important starting point for a proper treatment of the sleep disorder.

*Bernhard Widner, Maximilian Ledochowski, *Dietmar Fuchs*

*Institute of Medical Chemistry and Biochemistry and Department of Internal Medicine, University of Innsbruck, Innsbruck A-6020, Austria

1 Foley D. Sorting out sleep in patients with Alzheimer's disease. *Lancet* 1999; **354:** 2098–99.
2 McCurry SM, Logsdon RG, Teri L, et al. Characteristics of sleep disturbance in community-dwelling Alzheimer's disease patients. *J Geriatr Psychiatry Neurol* 1999; **12:** 53–59.
3 Vitiello MV, Bliwise DL, Prinz PN. Sleep in Alzheimer's disease and the sundown syndrome. *Neurology* 1992; **42:** 83–94.
4 Widner B, Leblhuber F, Walli J, Tilz GP, Demel U, Fuchs D. Tryptophan degradation and immune activation in Alzheimer's disease. *J Neural Trans* (in press).
5 Wiegand M, Möller AA, Schreiber W, et al. Nocturnal sleep EEG in patients with HIV infection. *Eur Arch Psychiatry Clin Neurosci* 1991; **240:** 153–58.

Sickness and sex of child

Sir—Johan Askling and colleagues (Dec 11, p 2053)[1] claim that, "Despite efforts to find reliable physical signs or symptoms during pregnancy to indicate the sex of the offspring, none have been found". Now there is a way (apart from the ultrasound scan). They showed that 55·7% of babies whose mothers were admitted for hyperemesis gravidarum in the first trimester were female. What about failure to progress in labour? There is a correlation between mode of delivery and sex of the baby. It can be calculated from a study of 52 282 deliveries in Jerusalem[2] that normal vaginal deliveries resulted in 50·7% males, caesarean sections in 52·2%, vacuum extractions in 57·1% and forceps deliveries in 58·1%. A 42-month retrospective study of deliveries in the two large government hospitals in Bulawayo, Zimbabwe, showed that in failed trials of scar (TOS) 2048 (57·8%) of the babies were male, 1344 (60·6%) in vacuum extractions, and 57 (66·6%) of symphysiotomies. We also found that not only the sex of the baby influences the mode of delivery but also the sex of the previous baby. If a TOS fails 57·8% of the previous pregnancies were found to be of female babies.

Boys have somewhat larger heads.[3] If, as is our experience a caesarean section is mostly done for the mechanical reasons and not for legal, financial, or psychological ones, the sex of the baby makes a significant difference.

Our colleagues in Sweden can say with confidence to a woman who has hyperemesis gravidarum that she has a 55·7% chance of delivering a girl. We can say with as much confidence that a woman facing vacuum extraction has a 60·6% chance of having a boy. If the vacuum extraction fails and we proceed to a symphysiotomy (or caesarean section) the odds of a boy are even higher.

Douwe A A Verkuyl

United Bulawayo Hospitals, PO Box 958, Bulawayo, Zimbabwe
(e-mail: dverkuyl@healthnet.zw)

1 Askling J, Erlandsson G, Kaijser M, Akre O, Ekbom A. Sickness in pregnancy and sex of child. *Lancet* 1999; **354:** 2053.
2 Seidman DS, Laor A, Gale R, Stevenson DK, Mashiach S, Danon YL. Long-term effects of vacuum and forceps deliveries. *Lancet* 1991; **337:** 1583–85.
3 Henriksen TB, Wilcox AJ, Hedegaard M, Secher NJ. Bias in studies of preterm and postterm delivery due to ultrasound assessment of gestational age. *Epidemiology* 1995; **6:** 533–37.

Sir—After an extensive nationwide Swedish survey, Johan Askling and colleagues[1] conclude that women presenting with hyperemesis gravidarum are more likely to give birth to girls than to boys and highlighted that Hippocrates had associated a female fetus with the pale face of a pregnant woman.

Throughout history prediction of the sex of an unborn child must have been a great challenge for empirics, physicians, and midwives. In *Corpus Hippocraticum* (5th–4th century BC) a woman pregnant with a female fetus would have an unhealthy pale appearance, freckled face, enlarged left breast, and turned downward nipples. Also, some advice was provided on how to choose the sex during coitus.[2] Even Aristotle (4th century BC), a physician and an embryologist himself, could not resist the temptation to describe a woman pregnant with a female fetus as paler, suffering more, subject to swellings of the legs and eruptions of the body, and more prone to longings and to rapid changes of mood.[3] Aristotle was a keen observer and long before the development of statistics and confidence intervals, noted that this was a rule subject to exceptions. Interestingly, neither the authors of *Corpus Hippocraticum* nor Aristotle mentioned hyperemesis gravidarum.

Seemingly, more signs of the sex of an unborn child were added during the forthcoming centuries. Towards the twilight of the Greco-Roman World, Soranus of Ephesus (2nd century AD) found it worthwhile to summarise all this previous long experience under a short chapter titled "What are the signs, according to the ancients, whether the fetus is male or female?"[4] Soranus decried the Hippocratic signs as based on obviously false assumptions and added that other people had said that the movements of the female fetus would be slower and more sluggish and the gravida would move with less ease and have a stronger inclination to vomiting. He concluded that although these forecasts were plausible, the opposite might well happen.

Throughout antiquity boys were strongly preferred and families would much appreciate the correct prediction that a boy was expected. Probably the biased association of bad health during pregnancy with a female embryo made the most enlightened physicians reject these omens. However, regarding this particular issue, the unknown physician who, between the 4th century BC and the 2nd century AD, first related hyperemesis gravidarum to the female embryo, was obviously correct.

Emmanouil Galanakis

Department of Paediatrics, University of Ioannina, PO Box 1186, 45110 Ioannina, Greece

1 Askling J, Erlandsson G, Kaijser M, Akre O, Ekbom A. Sickness in pregnancy and sex of child. *Lancet* 1999; **354:** 2053.
2 Hippocrates. Aphorisms v, 42; on barren women, 4; on superfetation, 26. In: É Littré, ed. Oevreus d'Hippocrate. Amsterdam: AM Hakkert, 1961.
3 Aristotle. Historia Animalium, 584a. In: The works of Aristotle, vol 4. Smith MA, Ross WD, transl. Thompson DW, ed. London: Oxford University Press, 1962.
4 Soranus, Gynecology, 45. Temkin O, transl. Baltimore: Johns Hopkins Press, 1956.

The QUORUM statement

Sir—The QUORUM statement (Nov 27, p 1896)[1] should prove useful to people writing and intepreting reports of systematic reviews. The promised update should include a recommendation that authors of a systematic review clearly indicate whether any other versions of the review have been published and the status of these versions, to show which is the most up-to-date. Reviewers have struggled for some time with difficulties caused by multiple publication of randomised trials without appropriate cross referencing.[2] They should ensure that the same traps are not set for users of reviews. For example, all Cochrane reviews contain a section giving details of other published versions of the review, and the QUORUM statement and journals should urge all reviewers to do likewise.[3]

Mike Clarke

UK Cochrane Centre, Summertown Pavillion, Oxford OX2 7LG, UK

1 Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF, for the QUORUM

Group. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUORUM statement. *Lancet* 1999; **354:** 1896–900.
2 Rennie D. Fair conduct and fair reporting of clinical trials. *JAMA* 1999; **282:** 1766–68.
3 Clarke M, Oxman A. Cochrane reviews will be in Medline. *BMJ* 1999; **319:** 1435.

Amyloid-β junkies

Sir—Evidence indicates that, in the very near future, by either snorting or injecting amyloid-β, it will be possible to remove amyloid-β-laden senile plaques from the brains of individuals with Alzheimer disease.[1] Given the wealth of in-vitro, genetic, and pathological criteria, it is generally thought that removal of senile plaques will have a beneficial effect and may arrest or reverse Alzheimer's disease.[2] However, before we all rush to become amyloid-β junkies, there are several biological issues that indicate that such a regimen may ultimately be detrimental.

First, analysis of many aged and even middle-aged individuals shows that amyloid-β deposits are often extensive in cognitively intact people. Amyloid-β deposition is clearly insufficient to develop frank Alzheimer's disease and, in fact, there is only a weak correlation between amyloid-β burden, neuronal cell loss, and cognitive status.[3] Second, animals with amyloid-β even more extensive than that found in Alzheimer's disease do not replicate the full range of Alzheimer's disease pathology nor the dementia associated with Alzheimer's disease. Furthermore, the net result of neurotoxic and neurotrophic effects of amyloid-β in in-vitro experiments and their relationship to in-vivo conditions remains unresolved. Third, amyloid-β is produced in response to injury to the nervous system in various diseases and experimental paradigms and its precursor, βPP, is one of the best markers of neurological injury and is used as such in pathological diagnosis in a clinical setting.[4] Indeed, amyloid-β may, in fact, rather than being detrimental, play a part in the defence of the aged brain.[5] Amyloid-β, like ubiquitin, heat-shock protein, or antioxidant proteins, is increased as a consequence of the aetiological process. It would be preposterous to suggest these responses to the primary aetiological event actually mediate pathogenesis, and to invoke amyloid-β as the primary agent is equally so. Given this uncertainty, we are playing a dangerous game in focusing efforts on the removal of amyloid-β, which could quite likely have the opposite effect to that promised: of a return to cognition.

**George Perry, Akihiko Nunomura, Arun K Raina, Mark A Smith*

*Institute of Pathology, Case Western Reserve University, Cleveland, OH 44106-2622, USA; and Asahikawa Medical College, Asahikawa, Japan
(e-mail: gxp7@po.cwru.edu or mas21@po.cwru.edu)

1 Schenk D, Barbour R, Dunn W, et al. Immunization with amyloid-beta attenuates Alzheimer-disease-like pathology in the PDAPP mouse. *Nature* 1999; **400:** 173–77.
2 Selkoe DJ. Translating cell biology into therapeutic advances in Alzheimer's disease. *Nature* 1999; **399** (suppl II): A23–31.
3 Davies L, Wolska B, Hilbich C, et al. A4 amyloid protein deposition and the diagnosis of Alzheimer's disease: prevalence in aged brains determined by immunocytochemistry compared with conventional neuropathologic techniques. *Neurology* 1988; **38:** 1688–93.
4 Roberts GW, Gentleman SM, Lynch A. βA4 amyloid protein deposition in brain after head trauma. *Lancet* 1991; **338:** 1422–23.

Medicolegal aspects of international teleconsultancy

Sir—The Internet has given new dimensions to medicine. E-mail teleconsultancy, by which the physician transfers the patient's data, including images, through the Internet to an expert (consultant) for a second opinion, is one of them. Reports and guidelines on teleconsultancy, however, hardly mention the legal aspects of this new means of consultation.[1,2] This lack of legal guidelines is caused by lack of legislation.

If teleconsultancy is done internationally, two legal questions are of importance: what court will have jurisdiction and which law will be applicable to the liability dispute?[3] In a conflict brought before the courts of a Member State of the European Community (EC), the courts will apply the Brussels Convention to settle jurisdiction,[4] provided the defendant is domiciled in a Member State. Otherwise, the Member State court will apply its national law to settle whether it has jurisdiction. Parties to the teleconsultancy contract may also agree on which court has jurisdiction to settle any future disputes. Liability disputes brought before courts outside the EC will be subject to the national law rules on international jurisdiction in that particular country.

With respect to the applicable law, the competent court of an EC Member State will apply the Rome Convention,[5] provided that it has qualified the liability dispute as a contractual dispute. The rules of the Rome Convention has universal applicability and will be applied by each court within the EC to decide applicable law to a contractual dispute. Whether the liability dispute is a contractual dispute is decided by the national law of the relevant court. If a written contract exists between both teleconsulting parties, and the plaintiff (treating physician or patient) alleges breach of contract by the teleconsultant, the court will apply the law chosen (if any) in this contract. This means that the court can apply the law of another country. If no choice of law has been made, the court will apply the law of the State of domicile of the characteristic performer of the contract. In the case of teleconsultancy, the consultant is the characteristic performer and the court will probably apply the law of the consultant's State of domicile. Liability disputes brought before courts outside the EC will be subject to the national law rules on the law applicable to contractual disputes in that particular country.

Because the patient is not a party in the teleconsultancy agreement, it is more likely that the patient will assert a tortious claim against the consultant, instead of a contractual claim. If the court qualifies the liability dispute as a tort, the court will apply its national rules to determine applicable law. In most jurisdictions the law of the place where the tort or harmful event occurred is applicable. With teleconsultancy it is difficult to establish where the harmful event occurred.

Liability can be excluded by contract. However, this can be overruled by the court if it finds that such exclusion is not in the interest of the patient. To decide which party has the burden of proof regarding the alleged liability on the part of the defendent (consultant), the court must decide whether it regards the teleconsultation as a result commitment or an effort commitment. Most likely, the court will decide that the teleconsultation is an effort commitment on the part of the consultant, which means that in accordance with EC regulations, the plaintiff will have to prove the liability of the consultant.

Experts might be reluctant to be consulted if there is a high financial risk. To minimise these risks it is advisable to agree on the competent court and applicable law and to force the consultancy party (the treating physician) by contract to assume the financial risks in case of a lawsuit. To ensure that the consultancy party can sustain the costs, it might be advisable to include a cause requiring the consultancy party to obtain adequate insurance coverage against these risks.