

Hippocrates

The risk that never was

In hunting down risk in medicine, the danger is always present that one will take to task some entirely innocuous practice, doing so with such crusading zeal that the mission to destroy it becomes unstoppable; phantoms of risk arise where real risks are lacking, ready to be exorcised with bell, book and candle.

The story of what happened to Bendectin and Debendox – the drugs once used to treat nausea of pregnancy – which were chased off the market more than a decade ago because of flimsy suspicions that they were teratogenic, has been told many times. Essentially, because they were used on a large scale, their use inevitably coincided with all sorts of spontaneous congenital malformations, and with that the seeds of persecution were sown. The only reason for mentioning the story now is that very few writers dealing with the history of adverse drug reactions get the story entirely straight. The best analysis is a little-known one published by Lasagna and Shulman several years ago, in which they showed how ill-fitted the American litigation process was to dealing with the subtleties of epidemiological evidence [1]; in several cases, courts dealing with precisely the same material reached diametrically opposite conclusions. Their paper deserves to be read in the original. Yet even Lasagna and Shulman drifted past one basic conclusion; when any drug is suspected of causing problems, the evidence needs to be set against the drug's usefulness. Were Bendectin and Debendox of any value? Oddly, they existed only in the Anglo-Saxon countries; elsewhere this type of treatment for nausea in pregnancy was generally condemned. Somehow, the world goes on turning without them, and apparently without anything having taken their place.

Reference

- [1] L. Lasagna and S.R. Shulman, Bendectin and the language of causation, in: *Phantom Risk – Scientific Inference and the Law*, K.R. Foster, D.E. Bernstein and P.W. Huber, eds, MIT Press, Cambridge, MA, 1993.

Endoscopic surgery comes to adulthood

The surgeon has always been much more a master of fine detail than the world gave him credit for. Operation through the endoscope is hardly new, but from its earliest days it promised to provide a fine challenge to any surgeon having the instincts of a watchmaker, and the only question was how much could be achieved, how accurately and how safely, in this way as compared with open surgery. Progress has been astonishing. A little earlier this year, a surgical group at Kyoto University reported a clinical trial of prophylactic endoscopic ligation of oesophageal varices. Twenty-two patients with enlarged, tortuous varices and “red colour signs” were selected and treated with this method alone; there was a follow-up endoscopy after four months and if the varices had reappeared or there was

evidence of bleeding the ligation was repeated. The total reduction rate was over 86%, and eradication required on average only thirty days in hospital. One patient showed some oesophageal injury and another bled after ligation, but both complications were mild and easily controlled. A year later there was no mortality from haemorrhage [1].

A similar but larger study from Taiwan, using a control group, has even produced promising results in patients with cirrhosis, in whom the aim was again to ligate the oesophageal varices in time, before any frank haemorrhage occurred. These patients were in much poorer condition than those at Kyoto, many being at risk for hepatic failure. Despite this, the bleeding rate during a two-year follow-up period was only 28%, as compared to 58% in a controlled group. The risks of the operation itself seemed to be negligible [2].

References

- [1] H. Kishimoto, M. Sakai, T. Kajiyama et al., Clinical trial of prophylactic endoscopic variceal ligation for esophageal varices, *J. Gastroenterol.* **32**(1) (1997), 6–11.
- [2] C.S. Lay, Y.T. Tsai, C.Y. Teg et al., Endoscopic variceal ligation in prophylaxis of first variceal bleeding in cirrhotic patients with high-risk esophageal varices, *Hepatology* **25**(6) (1997), 1346–1350.

Communicate, communicate

The campaign to open up the secret places of drug regulation and adverse reaction monitoring, launched in this Journal's special issue last year [1], continues apace. The latest fireworks came from a broadly based meeting in Erice in September 1997 under the auspices of the Sicily's renowned Ettore Majorana Foundation and Centre for Scientific Culture. Rather than merely complaining that regulators are so secretive, the meeting's closing "Declaration" tried to explain why facts are hidden away and how the situation might be improved. The meeting seems to have had little patience with the paternalistic approach to the public; in its view, it is generally possible to deal with the misunderstanding or misuse of publicly available data, but not possible to foresee or counter the dangers to the public which result from withholding information. Unfortunately, neither doctors nor drug controllers are born or trained communicators; it would be as well if every doctor and pharmacist moving into the drug administration were trained in communication. One of the essential lessons must be in communicating uncertainty without engendering fear; information on possible new medical risks often needs to be disseminated at a time when there is no certainty to be had. If one can move towards that norm, and at the same time uproot the mutual mistrust which often underlies secrecy, one may truly get somewhere. The full proceedings of "Erice", due in 1998, are worth waiting for.¹

Reference

- [1] Special issue on Secrecy in Drug Regulation, *Int. J. Risk & Safety in Medicine* **9**(3) (1996).

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Diabetes and the heart: managing the risks

Just 75 years after the arrival of insulin, one sometimes gets the impression that we are now content to rest on our laurels where the treatment of diabetes is concerned; yet there is a great deal left to do, particularly with the insidious complications which affect so many diabetics in middle and later life. Cardiovascular disease – particularly coronary disease and heart failure – are clearly a great deal more frequent in non-insulin-dependent type I or type II diabetics than in the remainder of the population; where by-pass surgery is needed it also carries a higher risk of morbidity and mortality in these patients. All the same it looks increasingly as if an aggressive surgical approach is likely to bring more benefit and less risk than purely medical efforts; percutaneous transluminal coronary angioplasty or coronary surgery may be justified where there is stable angina and thus an obvious temptation to persist with drug therapy alone. Drugs on the other hand may be the best or only approach where there is cardiac failure. All these conclusions are provisional; as Julien from the Hotel-Dieu de Paris has stressed in a thoughtful new paper [1], we still need much more careful study if we are to individualize care in these high-risk patients, and to find ways of monitoring their course adequately.

Reference

- [1] J. Julien, Cardiac complications in non-insulin-dependent diabetes mellitus, *J. Diabetes Complications* **11**(2) (1997), 123–130.

Dog's lives

Do our veterinary colleagues bestow more care on their patients than we do? One is always a little taken aback by veterinary discussions as to whether it is cheaper to kill or cure; but such debates apply only to farm animals, and for domestic pets quite different considerations apply. It has been calculated that a few years ago Canadians were spending on average \$479 a year on health care for their pets, which was more than what they paid the dentist and twice as much as they spent on pharmaceuticals for the entire family [1]. If the same source is to be believed, the fees paid to veterinary surgeons in Ontario for treating dogs and cats are way beyond what the Ontario Health Insurance Plan pays to physicians. Ultrasound in pregnancy brought the doctor \$77.90, a veterinarian \$104.00. That an X-ray of the femoral joint cost four times as much in a cat as in a human patient might be explained by the problem of keeping the animal still long enough to take the picture. But when a doctor gets \$16.70 for a house call and a veterinary surgeon \$52.50 one just begins to wonder. And for an amputation of the lower arm the medical man receives \$266.40, while the corresponding operation in a cat will cost you \$353.00... Can anyone tell Hippocrates why?

Reference

- [1] *Ottawa Citizen* newspaper, cited in News and Analysis, *Can. Med. Ass. J.* **156**(12) (1997), 1689.