

mention of asbestos-like bodies in describing the effects in the lung of inhaled glass wool fibres in two animal species, including a species which consistently forms asbestos bodies when exposed to asbestos dust. There are few reports in the literature on the effects of glass fibre in man, but Murphy,⁵ in a human case of "fibre-glass pneumoconiosis," describes and illustrates numerous uncoated glass fibres in the lung tissues without mentioning asbestos-like bodies. It is also likely that, as used in industrial conditions, much of the dust derived from glass fibres consists of particles too large to be respirable.⁴ For these reasons I consider it is very unlikely that any of the "asbestos bodies" in my series can be attributed to glass fibres.

The role of diatomaceous earth is likewise doubtful. Vigliani and Mottura⁶ describe in detail the post-mortem histological appearances in the lungs of a man exposed to pure calcined diatomite dust without mentioning asbestos-like bodies. That they were aware of the possibility of finding such bodies is clear from their reference to the work of Nordmann,⁷ who described asbestos-like bodies in lung tissue at necropsy in patients exposed to diatomaceous earth and quartz dust. Nordmann, however, is careful to distinguish between "pseudoasbestos bodies" present in two of his six cases and "true asbestos bodies" found in another two cases known to have been exposed to asbestos as well as diatomaceous earth. Some of the "pseudo-asbestos" bodies he illustrates do not resemble asbestos bodies.

Filamentous aluminium silicate has been shown in hamsters to evoke the formation of asbestos-like bodies, but I do not know of any human case in which the presence of such bodies has been attributed to this material. Furthermore, I understand that aluminium silicate has only been used as an insulator in this country for about the last three years (and then only in small quantities for specialized purposes), and thus it also seems unlikely to be an important source of confusion in my survey. None of the histological sections in my series showed any evidence of haemosiderosis of elastic fibres.

By contrast, there is strong circumstantial evidence that many of the bodies I found are in fact true asbestos bodies. More than half of the patients for whom an occupational history is available had either worked with asbestos or had worked in an environment where incidental inhalation of asbestos at some time is virtually certain to occur. The fact that such evidence has been elicited by the comparatively crude methods employed in obtaining retrospective occupational histories from relatives of deceased patients suggests that occupational exposure is probably a more important source of asbestos fibres in the population than the general environmental contamination by asbestos suggested by previous writers.—I am, etc.,

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Genetics of Finger-prints

SIR,—The erudite and amusing article on finger-prints by Professor L. S. Penrose (11 May, p. 321) contains an idea which may prove to be of major importance to our understanding of the mode of action of chromosomes.

After presenting his findings that total ridge count of the fingers varies in inverse proportion to the number of sex chromosomes present the author states (p. 324): "The queer thing is that the effect is produced by the whole chromosome, or a large segment, rather than by its constituent genes." A few years ago I put forward a similar view to account for the process of sex differentiation: "there seems to be strong evidence that the inheritance of sex . . . is controlled not by individual genes but by whole chromosomes or at least large parts of chromosomes."¹ There is increasing evidence that the biological difference between males and females is basically a quantitative one,²⁻⁵ and Professor Penrose's findings appear to support the view that genetically determined quantitative variation can be affected by entire chromosomes or large chromosomal sections.

Professor Penrose's studies emphasize the value of dermatoglyphics, for here we are dealing with a quantitative variable which is fixed in embryonic life and is subsequently unaffected by either environment or hormones. For this reason the sex chromosome constitution may be reflected more directly in ridge counts than in variables of more obvious biological and medical significance.—I am, etc.,

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Crohn's Disease and Carcinoma of Colon

SIR,—With reference to the article by Drs. A. D. Perrett, S. C. Truelove, and G. R. Massarella (25 May, p. 466), in which the authors report a possible association between the two diseases, they give seven references to reports of cases in which carcinoma of the small intestine developed in relation to pre-existing Crohn's disease of the ileocaecal junction. They omitted, however, reports by Martinelli and Belluci,¹ Steele and McNeely,² Almond *et al.*,³ and Davis and Caley.⁴ Since carcinoma of the small intestine is very rare, such reports would seem highly significant in pointing to the premalignant nature of Crohn's disease. In addition, Hughes,⁵ case records of Massachusetts General Hospital, Case 43292,⁶ and Wyburn-Mason⁷ have reported cases in which Crohn's disease in the ileocaecal region developed into malignant lymphoma. One of my surgical colleagues also had a male patient of 55 years of age who developed intestinal obstruction due to a lesion in the upper part of the ileum, which was resected with end-to-end anastomosis. Sections of the lesion showed the typical changes of Crohn's

disease. Seven years later intestinal obstruction recurred and laparotomy now showed a tumour at the site of the anastomosis. Histologically this proved to be a reticulo-sarcoma. Such observations lend weight to the suggestion that Crohn's disease may be a premalignant condition.—I am, etc.,

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Guanethidine and Diabetes

SIR,—Diabetes and hypertension are often found in the same patient. Although many patients with diabetes must have received guanethidine for control of coexistent hypertension, we have been unable to trace any direct reference to the effect of guanethidine on clinical severity or insulin dosage in diabetic patients. An inquiry to the manufacturers of guanethidine revealed the same lack of published data in this regard. This prompted us to record briefly the following case, where a striking increase in insulin requirements and a rise in blood sugar levels was noticed when guanethidine was discontinued in a diabetic patient.

A 43-year-old housewife was a known diabetic for the last 14 years. Her fundi showed advanced diabetic retinopathy, and she had gradually lost vision over the last three years with development of retinitis proliferans in the right eye. She has been taking soluble insulin 40 units twice daily since 1964, and was quite well controlled. She developed the nephrotic syndrome, with proteinuria, oedema, hypercholesterolaemia, and her blood pressure, which was 150/90 in 1964, gradually rose to 210/120 in June 1967. She was started on bendroflumazide 5 mg. daily and methyl dopa 250 mg. three times a day, which was replaced by guanethidine 10 mg. twice daily in December 1967. She needed a little less insulin after this, and was well controlled on soluble insulin 40 units in the morning and 30 units in the evening. She was admitted on 1 March 1968 with a history of several fainting attacks over the previous week. Her blood pressure on admission was 200/100 lying, and 120/80 standing. Her blood sugar was 220 mg./100 ml. It was thought that the fainting might have been due to postural hypotension due to guanethidine, and this was discontinued on 5 March. A progressive increase in glycosuria was noted over the next few days, and she complained of increased thirst while on the same insulin dosage. Her insulin was increased by 8 units on 11 March. The blood sugar levels were found to have gone up in spite of this. On 13 March the blood sugar was 429 mg./100 ml. at 10 a.m. and over 500 mg. at 3 p.m. Insulin was increased by 8 units. On 16 March the blood sugars were 327 mg./100 ml. at 10 a.m. and 478 mg./100 ml. at 3 p.m. Insulin was further increased by 8 units on 19 March to 52 units in the morning and 42 units in the evening. Blood sugars on 20 March were 244 mg./100 ml. at 10 a.m. and 378 mg./100 ml. at 4 p.m. On 22 March these were 347 mg./100 ml. at 10 a.m. and 468 mg./100 ml. at 3 p.m.

Thus within a few days of discontinuing guanethidine the requirements of insulin had increased considerably. Since there was no

other change in treatment or general condition of the patient, such as acute infection, the stoppage of guanethidine appears to have been responsible for this increase in blood sugar levels and increased insulin requirements. There is no published report on the effect of guanethidine on severity of diabetes. However, Woeber *et al.* reported reversal by guanethidine of abnormal glucose tolerance in patients with thyrotoxicosis.¹ In rats, guanethidine 20 mg./kg. intraperitoneally daily for four days produced a slight fall in blood sugar. Chronic pretreatment with guanethidine in a dose of 20 mg./kg. daily has been found to modify the hyperglycaemic response to ether anaesthesia. The maximum increase in blood sugar was diminished, but the overall rise appeared to be somewhat prolonged.^{2,3} In rabbits, on the other hand, Parikh *et al.*⁴ showed a hyperglycaemic action of guanethidine and also that it potentiated the hyperglycaemic action of epinephrine in a smaller dose, which itself had no effect on blood sugar. Intravenous administration of guanethidine 0.4 mg./kg. in seven patients with hypertension was found to cause slight hyperglycaemia after three hours.⁵ Guanethidine causes release of epinephrine, and epinephrine has been experimentally shown to inhibit pancreatic insulin release.⁶ However, the results of chronic administration of guanethidine, when tissues are depleted of epinephrine, may well be different from this acute effect. Guanethidine significantly reduced the hyperglycaemic response to diazoxide in adrenal demedullated rats.⁷

This last finding may have some relevance to the present case, since she had been on bendrofluazide 5 mg. daily for the last six months. It is possible that guanethidine was blocking the hyperglycaemic action of bendrofluazide, which became manifest dramatically when the former was discontinued. This case is being reported as an interesting clinical observation. The explanation of this phenomenon would need further clinical and experimental pharmacological investigations. We would be most interested in knowing if such a tendency has been noted in other patients in similar clinical situations.—We are, etc.,

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Deaths from Asthma

SIR,—I have followed the correspondence on deaths from asthma with interest, and I am grateful to Drs. I. W. B. Grant and others (18 May, p. 429) for their comments on four cases of cardiac arrest due to status asthmaticus occurring in hospital. However, their statement that "when a patient with status asthmaticus develops cardiac arrest in

hospital and this is shown to be due to ventricular asystole the proper course is to undertake open cardiac massage without delay" appears to be rather dogmatic. My experience of one case is reported below, in which the conventional conservative measures for the treatment of asystole were effective—namely, intracardiac adrenaline (1:10,000) with or without calcium chloride 10% intravenously.

A female asthmatic aged 44 years was readmitted with status asthmaticus on 13 February 1967. She was obese, her pulse rate 120/min. She was treated with intravenous A.C.T.H., oral prednisone, and ampicillin, and during the next 24 hours her condition improved. In the early hours of 15 February she awoke with sudden dyspnoea and collapsed within minutes. External cardiac massage and artificial ventilation were started promptly by the nursing staff, and intravenous sodium bicarbonate was given. Chest compression produced palpable femoral pulses, while the E.C.G. showed asystole. Five millilitres of adrenaline 1:10,000 was injected into the heart, and external massage continued for a further minute. Cardiac rhythm was restored, the E.C.G. showing a supraventricular tachycardia, rate 170/min. She was intubated, and ventilated with an East Radcliffe respirator. An intravenous infusion of hydrocortisone was also given, and she made an uninterrupted recovery from this episode. She was discharged home on 1 March.

The experience of this single case agrees with the view of Dr. Grant and his colleagues that ventricular asystole occurs in status asthmaticus. In this instance conservative measures were successful in restoring an effective cardiac rhythm. This case shows that intracardiac adrenaline, with or without intravenous calcium chloride, has a place in the treatment of asystole due to status asthmaticus, and should be considered before resorting to open cardiac massage.

I wish to thank Dr. Byron Evans for his permission to publish the details of this case, and Dr. D. A. Williams for his helpful advice.

—I am, etc.,

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Pregnancy and Monoamine Oxidase Inhibitors

SIR,—Neither your article (6 April, p. 35) nor your correspondents Mr. A. G. Johnson and Dr. M. F. Cuthbert (18 May, p. 433) mentioned the hazard of monoamine oxidase inhibitors (M.A.O.I.) during pregnancy. The literature makes it perfectly clear that it is not safe to give a patient who is on a monoamine oxidase inhibitor a local anaesthetic, a general anaesthetic, amphetamines, barbiturates, tricyclic antidepressants, or pethidine, not to speak of another M.A.O.I.¹ This is a formidable risk when one considers that any pregnancy may abort and the mother need at least sedation or even evacuation of the uterus. In later pregnancy there are all sorts of eventualities to consider, quite apart from the fact that the onset of labour is something which cannot be predicted or anticipated.

According to the excellent survey of the literature given in chapters 11 and 12 of *Psychopharmacological Agents*,² it takes a month for the effects of an M.A.O.I. to wear off completely. Unfortunately neither a threatened abortion nor a premature labour

will wait two weeks before treatment can be begun. Hence it would seem wise to wean women from M.A.O.I.s at the beginning of pregnancy, and it has been my practice to do this. Unfortunately the weaning process is difficult, and my last three patients have experienced a number of discomforts from the second to the tenth day after withdrawal. These discomforts included headache, agitation, sweating, and changes in the pattern of sleep. The agitation produced what sounded like acute anxiety attacks, and two of the patients felt driven to ask another doctor for supplies of their drug, but refrained from doing so because they knew their state was temporary. The most difficult symptom to deal with was their depression. Nobody who has seen the headache which develops when a patient on an M.A.O.I. is given imipramine wishes to repeat the experiences.

I understand that M.A.O.I.s are being used to induce abortion. The sort of women who are likely to wish for a termination of pregnancy will include patients already taking M.A.O.I.s. The risk of a fatality from cerebral haemorrhage when such a technique is used must be carefully considered, and the patient will have to face either a period of acute stress while her drug is being withdrawn or the slightly smaller but still considerable risks of other methods of terminating pregnancy.—I am, etc.,

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Oral Contraceptives in the Post-partum Period

SIR,—We wish to draw attention to some of the limitations of the paper by Dr. A. Nilsson and Mr. P.-E. Almgren on psychiatric symptoms during the post-partum period as related to the use of oral contraceptives (25 May, p. 453). The authors conclude a causal relation between oral contraceptives and psychiatric symptoms, and that these symptoms should be ascribed to hormonal factors. Our first point concerns the observation that the group of women who take oral contraceptives in the post-partum period must show some psychological differences from the group of women who use other methods of contraception, because the first group were "more anxious to use a safe method." It might therefore be hypothesized that those women who were more anxious for reliable contraception are less able to cope with a new baby in the family, and therefore at greater risk from post-partum psychiatric symptoms—hormonal factors are not a necessary condition of the findings of this paper, and the relation is not necessarily causal. Our second point is that the choice between oral contraception and other methods is made in the post-partum period, and that is just the period during which the differences in incidence of psychiatric symptoms have been demonstrated in this paper. The possibility that oral contraception is chosen because of the high incidence of post-partum psychiatric