decreased. The strains isolated in the other 11 patients were fully sensitive to these antibiotics.

In the recalcitrant cases, some of which were symptomless, gonococci were harboured in the tonsils for up to eight weeks. Re-exposure to orogenital contact was denied in each case.

Discussion

Eleven of the 13 patients suffering from tonsillar gonorrhoea had practised orogenital contact at their most recent intercourse, so it is most probable that the infection was acquired in this way. The two exceptions were a heterosexual Mohammedan who denied cunnilingus and a woman who claimed never to practise orogenital contact. Other modes of transferring gonococci to the tonsils must therefore be considered.

In none of our cases was there any indication that the infection had been transferred by kissing. The tonsillar infection was always associated with genital gonorrhoea. However, patients who may have contracted an isolated tonsillar infection, perhaps innocently, are unlikely to consult a venereologist. The throat symptoms when present in our cases were no different from those expected in common nasopharyngeal infections, but their persistence and the fact that cultures remained positive indicate that in our cases they were probably attributable to the gonococci. That gonococcal colonization of the tonsils was most often asymptomatic is suggestive of a carrier state.

Tonsillar gonococcal infections seem to be extremely recalcitrant to treatment. Our routine single-dose treatment failed

in about half the cases, whereas it has proved almost completely successful in curing uncomplicated gonorrhoea in both sexes (Bro-Jørgensen and Jensen, 1971). Tetracycline was also ineffectual, and though other regimens have been tried we have not as yet found a reliable therapy. An added difficulty in diagnosis and in assessing the efficacy of treatment is the unreliability of a single negative culture finding. We may have missed some cases on initial examination on account of this.

The high incidence of gonococcal tonsillar infections, their resistance to treatment, the lack of any characteristic signs and symptoms, and the possibility of innocent acquirement of the disease by kissing are factors which presumably may result in a rather high prevalence of this hitherto disregarded gonococcal infection. We suggest that tonsillar gonorrhoea may account for some obscure septicaemic and allergic manifestations as well as for some of the so-called "false-positive" gonococcal complement fixation tests.

References

- Bro-Jørgensen, A., and Jensen, T. (1971). *British Journal of Venereal Diseases*, 47. In press.
 Cowan, L. (1969). *British Journal of Venereal Diseases*, 45, 228.
 Fiumara, N. J., Wise, H. M., and Many, M. (1967). *New England Journal of Medicine*, 276, 1248.
 Høllgren, L. (1971). *Läkartidningen*, 68, 569.
 Iqbal, Y. (1971). *British Journal of Venereal Diseases*, 47, 144.
 Metzger, A. L. (1970). *Annals of Internal Medicine*, 73, 267.
 Schmidt, H., Hjørtting-Hansen, E., and Philipsen, H. P. (1961). *Acta Dermato-Venereologica*, 41, 324.
 Thatcher, R. W., McCraney, W. T., Kellogg, D. S., and Whaley, W. H. (1969). *Journal of the American Medical Association*, 210, 315.

MEDICAL MEMORANDA

Polyuric Acute Renal Failure after Methoxyflurane and Tetracycline

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British Medical Journal, 1971, 4, 661-662

Methoxyflurane has been in use as an anaesthetic agent for over a decade. Initial studies on this drug failed to show any hepatic or renal toxicity. There have, however, been several reports since 1964 associating methoxyflurane anaesthesia with a post-operative raised urine output and azotaemia. Tetracycline drugs have been reported to produce a similar picture and it has been suggested that the combination of methoxyflurane anaesthesia with tetracycline administration is more likely to result in this clinical syndrome (Kuzucu, 1970). We present such a case and discuss some of the unusual features.

Case Report

A previously healthy 33-year-old man was admitted to the intensive care unit with severe chest injuries after a car accident. He was shocked, had a four-rib flail segment of the left mid-chest anteriorly, fractures of his second, third, and fourth ribs on the

right, a right-sided tension pneumothorax, and a progressively widening mediastinum. This latter feature was a haemomediastinum due to an avulsed right subclavian artery, which was repaired under heart-lung bypass. The surgical management of this case is dealt with more fully in a report by Girdwood *et al.* (1972).

Postoperatively he made good progress; his cardiac output and renal function were good. His early postoperative management and therapy consisted of intermittent positive-pressure ventilation to control the flail segment, blood and fluids as necessary, regular bronchial toilet, and chest physiotherapy four times daily, with intravenous fentanyl 0.1 mg for analgesia. In addition the following drugs were given: ampicillin 250 mg plus cloxacillin 250 mg intramuscularly four times daily and streptomycin 500 mg intramuscularly twice daily for six days, ascorbic acid 500 mg intramuscularly twice daily (later 400 mg by mouth), and diazepam 5 mg intramuscularly or papaveretum 5 mg intramuscularly or both as required for analgesia and sedation.

From the seventh postoperative day, because of the large amounts of papaveretum and fentanyl that he was receiving, chest physiotherapy was carried out three times daily under methoxyflurane analgesia. Methoxyflurane (0.1-3%) was delivered together with 50% nitrous oxide in oxygen via a Pentec vaporizer on a Boyle's anaesthesia machine using a 10-l. fresh gas flow and a Mapleson C circuit for about 20 minutes each time. On the same day, because *Klebsiella aerogenes* was isolated from his bronchial secretions, the antibiotics were changed to tetracycline 100 mg intramuscularly four times daily after a loading dose of 500 mg, plus streptomycin 0.5 g twice daily. Then, because of the appearance of *Pseudomonas pyocyanea* in his secretions, antibiotics were stopped after the 10th postoperative day in the hope of avoiding further superinfection after the antibiotic suppression of normal flora.

His general condition continued to improve until the 13th postoperative day, when he was noticed to be dehydrated. He improved both clinically and biochemically with rehydration. He was then maintained with a fluid intake of 4.5 l./day, but within three days he was again dehydrated and we realized that he was suffering from an iatrogenic diabetes insipidus. He was not hyper-

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Biochemical values throughout the patient's illness.

glycaemic, hypokalaemic, or hypercalcaemic. Because of the reports that this condition can occur after methoxyflurane anaesthesia he received no more of this drug.

After rehydration it was noticed that the urinary urea concentration had fallen while the blood urea level was raised. This situation of "polyuric acute renal failure" was treated with three daily injections of nandrolone phenylpropionate 25 mg intramuscularly, maintenance of a high calorie intake, and encouragement of the high urine output by maintaining good hydration with a fluid intake of up to 7 l./day. This proved very successful.

The possibility that the diabetes insipidus was due to a hypothalamic lesion was investigated by observing the response to exogenous pitressin tannate in oil. The absence of any response at all in urinary output or osmolarity, even after repeating the dose one day later, was thought significant.

The serum and urinary oxalate levels were measured and a very high urinary output of oxalate and a serum level raised to

about three times normal were shown. A slightly lowered plasma calcium level was also found (see Chart). These values slowly returned to normal, though the response to pitressin was still reduced when the patient was discharged home six weeks after his accident.

Comment

The mechanism of the nephrotoxicity of methoxyflurane is not clear but would appear to be dose-dependent. Metabolic degradation products of methoxyflurane including oxalate and inorganic fluoride have been incriminated (Mazze *et al.*, 1971). Its use has been associated with an increased oxalate excretion in the urine of all cases studied (Silverberg *et al.*, 1971). In the present case the plasma level of oxalate was far greater than could be accounted for by the degree of renal failure.

The source of the excess oxalate remains in doubt. Usually 60% of it is derived from glycine and ascorbic acid (Atkins *et al.*, 1964). It has been suggested that antibiotics might upset the intestinal flora, causing abnormal bile acid deconjugation, freeing glycine which could be metabolized to oxalate (Greenberg *et al.*, 1970). Another possible mechanism for the increased oxalate load from glycine lies in the antianabolic effect of tetracyclines. The amino-acids freed by continued protein catabolism are no longer utilized for protein synthesis (Shils, 1962).

In view of the increased utilization of methoxyflurane in Britain and the possibility of its use concurrently with antibiotics of the tetracycline group the nephrotoxic effects of these drugs should be thoroughly appreciated.

We wish to thank Mr. M. I. Ionescu for permission to report details of this case, and Dr. F. M. Parsons and Dr. J. J. L. Ablett for their interest and help in the preparation of the manuscript. We would also like to thank Dr. A. Hodgkinson and Mr. F. Knowles, of the M.R.C. Mineral Metabolism Unit, for the oxalate determinations, and the department of chemical pathology for many of the biochemical determinations.

References

- Atkins, G. L., Dean, B. M., Griffin, W. J., and Watts, R. W. E. (1964). *Journal of Biological Chemistry*, **239**, 2975.
- Girdwood, R. W., Holden, M. P., and Ionescu, M. I. (1972). *Thorax*. In press.
- Greenberg, S. R., Frobese, A. S., and Pezzi, P. (1970). *New England Journal of Medicine*, **283**, 1226.
- Kuzucu, E. Y. (1970). *Journal of the American Medical Association*, **211**, 1162.
- Mazze, R. I., Trudell, J. R., and Cousins, M. J. (1971). *Anesthesiology*, **3**, 247.
- Shils, M. E. (1962). *Clinical Pharmacology and Therapeutics*, **3**, 321.
- Silverberg, D. S., McIntyre, J. W. R., Ulan, R. A., and Gain, E. A. (1971). *Canadian Anaesthetists' Society Journal*, **18**, 496.

Nocturnal Enuresis as a Late Complication of Meningitis

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British Medical Journal, 1971, **4**, 662-663

Enuresis is described as primary when referring to a child who has never learnt to be consistently dry, and secondary in the situation where someone who has been dry for a period of months or years starts wetting again. After the age of 6 years secondary enuresis is more common (Meadow, 1970). While

psychological stress, insecurity, and immaturity are among the usual causes, organic factors do occur. These include diabetes mellitus and other causes of polyuria, urinary tract infection, and neurological conditions, of which spina bifida occulta and spinal tumour are the most commonly described. The case reported here is that of a child who developed nocturnal enuresis about two years after recovery from severe meningitis. The underlying lesion was found to be chronic adhesive arachnoiditis with an associated cyst, and freeing of the nerve roots of the cauda equina and excision of the cyst resulted in a cure.

Case Report

A 13-year-old girl was seen because of nocturnal bedwetting for five years and headaches of recent onset. She was healthy, of normal intelligence, and a sacrococcygeal sinus was the sole positive clinical finding. Review of her past history disclosed that at the age of 6 years she had a severe attack of meningitis associa-

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