and transient swelling of face, body, and limbs (1); hypopyon of left eye (1); acute monarticular arthritis (1); and sulphonamide crystalluria (1).

Of the 12 meningococcal isolates obtained so far only one has shown sulphonamide resistance employing standard disc diffusion methods. Three of the four most recent strains have been found to be group I meningococci, the fourth belonging to group C. The minimum inhibitory concentration of the group B strains to sodium sulphadiazine was 1·6 μg/ml, and in two of them it was 0·4 μg/ml to benzylpenicillin. Follow-up studies on six patients (including four infants less than 1 year of age) 4-10 weeks after discharge showed no evidence of residual damage.—We are, etc.,

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Gonorrhoea in Obstetrics and Gynaecology

SIR,—Gonorrhoea is still on the increase, with 18,341 postpubertal female cases in 1972.[1] From the low incidence reported from antenatal screening (the highest figure obtained by British investigators being only 0·6%[2]) and the screening of gynaecological patients[3,4] it is easy to conclude that gonorrhoea is not a problem in obstetrics and gynaecology in Britain, but caution is required, especially in gynaecological patients. Many units still erroneously rely on a high vaginal swab for diagnosis, which may or may not be placed in Stuart's transport medium before plating is possible. The most effective means of diagnosis is to take samples from the cervix and urethra and plate them at the bedside on to prewarmed selective gonococcal medium,[5] the cultures being immediately placed in an incubator with a carbon dioxide-enriched atmosphere. At the same time Gram-stained smears are made from further samples.

In the 6½ months between November 1973 and mid-May 1974 10 cases of gonococcal salpingitis and one of gonococcal cervicitis have been found by this active approach in gynaecological patients. In six of these the Gram film gave immediate warning of the positive culture to come. It can be argued that it is immaterial to indentify the causative organism as antibiotics would be given anyway once a diagnosis of salpingitis has been reached. This is fallacious as it fails to identify the cases in which sexual contacts should be investigated by the venereology department.

No cases of Bartholin's abscess due to gonococcal infection were found during the same period. Most patients had already received antibiotics from their general practitioner so this is not surprising. It should be stressed that patients with a Bartholin's abscess should be admitted for surgical drainage and not treated first with antibiotics as they are ineffective and also confuse the bacteriological diagnosis.

Despite the screening of "at risk" antenatal patients, three cases of gonococcal ophthalmia neonatorum were found between September 1972 and September 1973. The mothers were confirmed as having gonorrhoea. One disturbing feature is that the conjunctivitis developed between the sixth and ninth days after delivery. With the now common practice of early discharge after delivery in most obstetric units it is easy to miss the diagnosis unless the district midwife and general practitioner are alert to the possibility of a gonococcal cause.

In a recent circular the Royal College of Obstetricians and Gynaecologists recommends trainees in obstetrics and gynaecology to consider a post in venereology as part of the elective year. This would be beneficial in developing an insight into the problems of gonorrhoea detection and control.—I am, etc.,

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1 Chief Medical Officer, Department of Health and Social Security, *British Journal of Venereal Diseases*, 1974, **50**, 73.
2 Rees, D. A., and Hamlett, J. D., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, **79**, 344.
3 Hughes, W. M., and Davies, J. M., *British Medical Journal*, 1971, **4**, 424.
4 Silverston, P. I., Snodgrass, C. A., and Wigfield, A. S., *British Journal of Venereal Diseases*, 1974, **50**, 53.
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Haemophilus influenzae Meningitis in Adults

SIR,—So far as I know, the interesting report by Dr. Susannah J. Eykyn and others (1 June, p. 463) is unprecedented in that half of their cases of haemophilus meningitis occurred in adults. Could this distribution be related to the location of St. Thomas's Hospital? The population of that area, particularly during the working day, must contain an exceptionally large preponderance of adults.

Dr. Eykyn and her colleagues comment several times on the difficulty of identifying *H. influenzae* in the Gram-stained deposit of cerebrospinal fluid. I should like once again to draw attention to the value of a good typing serum for *H. influenzae* type b in this situation. Typing is not mentioned in Dr. Eykyn's paper, but as your leading article (p. 462) pointed out capsulated strains of type b are responsible for the great majority of cases of haemophilus meningitis. The practical relevance of this is that a capsule-swelling test with a good type b antiserum (such as that made by Hyland Laboratories) makes possible the firm identification of type b *H. influenzae* in C.S.F., even if they are few in numbers, within minutes of the arrival of the specimen in the laboratory.[1]

Your leading article was a joy to read and I am sorry to have to point out any fault in it; indeed, the fault lies not in the article but in its title. It dealt not with "*Haemophilus influenzae* infections" but with one group of such infections, making no reference, for example, to the activities of non-capsulated strains in the bronchi, which account for the great majority of *H. influenzae* infections in Britain.—I am, etc.,

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1 Turk, D. C., and May, J. R., *Haemophilus influenzae. Its Clinical Importance*, pp. 35 and 120. London, English Universities Press, 1967.

Interaction of Nalidixic Acid and Warfarin

SIR,—It has been demonstrated in vitro that nalidixic acid can displace warfarin from binding sites on plasma proteins.[1] This does not appear to be significant clinically.[2] Dr. J. C. Petrie and his colleagues (4 May, p. 262) in their interesting study of the awareness of selected drug interactions go so far as to call the nalidixic acid-warfarin interaction "theoretical." The following case suggests that nalidixic acid given to patients stabilized on warfarin can produce potentially dangerous excess anticoagulation and should be avoided.

A 55-year-old woman was knocked down by a car in March 1972 fracturing her pelvis and left femur. This was followed by a left ileofemoral venous thrombosis, venous gangrene of the toes, and acute renal failure requiring peritoneal dialysis over a period of several weeks. Her anticoagulation with warfarin was maintained after discharge and was well controlled with a prothrombin ratio around 2·0 on 11 mg/day. The ratio was satisfactory on 20 December. She then developed *Escherichia coli* urinary infection and was given nalidixic acid 500 mg four times daily by her family doctor on 8 January 1973. She was readmitted to hospital on 14 January with a purpuric rash on her abdomen and bruises on her left leg and back, which came on a few days after starting nalidixic acid. Her prothrombin time was 45 seconds (control 13). The platelet count was normal. Both drugs were discontinued. She was later discharged well with a prothrombin time of 22 seconds on 10 mg of warfarin daily.

—I am, etc.,

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1 Sellers, E. M., and Koch-Weser, J., *Clinical Pharmacology and Therapeutics*, 1970, **11**, 524.
2 Smith, S. E., and Rawlins, M. D., *Variability in Human Drug Response*. London, Butterworths, 1973.

Antibacterial Preparations in the B.N.F.

SIR,—The section of the new edition of the *British National Formulary*[1] dealing with "Drugs Acting on Infections: Antibacterial Preparations" contains a number of statements which might be challenged. Some of these are listed below.

(1) Carbenicillin. It is advised that for systemic infections this be given by continuous intravenous infusion. The data sheet issued by the makers advises that carbenicillin be given intravenously either by bolus injection or rapid infusion on the grounds that infusion over longer periods may result in subtherapeutic concentrations. Whatever the relative therapeutic merits of intermittent versus continuous administration, one is left with the other potential drawback of continuous infusion of the penicillins —that is, their possible inactivation by other components of the intravenous solution or incompatibility with other additives, notably gentamicin in the case of carbenicillin. This is not mentioned by the *B.N.F.*

(2) Ampicillin. Amoxycillin and its better absorption by the oral route should have been mentioned in a volume published in 1973.

(3) Gentamicin. This is said usually to have "a slightly wider margin of safety" than kanamycin. In fact the margin between therapeutically active and toxic serum levels is greater with kanamycin.[2] For some reason the intravenous use of gentamicin is vetoed, though this mode of administration must be widespread for serious systemic infections, notably with *Pseudomonas aeruginosa*.

(4) Tetracyclines. It is recommended that, given parenterally, "the total dose should never exceed 1 g in 24 hours (less in patients with impaired renal function) because of the danger of liver damage." Nothing whatever is said in this section about the anti-anabolic action of these agents and other possible effects on the kidney, which have led the authors of at least three standard texts,[2-4] to interdict the use of tetracyclines altogether (with the exception of doxycyline) in patients with impaired renal function.

(5) Fusidic acid (Fucidin) is stated to be "active against a wide spectrum of organisms." How can fusidic acid possibly be described as a wide-spectrum drug? All "coliform" organisms are resistant to it, and even in the Gram-positive range its activity against the pneumococcus and other kinds of streptococci is poor.

(6) The section ends with some advice on the choice of drugs for various infections, among them acute meningitis and peritonitis. The paragraph describing the chemotherapy of meningitis caused by "coliform" organisms is written in a particularly confusing way. At one point, dealing with the treatment of pyocyaneus (sic) meningitis in an infant, the author could be read as saying that though gentamicin is the drug of first choice chloramphenicol and kanamycin are permissible alternatives. For the chemotherapy of peritonitis when no bacteriological information is available ampicillin is said to be "the drug most likely to be effective." The blind chemotherapy of peritonitis is a highly debatable topic, but there is one point at least on which I think there would be wide agreement and that is that ampicillin, if given alone, is not the drug most likely to be effective in this condition.

Considerations of space forbid me to make more than a selection of the criticisms which might be levelled at this section of the *B.N.F.*, which I suggest is in urgent need of revision. The prospect of its use until 1976 by any who are inexperienced in this field is one that I find alarming.—I am, etc.,

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1 *British National Formulary 1974-76*, pp. 94-110. London British Medical Association and Pharmaceutical Society of Great Britain, 1973.
2 Kucers, A., *The Use of Antibiotics*, pp. 146, 288. London, Heinemann, 1972.
3 Garrod, L. P., Lambert, H. P., and O'Grady, F., *Antibiotic and Chemotherapy*, 4th edn., p. 157. Edinburgh and London, Churchill Livingstone, 1973.
4 de Wardener, H. E., *The Kidney*, 4th edn., p. 312. Edinburgh and London, Churchill Livingstone, 1973.

Isolation System for General Hospitals

SIR,—Dr. A. G. Ironside (1 June, p. 501) poses the rhetorical question whether "dermatitis with severe sepsis [is] more infectious than any other wound or burn infection." In fact for many years infected, non-surgical skin lesions have been recognized to be a peculiarly dangerous source of hospital cross-infection. Numerous demonstrations of this can be found in the literature. For example, 14 patients died as a result of the admission of a patient with skin sepsis to a medical ward[1]; and similar catastrophes have occurred in surgical wards.[2]

The bacterial contamination of the hospital environment by patients with infected dermatological lesions can be truly prodigious.[3] It is important, however, to note that similar bacterial dispersal can follow simple colonization of lesions with *Staphylococcus aureus*, *Streptococcus pyogenes*, or Gram-negative bacilli such as *Proteus vulgaris* and *Pseudomonas aeruginosa*.[4] Though eczema with clinically apparent infection is rightly regarded as a particularly dangerous hazard in hospital, experiments on bacterial dispersal from individual patients have shown that clinically non-infected conditions, notably psoriasis, are the sources of some of the highest air counts.[4] This is a reflection of the greatly increased turnover of the epidermis and the production of profuse air-borne squames in such diseases.

The traditional practice of nursing dermatological patients in surgical wards is now clearly indefensible. Many cases of post-operative sepsis over the years have been due to this form of negligence. But the risks of treating skin patients in general medical wards are also considerable. Whenever possible, patients with extensive skin disease should be nursed in single-bedded rooms with exhaust ventilation. The practicability of converting existing ward accommodation to house dermatological cases at only modest expense has been shown at Westminster Hospital. For a medium-sized general hospital suitable facilities for seven or eight patients should be adequate. In the absence of suitable accommodation the minimum requirement is that the lesions of dermatological patients should be declared bacteriologically safe before admission to an open ward. Further bacteriological examination is essential during each patient's stay since skin lesions readily become colonized with pathogens in hospitals.[4]—I am, etc.,

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1 Vogel, R. A., *et al.*, *New England Journal of Medicine*, 1959, **261**, 1301.
2 Barber, M., and Dutton, A. A. C., *Lancet*, 1958, **2**, 64.
3 Selwyn, S., *Journal of Hygiene*, 1965, **63**, 59.
4 Selwyn, S., and Chalmers, D., *British Journal of Dermatology*, 1965, **77**, 349.

A Case of Pyrexia of Undetermined Origin

SIR,—I would like to suggest another possible, if unlikely, condition to explain the P.U.O. in the patient considered in a recent Clinicopathological Conference (20 April, p. 157). This is the protozoal disease babesiosis, which many features in the patient's illness might suggest.

(1) She spent her holidays in a caravan in Devon, where "red water fever" in cattle occurs and ticks transmitting the infection are ubiquitous. In the only other human case of babesiosis in the British Isles the patient contracted the disease on a caravan holiday under similar circumstances in Ireland.

(2) Haematuria is a cardinal feature in babesiosis.

(3) Splenomegaly and anaemia are characteristic features in babesiosis.

(4) The P.U.O. which failed to respond to medication would favour a babesial infection not treated appropriately.

(5) Finally, the failure to see *Babesia* parasites in the blood film would not exclude the infection; after the acute stage parasitized red cells may be extremely few and very difficult to find.

Babesia sp. is probably the most widely distributed blood parasite in mammals throughout the world and the sources of infection are therefore equally ubiquitous. In the British Isles alone *Babesia* sp. is found in bovines, rodents, insectivora, and chiroptera. Nevertheless, my observations do not profess to have cleared up this problem but only suggest one further line of research which might have been followed in an otherwise extremely thorough investigation of a very puzzling case which under the circumstances must remain a case of P.U.O.—I am, etc.,

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The Coroners' So-called 24-hour Rule

SIR,—There has been and still is a general belief among medical staff of junior and senior grades that patients dying within 24 hours of admission to hospital are "cases to be referred to the coroner." Even in 1974 this view obtains, as is confirmed by answers given by postmortem room technicians in many parts of the country to a recent examination question on the kinds of cases referred to the coroner.

This belief is erroneous. The Human Tissue Act 1961 contains specific provisions relating to postmortem examinations and section 2(1) affords clear permission for such an examination to be carried out on any patient to establish or confirm the causes of death.—I am, etc.,

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Anticonvulsant Osteomalacia and Vitamin D

SIR,—Mr. D. J. F. Rowe and Dr. T. C. B. Stamp (2 March, p. 392) make some critical comments on our paper on anticonvulsant osteomalacia (22 December 1973, p. 695). Contrary to their previously expressed opinions they now seem to believe that epileptics on anticonvulsant therapy do not have osteomalacia but osteoporosis, though they do not give any direct evidence to support this statement. Their arguments are: hypocalcaemia is seen without other biochemical changes and without histological sign of osteomalacia; mean levels of alkaline phosphatase of bone origin are no higher in adult epileptics than in normal adults; the low levels of bone mineral content (B.M.C.) found with our method can be caused by osteoporosis, since the method cannot distinguish this condition from osteomalacia; and the effect of treatment with vitamin D_2 (not vitamin D_3, as incorrectly stated by Mr. Rowe and Dr. Stamp) observed by us is at variance with the results of calcium balance studies.

The fact that hypocalcaemia is common in epileptics in the abscence of histological bone abnormalities may be due to bone biopsy being a rather insensitive method for estimating osteomalacia in its milder forms. As to our findings of elevated serum alkaline phosphatase levels, we should like to draw attention to the fact that three years previously Mr. Rowe, together with Dr. A. Richens,[1] reported that 18 (38%) out of 47