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

IAN CRAFT

EZEAT IYOUSSEFNEJADIAN

Chelsea Hospital for Women,

London S.W.3

1 Wright, C. S. W., Campbell, S., and Beatley, J., Lancet, 1972, 1, 1278.

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 count in meningococcal meningitis is an "indicator" of the degree of inflammatory response in the meninges, the 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. may be beneficial in the treatment regimen.1 In meningococcal infection—especially of the fulminant type where relative little involvement of the meninges is uncommon—the major consideration is to deal with the systemic infection. Penicillin alone will do this adequately and if inflammation of the meninges occurs it will rapidly eradicate meningococci at that site without the need for the use of chloramphenicol.

The inclusion of sulphamides 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 sent from there to this laboratory for testing in 1973, 15% were fully resistant to sulphamides. 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 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 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 immunity" 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 the introduction of epidemics, as has been shown in Africa, and in service camps in the U.S.A., 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 reducing the spread of meningitis to a lower level to reduce the likelihood of acquisition by the non-carrier). However, there is evidence5 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 or rifampicin alone.6 Until rendering the account of Foster et al.2 I might have conceded that in a family group of meningococci, 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 breaking of an endemic, one or two members of a family have been reported5 and the experience in the Devon outbreak emphasizes that this can happen. Hence the urgency for reappraisal of the prophylactic treatment before prophylaxis is undertaken.

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

R. J. FALLO

Department of Laboratory Medicine,

Ruchill Hospital,

Glasgow


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 a lifelong abiding interest in Reye's syndrome1,2 may I develop her idea a little farther? I suggest that what she terms "toxic encephalopathy with fatty visceral changes due to a specific toxic agent" should be considered as a "toxic encephalopathy 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. 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 and therefore should be called Brain's syndrome, or Turnbull's syndrome as the late Lord Brain himself suggested.

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

A. G. BHAGWAT
Department of Pathology,
Post Graduate Institute of Medical Education and Research,
Chandigarh, India

Carinoid Pulmonary Embolism and Cor Pulmonale

Sir,—Multiple pulmonary metastatic emboli are a cause of acute or subacute cor pulmonale in different carcinomatous diseases.1,2 We have found no report in the literature of metastasizing malignant carcinoid causing this syndrome.

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. Roentgenogram of the chest revealed a space-occupying lesion in the iliac 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 malignant carcinoid of the caecum with metastases in the lymph nodes. The patient recovered up 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. Complete chest radiograms confirmed this diagnosis. The electrocardiogram showed right axis deviation which was not present preoperatively. This was compatible with peripheral localisation of emboli that could explain the source of the emboli. The patient died during one of these attacks. At necropsy macroscopic examination revealed 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 peri-vascular and peribronchial lymphatic infiltration with neoplastic cells. Also localized thrombi containing tumour cells in arterioles (see fig.).

Carcinoid of the caecum is rather rare among carcinoids of the alimentary tract. Usually extra-appendical carcinoids are considered to be of low-grade malignancy. This did not seem to be so in our patient, in whom there were no local invasion signs, as judged by the tumour after only six months of history. Following the operation there was rapid lymphatic and haemorrhagic spread.

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

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.3,4 There were no signs of carcinoid syndrome, nor did the patient show the characteristic carcinoid 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 1937.5 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.,

R. SHAFIR
A. DINBAR
D. B. TULINSKY
Chaim Sheba Medical Center,
Tel Hashomer,
and Tel Aviv University Medical School,
Israel

Urineal F.D.P. Excretion in Glomerulonephritis

Sir,—I am glad that Dr. P. Naish and his colleagues (23 March, p. 344) 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, 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 observed 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.

Recently the suggestion 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 stretches the glomerulus. As an isolated finding this is surely not an indication for anticoagulation. A study by Magde6 has noted that heparin does not influence urinary F.D.P. excretion and has called this "exudative" loss of fibrin.

The pathological principle is that anticoagulation until the fibrin deposits are reduced to a cause of intracapillary fibrin deposition which carries the threat of capillary occlusion. This is a dynamic event starting with immune complex damage to platelets,7 but apart from the fibrin deposits, it is the mere presence of glomerular fibrin 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 intra-vascular 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,8 including measurement of platelet factor 4, the radiofibrinogen catalysis study,9 or the detection of fibrinogen fibrin monomer complexes by chromatography.

Rapidly declining renal function is still the indication for consideration of anticoagulation. This is in line with my recommendation that it is a matter of concern that few hospitals have the service for safe monitoring of patients on heparin.—I am, etc.,

E. N. WARDLE
Wellcome Research Laboratories,
Royal Victoria Infirmary,
Newcastle upon Tyne.

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 was diagnosed by the 125I-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—