with the minimum of sequelae.—We are, etc.,

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Meningococcal Disease

SIR,—In their interesting account of an outbreak of meningococcal disease in Devon (16 March, p. 50) Dr. D. M. Easton and his colleagues raise several points worthy of discussion.

They used a combination of penicillin, sulphonamides, and chloramphenicol in the initial treatment of most cases and suggest that if the low cerebrospinal fluid cell count in three of their cases "indicates only minimal inflammatory response in the meninges penetration of penicillin into the C.S.F. may be poor, so that the inclusion of chloramphenicol which passes well into the C.S.F. might be a beneficial addition to the treatment regimen." In meningococcal infection—especially of the fulminant type where relatively little involvement of the meninges is not uncommon—the major consideration is to deal with the systemic infection. Penicillin alone will do this adequately and, if inflammation of the meninges occurs will rapidly eradicate meningococci at that site without the need for the use of chloramphenicol.

The inclusion of sulphonamides in the treatment of meningococcal meningitis is of less certain help than formerly owing to the presence of resistant meningococci. Of the strains isolated in Scotland and forwarded to this laboratory for testing in 1973, 15% were fully resistant to sulphonamides. What is also of importance when considering prophylaxis is that in addition 51·5% of strains were partially resistant—that is, would not be eradicated from the nasopharynx by sulphonamide therapy. Hence if prophylaxis is to be used sulphonamides cannot be recommended.

This raises the question as to who should be protected and how. Firstly, I cannot agree with Dr. Easton and his colleagues that "family contacts should be screened and should all be given an adequate course of prophylactic treatment" if they imply that prophylaxis should be *dependent* upon screening. Screening will not pick up all carriers and in any case I would agree with Wenzel *et al.*[1] that it is the acquisition rate of meningococci that is important in terms of the dynamics of meningococcal infection, not the carrier rate. In other words, meningococcal disease is, like poliomyelitis, a "failure of carriage" (and it is interesting to note that in both these diseases asymptomatic infection leads to the production of antibodies). Hence prophylaxis must be used early if at all and must cover the case contacts, not so much to eradicate carriage but to try to prevent acquisition leading to disease. There is no doubt that prophylaxis will abort epidemics, as has been shown in Africa[2] and in service camps in the U.S.A.[3] but the problem is how this should be carried out in the face of sulphonamide resistance and the knowledge that penicillin will not eradicate meningococci from the nasopharynx of carriers.[4] One approach might be to give penicillin in the hope of preventing disease (and maybe by reducing carriage rates to a low level to reduce the likelihood of acquisition by the non-carrier). However, there is evidence[5] that penicillin not only will not eradicate carriage but will not prevent the onset of meningitis. The other approach is to give eradicative treatment—for instance, using minocycline and rifampicin[6] or rifampicin alone.[7] Until reading the account of Foster *et al.*[5] I might have conceded that in a family group penicillin, especially if given by injection, should be adequate, but I now feel that, as in an institutional outbreak where long-term carriage following inadequate prophylaxis could result in the seeding of the susceptible population once prophylaxis had been ended, eradicative treatment should be considered. It would be interesting to hear the views of others on this important topic.

At one time the suggestion that family contacts should receive prophylaxis would not have been accepted because outbreaks in family groups were rarely reported, but in recent years outbreaks involving more than one member of a family have been reported[5 8] and the experience in the Devon outbreak emphasizes that this can happen. Hence the urgency for reappraisal of the problem of prophylaxis is underlined.

Finally, Dr. Easton and his colleagues noted that group B meningococci predominated in their series. Were other groups isolated or were some strains either untyped or untypable?—I am, etc.,

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SIR,—Recent experience in Wigan supports the suggestion of Dr. D. M. Easton and others (16 March, p. 507) that there is a recrudescence of meningococcal disease, often with complications, in Britain. In the six months from October 1973 to March 1974 we treated 10 such patients compared with four in the corresponding period a year earlier. Their ages ranged from 5 months to 7 years. All had confirmed meningitis and in nine the presence of meningococci was demonstrated bacteriologically. A petechial rash was noted in nine cases.

Two children died, a girl of 3 years with severe septicaemia and shock and a boy of 6 who had septicaemia and gross cerebral oedema with coning and superficial cerebellar haemorrhage. Two other children had brief convulsive episodes and a third who had prolonged convulsions went on to develop bilateral subdural effusions and has considerable residual brain damage. One child had definite arthritis of the right elbow joint and another a transient arthralgia affecting the left knee.

None of these children had any history of prior contact with meningococcal disease and their homes were scattered throughout the area served by this hospital.—I am, etc.,

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Misleading Discs

SIR,—The antibiotic discs described by Mr. D. F. J. Brown and Dr. J. B. Selkon (23 March, p. 573) are not the only ones to mislead.

Bacteria of the *Haemophilus* genus require one or both of two growth-promoting substances for normal growth on culture. These are haematin, designated the "X-factor", and coenzyme 1, designated "V-factor". Coloured paper discs marked X, XV, and V, impregnated with standard quantities of these substances, are commonly used as a simple screening method for preliminary recognition of haemophilus species. Recently a culture of *H. influenzae* appeared as only a fine ring of growth around an XV disc, but *outside* a zone 14 mm in diameter without any growth. It was almost invisible without a hand lens. Another haemophilus grew as a ring around a zone without growth surrounding both the X and V discs. Experimental cultures of pneumococci and streptococci also showed zones of inhibition around the X and XV discs. The discs were in date and stored dry at 4°C.

A similar phenomenon was observed some years ago. The paper dye was not to blame since control blank discs of the three colours were inactive, and it was assumed that the X-factor (haematin) solution used must have been inhibitory. The makers were informed and corrected the matter, but the difficulty now seems to have recurred.—I am, etc.,

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Clinical Diagnosis of Reye's Syndrome

SIR,—I entirely agree with the views expressed in the last paragraph of Dr. Ellen S. Kang's letter (16 March, p. 518). Having an abiding interest in Reye's syndrome[1 2] may I develop her idea a little farther? I suggest that what she terms "toxic encephalopathy with fatty visceral changes due to a specific toxin" should be called the Reye-Bourgeois syndrome because it was the original intention of Reye *et al.*[3] to place the entity of "encephalopathy with fatty degeneration of

viscera" on a more specific basis, while it was Bourgeois *et al.*[4] who identified the specific toxin and produced a plausible experimental model. On the other hand the mere combination of fatty changes in viscera with encephalopathy was described much earlier (in 1929 to be precise) by Brain, Hunter, and Turnbull[5] and therefore should be called Brain's syndrome, or Turnbull's syndrome as the late Lord Brain himself suggested.[6]

Thus the confusion that Dr. Kang wishes to avoid can be averted by the use of two terms: (*a*) Brain-Turnbull syndrome to describe fatty degeneration of viscera with encephalopathy of undetermined cause and (*b*) Reye-Bourgeois syndrome to describe fatty degeneration of viscera and toxic encephalopathy due to a specific toxin.—I am, etc.,

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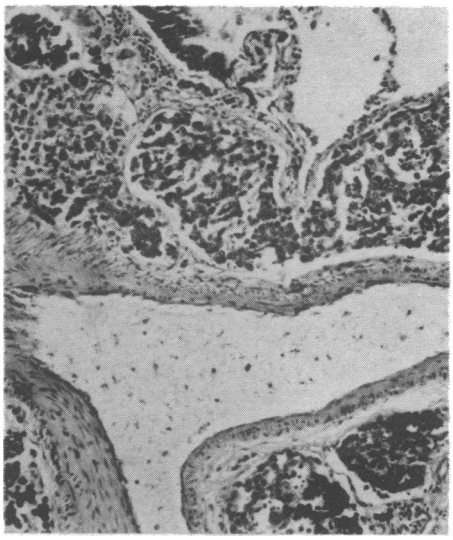
Carcinoid Pulmonary Embolism and Cor Pulmonale

SIR,—Multiple pulmonary metastatic emboli are a cause of acute or subacute cor pulmonale in different carcinomatous diseases.[1-3] We have found no report in the literature of metastasizing malignant carcinoid causing this symptom.

A 70-year-old woman was admitted to hospital with right lower abdominal pain and weight loss. There was neither history nor clinical finding of cardiac or pulmonary disease. A mobile, non-tender mass was palpated in the right iliac fossa. A prolonged blood sedimentation rate was the only pathological laboratory finding. Barium enema revealed a space-occupying lesion in the ileocaecal region. On laparatomy a hard mass was found in this region with extensive lymph node involvement along the mesenteric blood vessels. A right hemicolectomy with lymph node dissection was performed. Histological examination showed a malignant carcinoid of the caecum with metastases in the lymph nodes. From the third to the ninth postoperative day, when death occurred, there were recurrent episodes of respiratory distress characterized by extreme dyspnoea, cyanosis, and tachycardia compatible with recurrent showers of pulmonary emboli. Consecutive chest radiograms confirmed this diagnosis. The electrocardiogram showed right axis deviation which was not present previously. There was no peripheral thrombophlebitis that could explain the source of the emboli. The patient died during one of these attacks. At necropsy macroscopical examination showed metastases on the visceral pleura with many white nodules 1-3 mm in diameter in both lungs. Similar nodules were found in the mediastinal lymph nodes and ovaries. No liver metastases were found. Histological examination of the lungs showed perivascular and peribronchiolar lymphatic infiltration with tumour cells and organizing thrombi containing tumour cells in arterioles (see fig.).



Lung showing periarterial lymphatics distended by tumour cells. Haematoxylin and eosin x 100.

Carcinoid of the caecum is rather rare among carcinoids of the alimentary tract. Usually extra-appendiceal carcinoids are considered to be of low-grade malignancy. This did not seem to be so in our patient, in whom there was extensive local invasion by the tumour after only six months of history. Following the operation there was rapid lymphatic and haematogenous spread. This case is also unique in respect of the sites of spread of the tumour. We have found only three reported cases of lung metastases of alimentary tract carcinoid.[4-6] There were no signs of carcinoid syndrome, nor were there the characteristic cardiac findings of pulmonary stenosis. This case was characterized by a clinical picture of acute and subacute cor pulmonale caused by showers of pulmonary emboli. This entity was first described by Brill and Robertson in 1937.[3] The pathogenesis of cor pulmonale in cases of metastasizing tumours is explained either by invasion of lymphatic vessels by tumour cells compressing the alveoli and bronchioles or by compression of blood vessels by perivascular lymphatics filled with tumour cells. Another possibility is that multiple carcinomatous emboli obliterate pulmonary arterioles. The findings in our case seem to point to the recurrent pulmonary carcinomatous emboli as the cause of the clinical picture of acute and subacute cor pulmonale.—We are, etc.,

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Urinary F.D.P. Excretion in Glomerulonephritis

SIR,—I am glad that Dr. P. Naish and his colleagues (23 March, p. 544) have put into perspective the relation between urinary fibrinogen degradation products (F.D.P.) and non-selectivity of proteinuria. As I deduced from animal work,[1] the presence of high-molecular-weight fibrin products in the urine must mean membrane damage. Moreover, the graphs in their paper are similar to the one my colleagues and I showed[2] when we described what we then thought was a simple technique for estimating urinary F.D.P. In retrospect the discrepancy which we mentioned at that time stems from the fact that we were in fact relating F.D.P. to total proteinuria, since we have since found that protamine sulphate precipitates all proteins but so alters their antigenicity that they are not readily identifiable.

Unfortunately the main conclusion that biopsy fluorescence for fibrin will become the main criterion for anticoagulation could lead to confusion. High urinary F.D.P. excretion indicates "extra"-capillary fibrin deposition. This means that there is gross fibrinogen leakage so that crescent formation is stimulated, and in turn the crescent strangles the glomerulus. As an isolated finding this is surely not an indication for anticoagulation. Already Maggiore[3] has noted that heparin does not influence urinary F.D.P. excretion and has called this "exudative" loss of fibrin.

The theoretical principle is that anticoagulation is indicated for "intra"-capillary fibrin deposition which carries the threat of capillary occlusion. This is a dynamic event starting with immune complex damage to platelets,[4] but apart from the fact that fluorescence may detect fibrin monomer complexes, if fibrin is actually seen blocking capillaries, then local fibrinolysis of the vascular endothelium has already been lost and the damage done. Only further research will establish which functional tests will give early indication of the intravascular coagulation of immune complex disorders. We may well end up with the staggering conclusion that the more practical test is the E.S.R. In the meantime I would recommend consideration of platelet function tests,[5] including measurement of platelet factor 4, the radiofibrinogen catabolism study,[6] or the detection of plasma fibrin monomer complexes by chromatography.

Rapidly declining renal function is still the indication for consideration of anticoagulation, though this is a late stage. It should be a matter of concern that few hospitals have the service for safe monitoring of patients on heparin.—I am, etc.,

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Intermittent Calf Compression in Prevention of Deep Venous Thrombosis

SIR,—I was most impressed by the efficacy of preoperative intermittent calf compression in the prevention of postoperative deep vein thrombosis when this is diagnosed by the ^{125}I-labelled fibrinogen test as reported by Dr. V. C. Roberts and Mr. L. T. Cotton (2 March, p. 358). It is easy to accept that treatment given only during an operation might prevent immediate thrombosis, which is clearly demonstrated in their fig. 2. This figure suggests a further interesting conclusion. From the data it seems that treatment for up to a mean of 117 minutes only—that is, during the operation on day 0—