BRITISH MEDICAL JOURNAL

LONDON, SATURDAY 24 JUNE 1978

Covert bacteriuria—peril or partnership?

Chronic pyelonephritis is still an important cause of end-stage kidney failure even though effective treatment for urinary tract infection has been available for over 40 years.[1] In general practice urinary infections remain a major source of illness with an annual consultation rate of 12 per 1000 patients.[2] One reason for this therapeutic failure might be that urinary tract infections often remain undetected and untreated. Such covert infections might be the source of the continuing illness and death. Since these hidden infections can be detected simply and cheaply we need to know whether screening for them has preventive value. The answer to that question requires an understanding of the relation of covert to overt infection, knowledge of the long-term sequelae of covert infections, and study of their response to treatment.

Whether or not urinary tract infection produces symptoms depends on differences in host-parasite relations. In covert infections rough, untypable strains of *Escherichia coli* are more often isolated than in overt infections[3] and correspondence between the urinary and faecal strains of *E coli* is less often observed than in symptomatic infections.[4] These observations indicate that the surface structure of bacteria isolated from covert infections may have been altered, possibly[5] as a result of the action of locally produced immunoglobulin (S IgA). Several other findings support this view. Strains isolated from patients with covert infections are less antigenic[6] and show less adherence to uroepithelial cells than isolates from symptomatic cases,[7] and new infections which follow initially successful treatment of covert bacteriuria are more often associated with symptoms than the continuing or relapsing infections in untreated or unsuccessfully treated cases.[8] This all suggests that covert infections represent a symbiosis which is better left undisturbed by treatment. There is at least one important exception, however: the pregnant woman with symptomless infection should be treated, since she has a 30% chance of developing acute pyelonephritis. This risk can be avoided by detecting and treating bacteriuria in the antenatal clinic.[9]

Several groups have studied the long-term consequences of covert infections in adults and children. About 25% of adults with covert infection have kidney scars, but the damage does not seem to progress provided there are no complicating factors such as hypertension, obstruction, excessive analgesic intake, diabetes mellitus, or urolithiasis.[10–12] Much evidence suggests that kidney damage due to urinary tract infection develops in childhood. There have been four recent studies[13–16] of the fate of schoolgirls with covert infection and the effect of treatment of their infections, and the findings of three of these studies have now appeared. In Dundee 60 girls aged 5-8 years were followed for two years. One of the 26 children who received treatment and three of the 34 children who were left untreated developed new kidney scars. In Gothenburg 116 girls aged 7-15 were followed for three years. Only girls with normal *x*-ray appearances were allocated to the controlled treatment trial. In these girls persistent bacteriuria did not lead to scarring of the kidney, and bacteriuria alone did not affect urinary concentrating power or kidney growth. In the Cardiff-Oxford study 208 schoolgirls aged 5-12 were followed for four years, randomly allocated to a treatment and control group irrespective of the *x*-ray findings. As in the Gothenburg study, kidneys that were not scarred initially remained unscarred, and their growth was unimpaired even in the presence of persistent bacteriuria or vesicoureteric reflux or both. Nevertheless, in 12 of the 44 girls in whom the kidneys were scarred initially the scarring had progressed by the end of four years. The features of this high-risk group were that all had vesicoureteric reflux and that bacteriuria had been present for over two years in all except one.

Since 2% of apparently healthy schoolgirls have covert urinary infection the data from the Dundee and Cardiff-Oxford studies indicate that about one in every 1000 schoolgirls develops progressive kidney damage; yet this remarkable frequency is not reflected in the incidence of end-stage kidney failure in young women. What, then, causes kidneys with focal scarring to fail? Several possible mechanisms may be important —the development of hypertension; the effect of back pressure from associated vesicoureteric reflux; whether or not the renal papillae allow pyelotubular backflow[17]; whether or not glomerular disease accompanies the reflux[18]; and the possible deleterious effect of persistent or recurrent infection. Both the frequency of progression of focal scarring to kidney failure and the relative importance of the adjuvant factors in this progression need further evaluation.

Since new kidney scars rarely develop after the age of 4,[19] evidently screening schoolgirls for covert infection has little to offer. Effective prevention requires screening at an earlier age. Vesicoureteric reflux is of central importance in the pathogenesis of kidney scars associated with infection; in particular, the more severe degrees of reflux (which before the age of 4 may be associated with pyelotubular backflow) predispose to kidney scarring.[19] Clearly what we need is a screening procedure for vesicoureteric reflux. At present the best method is to screen for infection, but this is not foolproof. The Cardiff-Oxford group showed that during the first year of follow-up of 27 untreated girls with bacteriuria and reflux the bacteriuria

cleared in six even though the reflux persisted.[20] We need better methods, and several have been explored. The detection of anti-Tamm-Horsfall antibody proved unhelpful.[21] Screening relatives of patients with vesicoureteric reflux gives a much higher yield of reflux than in the general population.[22 23] A weak association of reflux with HLA B12 has been shown.[24]

Even when an acceptable technique for the detection of reflux in the very young has been found, however, controlled trials of medical versus surgical treatment will be required to establish the optimum method of preventing kidney damage. We still have far to go before we can prevent chronic pyelonephritis in childhood. Meanwhile we may be able to arrest its progress by early detection and control of raised blood pressure, by long-term antibacterial treatment,[25] and possibly also by surgical treatment of the most severe grades of vesicoureteric reflux.[26 27]

1 Parsons, F M, in *Proceedings of the 9th Conference of the European Dialysis and Transplant Association*, eds J S Cameron, C S Ogg, and D Fries, p 3. London, Pitman Medical, 1972.
2 Fry, J, *et al*, *Lancet*, 1962, **1**, 1318.
3 Hanson, L A, *Journal of Infectious Diseases*, 1973, **127**, 726.
4 Roberts, A P, *et al*, *Journal of Medical Microbiology*, 1975, **8**, 311.
5 Lidin-Janson, G, *et al*, *Journal of Infectious Diseases*, 1977, **136**, 346.
6 Hanson, L A, in *Symposium on Pyelonephritis*, eds E H Kass and W Brumfitt. Chicago, University of Chicago Press, 1978, in press.
7 Svanborg Eden, C, *et al*, *Lancet*, 1976, **2**, 490.
8 Asscher, A W, *et al*, *British Medical Journal*, 1969, **1**, 804.
9 Williams, J D, *et al*, in *Urinary Tract Infection*, eds W Brumfitt and A W Asscher, p 160. London, Oxford University Press, 1973.
10 Freedman, L R, in *Abstracts of the 5th International Congress of Nephrology*, ed H Villareal. Basal, Karger, 1972.
11 Gower, P E, *Quarterly Journal of Medicine*, 1976, **45**, 315.
12 Asscher, A W, *et al*, in *Urinary Tract Infection*, eds W Brumfitt and A W Asscher, p 51. London, Oxford University Press, 1973.
13 Savage, D C L, *et al*, *Lancet*, 1975, **1**, 358.
14 Newcastle Asymptomatic Bacteriuria Research Group, *Archives of Disease in Childhood*, 1975, **50**, 90.
15 Lindberg, U, *et al*, *Journal of Pediatrics*, 1978, **92**, 194.
16 Cardiff-Oxford Bacteriuria Study Group, *Lancet*, 1978, **1**, 889.
17 Ransley, P G, and Risdon, R A, *Urological Research*, 1975, **3**, 111.
18 Kincaid-Smith, P, *Kidney International*, 1975, **8**, suppl 4, 81.
19 Rolleston, G L, Maling, T M H, and Hodson, C J, *Archives of Disease in Childhood*, 1974, **49**, 531.
20 Verrier-Jones, E R, *et al*, *Kidney International*, 1975, **8**, suppl 4, 85.
21 Fasth, A, Hanson, L A, and Asscher, A W, *Archives of Disease in Childhood*, 1977, **52**, 560.
22 de Vargas, A B F, *et al*, *Journal of Medical Genetics*, 1978, **15**, 85.
23 *British Medical Journal*, 1975, **4**, 726.
24 Bailey, R R, and Wallace, M, *British Medical Journal*, 1978, **1**, 48.
25 Smellie, J M, *et al*, *British Medical Journal*, 1976, **2**, 203.
26 Smellie, J M, and Normand, I C S, *Archives of Disease in Childhood*, 1975, **50**, 581.
27 Orikasa, S, *et al*, *Journal of Urology*, 1978, **119**, 25.

The laparoscope: useful tool or dangerous weapon?

Obstetricians and gynaecologists stand apart from their colleagues in the almost masochistic zeal of their self-examination and self-criticism. Hospital statistical reports, maternal mortality surveys, and perinatal mortality and morbidity reviews, often highly critical, are all part of the obstetrician's way of life. Recently the same approach has been turned to gynaecological laparoscopy in a study[1] organised jointly by the Royal College of Obstetricians and Gynaecologists, the DHSS, and the medical defence organisations.

After Steptoe's pioneering work in the early 1960s laparoscopy was taken up by British gynaecologists with remarkable enthusiasm. The ability to see the pelvic organs without formal laparotomy proved a great attraction; to many gynaecologists the ingenious instrument had something of the fascination of a new toy. Soon techniques were developed to allow minor surgery, and laparoscopy proved particularly useful for tubal sterilisation. The increasing demand for irreversible contraception has made this the predominant use of the instrument today.

Yet, despite the general enthusiasm, there have been disquieting reports of serious complications and even deaths. Uncertainty as to the true extent of these ill-effects led to setting up the joint inquiry. What can we say of the results, which reviewed 50 000 operations? On the face of it gynaecological laparoscopy appears to be outstandingly safe, with a mortality rate of only 8 per 100 000. Nevertheless, only about 80% of the estimated number of laparoscopies occurring in the year covered by the study found their way into the survey. That might not be too important if it could be established that the deficit was attributable to some institutions' not taking part in the inquiry; but, in fact, a sample taken from co-operating hospitals showed that only 79% of their patients had been entered. Possibly some of those in whom serious complications arose might have been less likely to be reported because of worry about litigation. Fixing entry into the study at the time that laparoscopy was arranged rather than when it was performed would have avoided that source of bias. Furthermore, survey forms which for various reasons could not be processed showed a 9% incidence of complications compared with 3·6% in those which were entered in the survey.

The three parts of the laparoscopic procedure that most often gave rise to complications were inducing the pneumoperitoneum, introducing the trocar, and diathermy of the tubes or other structures. One reassuring finding was that the anaesthetic risk was very low. Two of the four deaths (and perhaps three) were such that they must be regarded as specifically related to the procedure and would not have occurred with an alternative technique. In one instance a bowel injury, unrecognised at sterilisation by electrocoagulation, ultimately led to death. In another, death occurred after induction of pneumoperitoneum and was confirmed at necropsy as being due to gas embolism. Another death occurred in similar circumstances, but the report gave no details of the necropsy findings. In the fourth case cardiac arrest occurred at the end of the procedure and was not obviously related to the pneumoperitoneum. These mortality and morbidity figures are roughly comparable with those reported in similar large reviews in the United States,[2-4] with similar designs and almost certainly similar types of bias. The report compares favourably the overall mortality rate with the recurrent annual mortality rate attributable to oral contraception. A more important comparison, perhaps, is with alternative methods of sterilisation, but this information is not available.

As tends to happen with computerised data collection on a large scale, some quite unexpected and interesting figures emerge. Many of these bear on the fundamental organisation of the NHS with its large proportion of operations performed by doctors in different trainee grades, many unsupervised. The higher rate of complications in operations performed in these circumstances is a general problem not specifically related to laparoscopy. Occasionally the report gives the impression that some of the data were processed through a computer to emerge untouched by the human mind. We are told, for example, that as the complication rate was higher in operations lasting over 35 minutes the operating time should be kept below this—bizarre advice indeed.

The commendable enthusiasm generated through the Royal College of Obstetricians and Gynaecologists for this survey encouraged the voluntary co-operation of doctors