with the minimum of sequelae. — We are, etc.,
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1 Wright, C. S. W., Campbell, S., and Beasley, J., Lancet, 1973, 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 cell count in meningococcal meningitis is "indolent" then 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 beneficial to the treatment regimen. 1

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 of meningococci isolated in Scotland and forwarded to this laboratory for testing in 1973, 18% were fully resistant to sulphonamides. What is also of importance when considering prophylaxis is that in addition 51% 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 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 meningococcal epidemics, as has been shown in Africa 2 and in service camps in the U.S.A. 1 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 reduce the risk 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 meningococcal disease. 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. 2 I might have conceded that in a family group of this kind, especially if penicillin 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 spreading of disease, the use of 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 point 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 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 untyped or untypable?—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 a lifelong abiding interest in Reye's syndrome 1 may I develop her idea a little further? I suggest that what she terms "toxic encephalopathy with fatty visceral changes due to a specific toxic agent" should come to be known as "Reye's syndrome" because it was the original intention of Reye et al. 2 to place the entity of "encephalopathy with fatty degeneration of
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.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 colonic carcinoma caused by showers of pulmonary emboli. This entity was first described by Brill and Robertson in 1937.7 The pathogenesis of colonic carcinoma in cases of metastasizing tumours is explained either by invasion of lymphatic vessels by tumour cells compressing the aleveoli 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 colonic carcinoma.—We are, etc.,

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Interventional Calf Compression in Prevention of Deep Venous Thrombosis

Str.—I was most impressed by the efficacy of preoperative interventional calf compression in the prevention of postoperative deep vein thrombosis when this is diagnosed by the 131I-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—

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.

Interestingly the authors' 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 stretches the glomerulus. As an isolated finding this is surely not an indication for anticoagulation. Lord Brain himself has noted that heparin does not influence urinary F.D.P. excretion and has called this "exudative" loss of fibrin.

The theoretical principle that anti-coagulation can be used in this fibrin-deposition syndrome is the fibrinolytic effect of heparin. In a recent experiment Lord Brain and colleagues have shown that heparin may increase the activity of plasminogen.

Rapidly declining renal failure is still the indication for consideration of anticoagulation, although it is a less common indication. A patient who is on a balanced diuretic regime and who has normal clotting tests will give early indication of the intravascular coagulation of immune complex disorders. We may well end up with the stipulating conclusion that the more practical approach is the E.S.R. In the future I would recommend consideration of platelet function tests, including measurement of platelet factor 4, the radiofibrinogen-cata
cleavage study, or the detection of plasma fibrin monomer complexes by chromatography.

Unfortunately renal function is still the indication for consideration of anticoagulation, although it is a less common indication. A patient who is on a balanced diuretic regime and who has normal clotting tests will give early indication of the intravascular coagulation of immune complex disorders. We may well end up with the stipulating conclusion that the more practical approach is the E.S.R. In the future I would recommend consideration of platelet function tests, including measurement of platelet factor 4, the radiofibrinogen-cata
cleavage study, or the detection of plasma fibrin monomer complexes by chromatography.

Carcinoid Pulmonary Embolism and Cor Pulmonale

Str.—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. At this time an enema revealed a space-occupying lesion in the ileocaecal region. On laparotomy 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. Pathological examination showed malignant carcinoid of the caecum with metastases in the lymph nodes. The patient died up to the ninth postoperative day, when death occurred, there were recurrent episodes of respiratory distress characterised by extreme dyspnoea, cyanosis, and tachycardia compatible with recurrent showers of pulmonary embolus. Consecutive chest radiograms confirmed this diagnosis. The electrocardiogram showed right axis deviation which was not present preoperatively. The peripheral circulatory signs, a few premonitory signs that could explain the course of the emboli. The patient died during one of these attacks. At necropsy macroscopic 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 peribronchial lymphatic infiltration with tumour cells adjoining throughout the lung, 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 a very slow local invasion was caused by the tumour after only six months of history. Following the operation there was rapid hypotension and haemorrhagic spread.

2. Mason, D. G., Archives of Internal Medicine, 1940, 12, 661.