CORRESPONDENCE

Correspondents are asked to be brief

Chaperones

SIR,—Dr. J. A. Henderson (30 January, p. 273) seems to argue that "modesty and prudishness" are the only reasons for the presence of a chaperone when a male general practitioner makes a gynaecological examination in his surgery; he considers these reasons to be inadequate in most cases, and prefers to rely on trust. The true reason for having a chaperone should be frankly acknowledged. For each occasion on which a doctor really behaves improperly towards a patient—and they are rare indeed—there is a host of false accusations and this should be fully appreciated, especially by new graduates.

One of the functions of the chaperone is to vouch for the doctor's conduct when his behaviour is attacked. Baseless allegations of improper conduct are common. Allegations of unprofessional conduct occur not once in a decade, as some appear to think, but several times every year. Quite often practitioners who have to appear in a magistrates' court, or before the Disciplinary Committee of the General Medical Council, to answer a charge of sexual assault made by a patient, are unable to call any supporting evidence because there was no-one else present at the time of the examination.

The Medical Defence Union was founded in 1885 largely as the result of a case in which a doctor was sentenced to two years' imprisonment with hard labour on the unsupported evidence of a woman who had attended his surgery during her pregnancy. He served eight months before belated evidence of the woman's previous psychiatric disorders led the Home Secretary of the day to arrange a free pardon.

In his book *Law for the Medical Practitioner*[1] Harcourt Kitchin, barrister at law, wrote: "The Medical Defence Union finds that practitioners are rather apt, through daily association with members of the other sex in somewhat intimate circumstances, to be lulled into a false sense of security and to believe that they are above accusation. That they are not so is shown by many instances in which, for various obscure reasons, women have falsely accused their medical men of seducing them." The views of the Union were accurately reported by Harcourt Kitchin in 1941 and the Union holds the same views now even more firmly.—I am, etc.,

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[1] D. H. Kitchin, *Law for the Medical Practitioner*, p. 102, London, Eyre and Spottiswoode, 1941.

Safety of Combined Antidepressant Drugs

SIR,—On several occasions in your correspondence column[1 2] you have allowed me to express the opinion that it is not dangerous to combine the tricyclic antidepressant drugs, such as trimipramine and amitriptyline, with the monoamine oxidase inhibitor drugs, provided certain precautions are taken. In general a sufficient dosage (25-150 mg) of the tricyclic drug should be given only at night to produce deep sleep and combat early morning waking, reducing it if the sleep is too deep or prolonged. The monoamine oxidase inhibitor drugs should be given during the day; the dosage again should be reduced if there are any postural hypotensive symptoms.

In this department we have used combined antidepressant drugs for nearly ten years now on some thousands of patients. We still wait to see any of the rare dangerous complications reported. But we have collected quite a lot of information as to why the combination was originally thought to be dangerous. For instance, I have reported a supposed death from combined drugs,[2] which turned out at post mortem to be due to undiagnosed cheese reaction. The stomach still contained cheese and it was found that the patient had taken a large amount an hour before the symptoms started.

Just recently two other cases have been seen which should be reported as throwing further light on this matter. One patient, who had sudden cardiovascular collapse after having been on combined antidepressants for six months, was admitted to an intensive care unit and died. The case was reported to the coroner as a possible combined drug death. But at post mortem a volvulus of the small intestine was found. Possibly too quick a diagnosis of a supposed combined drug reaction led to the abdominal lesion being overlooked.

A few weeks ago I was told that a patient I had put on combined drugs a week or two previously was now in hospital very seriously ill. He had clouding of consciousness, was continually plucking at the bedclothes, and was obviously hallucinated. He was twitching in all his limbs. His temperature was raised. There was tachycardia and profuse sweating. His physical condition was deteriorating rapidly. Some of these symptoms were described in the rare cases who have supposedly died with combined drugs. At first he seemed to me to be suffering from delirium tremens. But the general practitioner said that the patient had only had sodium amytal in ordinary doses before being put on the combined antidepressants. The mother was also quite insistent that no other drugs had been taken in excess, and he had become ill only after starting the combined antidepressants which I had prescribed.

After getting the patient into a better physical condition with fluid replacement, he was transferred to the intensive care unit at St. Thomas's Hospital. With further administration of fluids he quickly recovered consciousness. Then one was able to find out exactly what had happened. He had, in fact, been taking sedatives in very large doses and getting them from varied sources. At one time he was taking up to ten carbromal with pentobarbitone tablets a day and, before stopping them to start the combined antidepressants, was still taking up to four at night. He had actually taken very few of the tranylcypromine and trimipramine prescribed, but it was the stopping of all the sedatives which had produced a typical delirium tremens around the fourth day of sedative withdrawal.

All these cases naturally give one considerable anxiety. But so many patients in the past ten years have been helped by combining the antidepressants that one feels one must go on using them until proved to be unsafe for this purpose. What is so impor-

tant about the last patient is that if he had died the coroner would almost certainly have had had to bring in the death as being due to combined drugs, with both the mother and doctor denying that he had more than ordinary doses of sedatives. After recovery he was safely given the combined antidepressant drugs for a fortnight.—I am, etc.,

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1 Sargant, W. W., *British Medical Journal*, 1969, **2**, 49.
2 Sargant, W. W., *British Medical Journal*, 1969, **3**, 118.

Fatal Septicaemia due to Yersinia Pseudotuberculosis

SIR,—The usual presentation of *Yersinia pseudotuberculosis* (*Pasteurella*) infection in man is most frequently manifested as mesenteric lymphadenitis. It occurs in children and boys are mainly affected. The infection occurs in many European countries including Poland.[1-5] The diagnosis of *Yersinia pseudotuberculosis* infection is made on isolating the causative agent from the blood or lymph nodes. Serological and histopathological examinations are also of great importance. It is usually a benign infection, but fatal cases have been reported rarely.[4 5]

Our patient was a 12-month-old girl admitted to the hospital on 19 December 1969. She was febrile with a temperature of 39·8°C., and had a fine macular red rash and numerous petechiae on the skin of the face, trunk, and upper and lower limbs. The child was unconscious; she had irregular breathing with breaks of apnoea, a rapid arrhythmia of over 200/min with faint sounds; liver enlarged around 4 cm, and the spleen was palpable beneath the left costal margin. Investigations showed protein in the cerebrospinal fluid 24 mg/100 ml and W.B.C. 10,050/mm³.

On the basis of the clinical picture acute insufficiency of the suprarenal glands was diagnosed, due to septicaemia of unknown aetiology. Despite intensive care, including controlled respiration, circulation-stimulating drugs, cardiovascular stimulants, and high doses of hydrocortisone the patient died 45 minutes after admission, with symptoms of circulatory and respiratory failure. Only a few hours had elapsed between the onset of the first symptoms and death.

At necropsy blood and specimens of the intestine, lymph nodes, and spleen were delivered to the department of microbiology of the medical school in Bialystok for bacteriological examination. Gram-negative rods were isolated from the blood that we identified on the basis of their biochemical reactions as well as antigenic structure as being *Yersinia pseudotuberculosis* type I. The micro-organisms also in other features did not differ from the standard *Yersinia pseudotuberculosis* strains; the bacilli produced flagella and were motile only while incubated at 22°C.

Histopathological diagnoses were: acute haemorrhagic colitis; acute mesenteric lymphadenitis; haemorrhagic and necrotic foci in the suprarenals; degeneration of the renal parenchyma, of the liver, and of the myocardium. Definitive diagnosis: fulminating septicaemia.

On the basis of the data obtained, mainly on the isolation of *Yersinia pseudotuberculosis* from the blood taken at necropsy, the diagnosis of fatal septicaemia from this micro-organism can be made.

We have found that hens were probably the source of infection in this child. The girl lived in the country, and in the sera of hens belonging to her parents we found a high level of antibodies against *Yersinia pseudotuberculosis* type I.

This fatal case of septicemia due to *Yersinia pseudotuberculosis* is the only one thus far described in Poland and is therefore of special interest. Few similar cases have been described in the literature so far.—We are, etc.,

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1 Borowski, J., Kupryanow-Wolfart, K., Kurasz, S., and Sokolewicz, E., *Polski Tygodnik Lekarski*, 1970, **25**, 401.
2 Brown, G. W., Brown, J. M., and Leditschke, J. F. *Medical Journal of Australia*. 1966, **1**, 585.
3 Daniëls, J. J. H. M., *British Medical Journal*, 1961, **2**. 997.
4 Knapp, W., *New England Journal of Medicine*, 1958, **259**, 776.
5 Mollaret, H. H., *et al.*, *Presse Médicale*, 1964, **72**, 2671.

Bacillaemia in Leprosy

SIR,—It was interesting to read the suggestion by Dr. A. B. A. Karat and others (6 February, p. 307) that bacillaemia occurs in all forms of leprosy. Rhodes-Jones[1] demonstrated bacillaemia in both tuberculoid and lepromatous leprosy, while John Lowe[2] and Iyengar[3] have also reported bacillaemia. The fact that this occurs deserves wider recognition.—I am, etc.,

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1 Rhodes-Jones, R., *Leprosy Review*, 1963, **34**, 26.
2 Lowe, J., *Indian Medical Gazette*, 1933, **68**, 503.
3 Iyengar, K. R. K., *Indian Journal of Medical Research*, 1919, **7**, 235.

Jaundice after Treatment of Leukaemia with Busulphan

SIR,—We wish to report the terminal occurrence of cholestatic jaundice in a patient with acute relapse of chronic granulocytic leukaemia who had been treated with busulphan for more than six years. We have failed to find a similar instance of cholestatic jaundice attributable to busulphan recorded in the literature.

An engineer aged 25 years presented on October 1963 having been "off colour" for two years. In the last six months he had gradually lost weight and noted occasional discomfort under the left ribs. Pallor of skin and mucosae and firm splenomegaly reaching 4 cm below the costal margin were found. Relevant laboratory results were: Hb 9·1 g/100 ml; total W.B.C. 205,000/mm³ (promyelocytes 6%, myelocytes 20%, band cells 44%, polymorphs 28%, eosinophils 2%); platelets 155,000/mm³, bone marrow-smears consistent with chronic granulocytic leukaemia; leucocyte alkaline phosphatase score 12; Ph¹-chromosome positive.

He progressed satisfactorily on continuous treatment with busulphan, the dosage varying between 4 mg daily and 0·5 mg every third day, until 2 December 1969 when coryza had developed. Two weeks later the spleen was enlarging and the haemoglobin level had fallen to 10·3 g/100 ml from previously normal levels. The leucocyte count was 25,000 mm³ with no blast cells and the platelet count was 100,000 mm³. At this time nausea, occasional vomiting, mild intermittent fever, and backache developed, also icterus. The direct van den Bergh reaction was positive, serum bilirubin was 2·3 mg/100 ml and serum alkaline phosphatase level 38 K.A. units with normal thymol turbidity and flocculation. Examination of the urine showed a trace of bilirubin with slight excess of urobilin and moderate excess of urobilinogen. The stools were paler than normal. Progressive fall in haemoglobin level to 4·7 g/100 ml, rising total leucocyte count to 55,000/mm³ with 24% blast cells, falling platelet count to less than 10,000/mm³, a rising serum bilirubin up to 8 mg/100 ml, along with slightly increased levels of transaminases (SGOT 52 m I.U./ml, SGPT 32 mIU/ml) occurred during the next few days, together with rapid increase in splenomegaly. Despite supportive and "specific" therapy the patient died on 5 January 1970.

The total dose of busulphan was 4·075 g of which 0·7635 g was given in the 12 months preceding the onset of jaundice as compared with an annual average of 0·6623 g busulphan during the previous five years. The only other medicaments at the time of onset of icterus and for two years before this were ferrous fumarate and occasional sodium amytal at night. Necropsy revealed icterus and scattered petechiae. The enlarged and focally infarcted spleen showed diffuse infiltration by primitive granulocytic cells. The soft enlarged liver showed a very striking degree of centrilobular cholestasis while in other areas there was some swelling of liver cells. A portal tract infiltrate of variable intensity consisting of lymphocytes and plasma cells was noted and a few primitive granulocytic cells were seen scattered throughout the liver lobules. There was no evidence of extrahepatic biliary obstruction or gall bladder disease, and the degree of leukaemic infiltration of the liver was minimal. Vertebral bone marrow was cellular with aggregates of granulocytic precursors.

Toxic effects from busulphan are relatively rare. Pancytopenia is the main danger with excessive therapy, thrombocytopenia being the usual warning. Other toxic effects with prolonged therapy include melanotic pigmentation of the skin and, very rarely, interstitial pulmonary fibrosis, a syndrome resembling adrenocortical insufficiency but in which a specific endocrine defect has not been demonstrated, atrophic bronchitis, glossitis, anhydrosis, alopecia totalis, impotence, sterility, and cataracts along with nuclear abnormalities in many other cells.[1] Amenorrhoea and mild gynaecomastia[2] and renal failure due to hyperuricaemia[3] have also been noted.

The histological appearances of the liver strongly favour drug-induced cholestasis of hypersensitive type. The absence of an eosinophilic infiltrate in the liver that frequently accompanies this form of liver toxicity can be accounted for by the lack of circulating eosinophils during the terminal illness. Cholestatic jaundice in severe bacterial infections, with histology similar to that seen in this case has been described.[4] However, there was no evidence either clinically or at necropsy to suggest severe infection of any form. It could also be argued the cholestasis was related to acute relapse of the chronic leukaemia, but this view has no histological support.