlem Printing and Publishing Co, 1985: 11–5.

Sodelovanje avtorjev z uredništvom

Prispevke oddajte ali pošljite le na naslov: Uredništvo Zdravniškega vestnika, Komenskega 4, 1000 Ljubljana. Za prejete prispevke izda uredništvo potrdilo. V primeru nejasnosti so uredniki na voljo za posvet, najbolje po poprejšnjem telefonskem dogovoru (tel. 061 / 317 868).

Vsak članek daje uredništvo v strokovno recenzijo in jezikovno lekturo. Po končanem redakcijskem postopku, strokovni recenziji in lektoriranju vrnemo prispevek avtorju, da popravke odobri, jih upošteva in oskrbi čistopis, ki ga vrne s popravljenim prvotnim izvirnikom. Med redakcijskim postopkom je zagotovljena tajnost vsebine članka.

Avtor dobi v korekturo prvi krtačni odtis s prošnjo, da na njem označi vse tiskovne napake. Spreminjanja besedila ob tej priliki uredništvo ne bo upoštevalo. Korekture je treba vrniti v treh dneh, sicer uredništvo meni, da avtor nima pripomb.

Rokopisov in slikovnega materiala uredništvo ne vrača.

Dovoljenje za ponatis slik, objavljenih v ZV, je treba zaprositi na Uredništvo Zdravniškega vestnika, Komenskega 4, 1000 Ljubljana.

Navodila za delo recenzentov

Če zaprošeni recenzent prispevka ne more sprejeti v oceno, naj rokopis vrne. Hvaležni bomo, če v tem primeru predlaga drugega primernega recenzenta. Če meni, naj bi uredništvo poleg njega prosilo za oceno prispevka še enega recenzenta (multidisciplinarna ali mejna tema), naj to navede v svoji oceni in predlaga ustreznega strokovnjaka.

Recenzentovo delo je zelo odgovorno in zahtevno, ker njegovo mnenje največkrat vodi odločitev uredništva o usodi prispevka. S svojimi ocenami in sugestijami recenzenti prispevajo k izboljšanju kakovosti našega časopisa. Po ustaljeni praksi ostane recenzent avtorju neznan in obratno.

Če recenzent meni, da delo ni vredno objave v ZV, prosimo, da navede vse razloge, zaradi katerih delo zasluži negativno oceno. Negativno ocenjen članek po ustaljenem postopku skupaj z recenzijo (seveda anonimno) uredništvo pošlje še enemu recenzentu, kar se ne sme razumeti kot izraz nezaupanja prvemu recenzentu.

Prispevke pošiljajo tudi mladi avtorji, ki žele svoja zapažanja in izdelke prvič objaviti v ZV; tem je treba pomagati z nasveti, če prispevek le formalno ne ustreza, vsebuje pa pomembna zapažanja in sporočila.

Od recenzenta uredništvo pričakuje, da bo odgovoril na vprašanja na obrazcu ter bo ugotovil, če je avtor upošteval navodila sodelavcem, ki so objavljena v vsaki številki ZV, in da bo preveril, če so podane trditve in misli verodostojne. Recenzent mora oceniti metodologijo in dokumentacijo ter opozoriti uredništvo na ev. pomanjkljivosti, posebej še v rezultatih.

Ni potrebno, da se recenzent ukvarja z lektoriranjem in korigiranjem, čeprav ni napak, če opozori na take pomanjkljivosti. Posebej Vas prosimo, da ste pozorni na to, ali je naslov dela jasen in koncizen ter ali ustreza vsebini; ali izvleček povzema bistvene podatke članka; ali avtor citira najnovejšo literaturo in ali omenja domače avtorje, ki so pisali o isti temi v domačih časopisih ali v ZV; ali se avtor izogiba avtorjem, ki zagovarjajo drugačna mnenja, kot so njegova; ali navaja tuje misli brez citiranja; ali so literaturni citati točni. Preveriti je treba dostopne reference. Prav tako je treba oceniti, če so slike, tabele in grafi točni in da se v tabelah ne ponavlja tisto, kar je že navedeno v tekstu; da ne vsebujejo nepojasnjenih kratic, da so številčni podatki v tabelah ustrezni onim v tekstu ter da ni napak.

Če recenzent meni, da delo potrebuje dopolnilo (komentar) ali da bi ga sam lahko dopolnil (s podatki iz literature ali lastnimi izkušnjami), se lahko dogovori z urednikom, da se tak komentar objavi v isti številki kot ocenjevano delo.

Recenzij ne plačujemo.

Zdravniški vestnik

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