

THE LANCET

Asbestos

PUBLIC anxiety about asbestos has descended from its zenith a few months ago, but community-health and health-and-safety workers are still much exercised by control of the hazards in industry and the implications of environmental contamination. The major biological effects are asbestosis, carcinoma of lung, and mesothelial tumours. Research effort is now directed towards establishing the carcinogenicity of the different types of fibre and determining dose-response relationships on which a national standard for asbestos dust in air can be based.

During the past twelve months two important reviews have been published—the Zielhuis report¹ on the Public Health Risks of Exposure to Asbestos, a report of a working-group prepared for the Commission of European Communities; and the I.A.R.C. monograph no. 14 on asbestos.² The first concludes from information on environmental contamination that no convincing evidence exists in Western Europe of increased risk through true ambient exposure to asbestos—in air, water, drugs, beverages, or food—though the possibility of such a risk cannot be categorically denied. Para-occupational exposures of family and neighbourhood and leisure-time working with asbestos-containing products are singled out as an area of concern. The I.A.R.C. report, looking at experimental as well as epidemiological evidence, concludes more pessimistically that “it is not possible to assess whether there is a level of exposure in humans below which an increased risk of cancer would not occur”.

WHITWELL, SCOTT, and GRIMSHAW³ have

1. Public Health Risks of Exposure to Asbestos: report of working group of experts, Commission of European Communities. Oxford, 1977.
2. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Asbestos; vol. xiv. International Agency for Research on Cancer, 1977.
3. Whitwell, F., Scott, J., Grimshaw, M. *Thorax*, 1977, 32, 377.

approached the matter from a different angle. They obtained occupational histories from 100 patients who had died from pleural mesothelioma, 100 patients with cancer of lung but no industrial disease, and 100 controls (no industrial disease or lung cancer). The light-visible asbestos fibre content was examined by phase-contrast microscopy after potash digestion. 83% of the mesothelioma patients had a history of asbestos exposure. The dried lung tissue of these patients contained over 100 000 asbestos fibres per gram. The lungs of the 23 patients with histological evidence of asbestosis nearly always showed counts of over 3 million. Lungs from control patients and from patients with cancer of bronchus but no industrial disease had counts of less than 20 000 fibres per gram, and patients with pleural plaques had counts of over 20 000 per gram. The number of asbestos fibres was related to occupation but not to home environment. WHITWELL et al. conclude that a definite dose relationship exists between asbestos exposure and mesothelioma formation but that “sub-asbestosis” levels of asbestos exposure do not contribute to the formation of lung cancer in those not exposed industrially. The type of asbestos fibre was not identified in this investigation. NEWHOUSE and BERRY⁴ also found evidence of a dose-response relationship for mesothelial tumours among workers in a factory where most of the workers were exposed to crocidolite, amosite, and chrysotile asbestos; the incidence-rate per 100 000 man-years was six times higher among those with long and severe exposure than among the workers with low to moderate exposure for less than two years.

The true risks of mesothelial tumours and carcinoma of the lung are hard to assess. The latent period for both tumours is long—for mesothelial tumours usually between twenty and forty years, and for cancer of lung probably more than twenty years—so that even with lengthy follow-up the risks may be underestimated. For cancer of the lung the effects of smoking as well as asbestos must be taken into account. SARACCI⁵ has reanalysed data from five sources⁶⁻¹⁰ where risk from cancer of lung was considered in relation to both asbestos exposure and cigarette smoking. He finds the multiplicative model more plausible than the additive model, being consistent with work in animals. In the multiplicative model, both asbestos and smoking are independently capable of producing lung

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10. Martischniig, K. M., Newell, D. J., Barnesley, W. C., Cowan, W. K., Feinman, E. L., Oliver, E. *Br. med. J.* 1977, i, 746.

11. Jones, J. S. T., Pooley, F. D., Smith, P. G. in *IARC Scientific Publication* no. 13, 1976.

cancer in man but with exposure to both they act synergistically.

Except in miners, exposure to one fibre type has been little studied. JONES,¹¹ in the United Kingdom, and McDONALD and McDONALD,¹² in Canada, looked at people employed in making army gas-masks with crocidolite filters during the 1939-45 war. The incidence of mesothelial tumours is very high. The U.K. study covered 1600 workers, chiefly women, and 26 have so far died of mesothelial tumours. The Canadian study covered 199 workers, and 9 (16%) of the 56 deaths have been due to mesothelioma. SELIKOFF¹³ followed a cohort of 870 wartime workers in a factory in the United States using only amosite asbestos: by 1973 there had been 598 deaths, 9 (1.5%) due to mesothelioma. In McDONALD's¹⁴ study of 11 000 Canadian chrysotile miners and millers extending from 1910 to 1975, 11 (0.24%) of the 4547 deaths were due to mesothelial tumours. One group of anthophyllite miners followed-up till 1974¹⁵ had had no deaths from mesothelial tumours.

Evidently crocidolite, amosite, and chrysotile asbestos all predispose to the tumour, with crocidolite carrying the highest risk. Have the improved conditions in industry influenced the mortality of asbestos workers? PETO et al.¹⁶ have extended their study of asbestos textile factory workers by 8½ years. Dust levels in the factory have steadily diminished but there is little difference between mortality before and after 1951. There is still an excess of deaths from lung cancer and chronic respiratory disease, and 5 pleural mesotheliomas have occurred. Further observation will be needed to show the effects of recent and stricter control of dust levels. ELMES and SIMPSON¹⁷ have also extended their study of insulation workers in Belfast by 10 years. Of the original 162 men at work in 1940, all but 40 were dead by 1975. The excess mortality from lung cancer and mesothelial tumours has continued, but the mortality from non-malignant respiratory disease including asbestosis has declined, reflecting improved conditions in the industry. Little asbestos apart from 'Maronite' board has been used in shipbuilding in Belfast since the 1960s. An advisory committee of the Health and Safety Commission is examining not only health aspects of asbestos but also economic factors in the control of hazards and substitution by alternative materials such as man-made mineral fibres. A report is expected in 1978, and revised codes of practice and standards will doubtless follow.

Ultrasonography of the Pancreas

ULTRASOUND is a good test for pancreatic disease. In a series reported by DI MAGNO and others¹ it proved far more reliable than isotope scanning. A positive result from ultrasonography, or from a pancreatic-function test if the ultrasound examination was normal, warranted endoscopic retrograde cholangiopancreatography (E.R.C.P.). This sequence of tests correctly identified 90% of patients with and without pancreatic disease. DI MAGNO et al. classed their ultrasound scans only as normal or abnormal. Other workers use ultrasound to explore the nature of the pancreatic abnormality.^{2,3}

The performance and interpretation of an ultrasound scan of the pancreas demands considerable knowledge of anatomy and pathology coupled with skill and experience in ultrasonics. Absence of one of these ingredients jeopardises the examination. This may explain the wide disparity in the published reports on pancreatic ultrasonography. Leading workers have for several years been displaying the normal pancreas in detail.^{2,4} From a survey of 382 normal pancreases we can now state the normal antero-posterior and cranio-caudal diameters of the head, body, and tail⁵—so it is surprising to find WINSHIP and others saying, this year, that "the normal pancreas is difficult or impossible to show".⁶

In acute pancreatitis an enlarged, inflamed pancreas is seen in 83-90% of cases, even after the serum-amylase has returned to normal.^{2,7} More importantly, ultrasound shows whether pseudocysts are getting bigger or smaller and differentiates them from inflammatory masses, thus aiding surgical management.⁸ Ultrasound will detect over 90% of pseudocysts greater than 2 cm in diameter^{2,3,8-11} and is far more accurate than other methods.^{2,3,11} The 8% false-positive rate is due to the difficulty of differentiating small cysts from small areas of necrosis. Ultrasound reveals that about half of all attacks of acute pancreatitis are complicated by pseudocyst formation, 20-40% of the pseudocysts resolving spontaneously in the months that follow.^{8,11}

The ultrasound changes of chronic pancreatitis have been well described by French and German workers,^{2,3} who claim to detect specific changes of chronic pancreatitis in 40%¹² to 94%.² 90% accu-

acy has not been reported in other departments, so chronic pancreatitis is usually normal on ultrasound.³

In carcinoma of the pancreas, ultrasonography is specifically diagnostic. Most tumours of the head or body of the pancreas have been reported.¹³ With the pancreas in situ, carcinoma of the head or body of the pancreas is easily distinguished from a pseudocyst.^{2,15}

Percutaneous ultrasound-guided biopsy permits preoperative diagnosis of carcinoma of the pancreas. A positive result was obtained in 10 of 15 patients, and no positive result was obtained in 5 of 15 patients. Most of the re-punctured patients survived.¹⁶

Computer-aided ultrasonography of C.T. scan is a start, the scanner is still in development.^{19,20} The picture of the pancreas is 10-20% wider for C.T. scan than for ultrasound.^{19,21}

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12. Lutz, H. *Elect*

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acy has not been achieved in British or American departments, some of which still maintain that in chronic pancreatitis the ultrasonic picture is usually normal.⁷ E.R.C.P. is much more accurate than ultrasound in diagnosis of chronic pancreatitis.³

In carcinoma of the pancreas ultrasonic abnormalities are seen in 90%,^{9,12} and a carcinoma is specifically diagnosable in between 58%¹² and 83%.² Most tumours are over 2 cm in diameter and lie in the head or body. Lately, 11 carcinomas of the tail have been reported, 3 of them less than 2 cm in diameter.¹³ With the incidence of carcinoma of the pancreas increasing at a rate exceeded only by carcinoma of the lung,¹⁴ early diagnosis is important. At present a small tumour is hard to distinguish from localised chronic pancreatitis. Carcinomas are easily distinguishable from cystadenomas, which resemble a pseudocyst but are usually multilocular.^{2,15}

Percutaneous biopsy of the pancreas under ultrasound control, a technically simple procedure, permits preoperative cytological diagnosis of carcinoma of the pancreas. Of 20 carcinomas so sampled, a positive aspirate was obtained in 17; 2 tumours were too solid for aspiration and in 1 the aspirate was normal. There were no complications, and no positive results were obtained in patients without tumour.¹⁶ Pseudocysts have also been punctured and drained by this means. Out of 22 patients so treated 2 had mild complications.^{17,18} Most of the pseudocysts recurred and several were re-punctured. Even if not curative, repeated puncture may avoid operation in the acute phase, when the mortality-rate is highest,⁶ and allow the cyst wall time to mature.¹⁸

Computerised tomography of the pancreas is easier to perform and to interpret than pancreatic ultrasonography. With the increasing availability of C.T. scanners, why bother with ultrasound? For a start, the cost of buying and maintaining a C.T. scanner is ten times the equivalent cost for ultrasound.^{19,20} Ultrasound produces no ionising radiation. Though C.T. scanning gives an inadequate picture of the pancreas in only 7%,²¹ as against 10–20% with ultrasound,^{12,19} clinically the advantage for C.T. is slight: the patient with an unsuccessful ultrasound scan will usually be investigated further.^{19,22} The X-ray absorption values of nor-

mal, inflamed, and cancerous pancreas are so similar that these conditions cannot be distinguished by C.T. scanning.^{21,23,24} This is not so with ultrasound, which detects much smaller density differences than X-rays, and thus displays more contrast between structures.²⁰ Ultrasound should be the initial investigation for most patients with suspected pancreatic disease.

U.K. TRANSPLANT

SINCE U.K. Transplant was set up in 1972, to distribute cadaver kidneys between the 30 transplant centres in the United Kingdom and Ireland, over 3000 cadaver kidneys have been transplanted in the United Kingdom. A computer file of all patients awaiting a kidney transplant is kept at the organisation's centre in Bristol, and from this file the best-matched recipients are chosen whenever cadaver kidneys are offered to the organisation for distribution. According to the annual report¹ the number of patients waiting for a transplant continues to increase by about 100 each year. The latest figure is 1234. The rate of kidney transplantation has not increased correspondingly, although last year's total of cadaver grafts (691) was some improvement over the previous year (604). About half these kidneys were transplanted by the centre which retrieved them. As in previous years, no significant improvement in graft survival was apparent in those patients who received well-matched kidneys; however, a trend is discernible, and when the numbers are greater survival may prove to be correlated with matching. This is so in America, where a significant correlation between the number of HLA antigens mismatched and graft survival has at last become apparent in a series of nearly 5000 first cadaver-kidney transplants.² Achieving a perfect match for the four antigens at the HLA A and B loci remains a difficult task and last year this was accomplished in only 4% of cases transplanted in the U.K. Matching may be more important in patients who have acquired antibodies before grafting. This group of patients do surprisingly well, and with matching of A-locus antigens over 70% of grafts survive a year. A depressing feature of the report is the clear indication that the overall survival of kidney grafts is not improving as the years go by. In fact, cadaver-graft survival at one year has fallen from 62% to 50% during the past five years, a decline very similar to that in the United States.³ The introduction of a no-blood-transfusion policy for dialysis patients has been proposed as a cause for this, and in this year's report U.K. Transplant look carefully at the possible influence of previous blood-transfusion on graft survival. The analysis was done on 773 patients whose transfusion history was accurately known, and the group of transfused patients did prove to have benefited: their graft survival was 5–10% better than that of the non-transfused group. A previous pregnancy was also associated with better survival. Another noteworthy observation was the improved graft survival if recipients were blood-group ABO identical, rather than ABO compat-

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ible, with the donor. Whereas the age of the kidney donor did not significantly influence the results, the age of the recipient was all important. For patients over the age of 50 graft survival at twelve months was only 30–40%, and this was because many died in the first year with a functioning graft.

Tables prepared from data provided by the registry of the European Dialysis and Transplant Association permit comparisons of the treatment available in the U.K. with that in other European countries. Taking dialysis and transplantation together, 71 patients per million of the population received treatment in the United Kingdom in 1976. This is less than half the number treated by Switzerland, Denmark, and Israel, and at present the U.K. lies 13th in a table of 24 European countries. Most of the countries in Europe continue to open new dialysis centres and now have 3 per million of the population. By contrast, in Great Britain the number of dialysis centres is static at 1 per million of the population. The situation is not quite as bad as it seems, however, since through home dialysis these centres treat twice as many dialysis patients as do their counterparts, and the proportion of patients transplanted is higher than in most countries. Nonetheless Britain is clearly lagging, since it has the same incidence of renal failure as the rest of Europe. Last year the United Kingdom accepted 15 new patients per million of the population whereas France, the Federal Republic of Germany, and Italy were each accepting twice this number. Not only is the U.K. figure less than that for the previous year but it is also well below the average for Europe as a whole (19). Home dialysis in Britain has been a success but the number of patients who can be trained each year in existing dialysis centres is unlikely to increase. Nor is there much prospect of a substantial increase in the rate of kidney transplantation. At present the only way to help more patients with renal failure is to increase facilities for haemodialysis. This could be done by constructing more dialysis centres or by establishing satellite units linked to existing centres.

ON PISSING IN THE BEDDE¹—AND ELSEWHERE

Most children's doctors can be confident about the diagnosis and management of nocturnal enuresis. Results of treatment may vary with their enthusiasm, but with a spontaneous-cure rate of about 20% per annum time is on their side. Children with day-and-night wetting seem more difficult to treat and often have other symptoms (urgency, faecal soiling) which distinguish them from those with nocturnal enuresis alone. Berg and others,² in Leeds, have tried to identify such differences. They investigated 86 children—40 day-and-night wetters referred to a children's psychiatrist, 29 night wetters referred to a paediatrician, and 17 night wetters attending a child-psychiatry clinic. They assume that the degree of psychiatric disturbance dictates whether a child with nocturnal enuresis should be referred to psychiatrist or children's physician; in some parts of the country it indicates differing lengths of wait-

ing-list. During an interview with a single observer, mothers gave information about the presenting disorder, social behaviour, and school performance. Urgency, soiling (most commonly in boys), and parental exhortation to use the lavatory were more common in day-and-night wetters. Although some parents in all groups had a history of nocturnal enuresis, current urinary symptoms such as urgency or giggle incontinence were not asked about—a surprising omission since two-thirds of the whole group of children complained of urgency and this was more common in those with any wetting pattern referred to a psychiatrist than in children with nocturnal enuresis attending a paediatrician. Understandably, parental urging of the child to toilet followed a similar pattern: some mothers are probably anxious about their own continence and project their worries on the child; others, of course, are simply exasperated with a wet and smelly child. The children's schools were visited and a standard psychological profile was completed for the patient and a control child. Again, day-and-night wetters emerged with more psychiatric disturbance—neuroticism in girls and antisocial behaviour in boys. Night wetters differed little from controls. Each child was examined by a paediatrician and the urine was tested. Bacteriuria was virtually confined to girls who wetted day and night, and eradication of infection did not alter that pattern. Radiology of the urinary tract was mostly normal. Lastly, maximum bladder capacity (M.B.C.)—meaning the volume of urine obtained from a child at bursting point—was measured in most children and 88 controls; the M.B.C.s of all wetters were less than those of normal children. This has been reported before³ in nocturnal enuresis; by bladder training, capacity can be increased and enuresis cured at six-month follow-up.⁴

The doctor has to ask himself three questions about a child with urinary incontinence. Firstly, is the child old enough, sane enough, and intelligent enough to be capable of dryness? Secondly, does the incontinence result from physical disorder? It seldom does, and a careful examination of child and urine should resolve this point. Furthermore, as Berg and others² observe, urinary infection in girls with damp pants is probably a result rather than a cause of wetting. Radiography of spine and urinary tract are not therefore indicated in most children.⁵ Pressure studies of bladder function may yield interesting results, such as abnormal detrusor function in patients with urgency and day-and-night wetting.⁶ Therapeutic benefits are marginal so these investigations must never be a routine in childhood. Finally, is the incontinence one symptom of a wider emotional disorder? Nocturnal enuresis alone is usually a biological phenomenon which is likely to remit with tricyclic antidepressants—probably from their cholinergic effect—for as long as they are prescribed. An alarm system will be more permanently successful, if it is used in the right way by the right families and prescribed by the right doctor.⁷ Children who wet by day and night

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more usually have an emotional disturbance needing its own skilled treatment; children who wet by night are likely to have urgency. Might not this be a conditioned response which can be modified by behaviour therapy for the child—or its parents?

THIRD INTERNATIONAL CÆLIAC SYMPOSIUM

THE Californians have an original approach to dietary treatment of celiac disease: they are trying to breed a wheat lacking in alpha-gliadin. Meanwhile, work in Leiden, Oxford, and Galway is bringing nearer the day when the toxic fraction of gluten is fully identified; and groups in Boston, Paris, Bergen, Bern, and Hammar-smith are using intestinal organ cultures as indicators of toxicity or to study the nature of the intestinal damage. The results tend to be non-specific, so that some workers continue to rely on in-vivo absorptive tests (e.g., with xylose) and on sequential intestinal biopsies. These and other matters came up at the third international symposium, held in University College, Galway.

The prevalence of HLA B8 seems to be higher in the West of Ireland than elsewhere, presumably accounting for the high incidence of celiac disease there. The genetic basis of the disease is now becoming clearer; it seems that an individual with the tissue antigens HLA B8 and DWR3, and also with a B-lymphocyte-specific alloantigen, is very likely to get celiac disease.

How long does gluten intolerance persist? 97% of a large number of patients with celiac disease managed by members of the European Society of Paediatric Gastroenterology were judged to have permanent gluten intolerance. Groups from Galway, Paris, Geneva, and London described children with varying degrees of gluten intolerance or with apparent eventual gluten tolerance, but it was agreed that such children must be followed up assiduously and that a lifelong gluten-free diet will be the lot of almost all. A small panel was set up to clarify and unify diagnostic criteria, particularly in relation to mucosal morphology, as the basis for accurate prognosis and continued observation. No-one responding to the European Society of Paediatric Gastroenterology questionnaire knew of a case of lymphoma arising below the age of 18 years, or knew of a case of untreated childhood celiac disease which had not responded to a gluten-free diet.

The benefits of zinc and other trace metals in adults with unresponsive disease were reported from Belfast. Bristol and Oxford reported their results with Arthus-like skin reactions to gluten fractions, which, like serum antibodies to gluten, are not specific to celiac disease, being found in other forms of intestinal mucosal damage. Patients' views on gluten avoidance were reported from Bristol. Constipation is a big drawback of the gluten-free diet, and this is lessened by a rice-bran preparation. The patients can get much help from a celiac society—not least, with holiday arrangements and phrase sheets for use in foreign restaurants.

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WHICH MEDICINE?

How does a doctor decide which drug, or which preparation of a drug, to prescribe? In the existing system, the decision involves at least two processes. Firstly, the doctor must be made aware of the existence of a drug, and the continuing introduction of new products to a market which at present exceeds 30 000 formulations makes this a formidable proposition. Secondly he has to get information on the drug's usefulness in individual patients. In a sample of general practitioners,¹ drug-company representatives were the prime source of information about the existence of a drug, closely followed by *MIMS*. Almost half the practitioners admitted that they were unable to obtain an unbiased assessment of a new drug. The most helpful sources of advice were consultants, and articles in medical journals. These observations raise important questions about the role and responsibility of the pharmaceutical industry in postgraduate education, and particularly about the influence of the 3000 drug-company representatives, most of whom are not medically qualified and in no position to advise on treatment of an individual patient. The pharmaceutical industry contributes towards post-graduate education by medical meetings and films, but the cost of representatives and their activities is the main item, reckoned at about £20 million a year.²

Do we really have to continue with this two-stage approach to decision-making in prescribing? While information on a drug and its pharmacological properties is important, there has been a tendency to forget that clinical medicine is, or should be, directed towards the patient and his disease. At a symposium on the information needs of the prescribing physician, Hunter³ said that the prescriber would be helped if the emphasis in information systems could be shifted from the drug towards the disease. A clinical pharmacologist is, by training, both a pharmacologist and a clinician and should be able, in collaboration with his clinical colleagues, to build the basis of such a system in the hospital service^{4,5}—particularly if supported by a hospital pharmacy information centre.⁶

Alas, these facilities are rare in hospitals, and general practitioners with ready immediate access to such advice are few indeed. Most doctors are well aware of their shortcomings in prescribing, want to do something about it, but do not know where to turn for advice at the time when they most need it. Which brings us back again to a plea we have uttered before,⁷ for a publication—perhaps a redesigned, regularly updated, cost-conscious *British National Formulary*—which would provide advice on the best treatment for a particular condition, on how to administer it, and on the potential dangers and necessary precautions. The 1976–78 *B.N.F.* is already out-of-date in many respects, and it is disturbing that the Department of Health has said nothing about plans for a successor.

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