

Antihistamines and the Ovum

SIR,—At the Seventh Conference of the Federation on Planned Parenthood held recently in Singapore Professor M. C. Shelesnyak showed that for implantation of the fertilized ovum to be successful not only must oestrogens and progesterones be necessary but a third substance, histamine, is required, and successful "nesting" depends on the interplay of these three.

Presumably the temporary stoppage of the production of any of these three substances would halt the process of implantation and consequently impede pregnancy. It would appear, therefore, that antihistamines might prevent satisfactory implantation of the fertilized ovum and pregnancy.

If this is the case, surely considerable caution should be exercised in the giving of antihistamine drugs to those about to start a family?—I am, etc.,

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Resistance to the Newer Penicillins

SIR,—The recent paper by Dr. G. T. Stewart and Mr. R. J. Holt (February 2, p. 308) prompts us to report our experience of a methicillin-resistant staphylococcus in one of the surgical wards of this hospital. Methicillin has been in use here since September, 1960.

The first culture of a methicillin-resistant staphylococcus was isolated in October, 1962, from the sputum of a patient with a post-operative chest infection. He had never been treated with this drug, nor had he visited any other hospital in the past two years.

In the following four months we have had four further cases of infection with this staphylococcus (two urinary infections and two respiratory infections.) The organism has also been recovered from the floor dust of the ward concerned and was characterized by widespread resistance to other antibiotics including penicillin, streptomycin, chloramphenicol, and tetracycline. Three of the six cultures were also resistant to cloxacillin.

Dr. M. T. Parker, of the Staphylococcus Reference Laboratory, reported these cultures to be phage type 47/53/75/77. The last patient affected was admitted to hospital as a mild case of pancreatitis but became critically ill with staphylococcal lobar pneumonia on the fourth day. He recovered after treatment with intravenous erythromycin and novobiocin in addition to noradrenaline, steroids, and oronasal helium and oxygen.

No alteration was made in the routine practice of formalin autoclaving woollen blankets and boiling all other bed linen when a patient is discharged from this hospital. However, all the patients and staff of the affected ward were treated by a nasal cream of neomycin and chlorhexidine, the ward floor was washed with "savlon" (chlorhexidine and cetrimide) and the bed curtains were laundered.

Since adopting these measures we have encountered no further cultures of methicillin-resistant staphylococci.—We are, etc.,

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Amidopyrine and Agranulocytosis

SIR,—For many years amidopyrine has been widely recognized as a potentially dangerous drug capable of causing severe and often fatal agranulocytosis. Although

its use is generally condemned, preparations containing amidopyrine continue to be marketed and are still used. The following brief case history is described, not because it illustrates anything new or unusual, but to serve as a reminder to those who may be inclined to use proprietary drugs without full realization of their content.

An elderly lady, aged 67, was admitted to hospital in November, 1962, because of persistent sore throat of some two weeks' duration. She had enjoyed good health apart from bouts of fibrositis, which had been treated on two or three occasions in recent years with "novalgin" tablets.

Because of a recurrence of muscular pains she was again given a supply of "novalgin" (amidopyrine) by her family doctor, and had taken only three tablets when she became fevered and complained of a sore throat. No more tablets were taken, and she was treated with penicillin, followed by oxytetracycline. At the end of two weeks' treatment she was found to have extensive sloughing of the fauces, and examination of the blood revealed anaemia and leucopenia. At the time of admission to hospital she was found to be pyrexial with severe ulcerative and sloughing angina and stomatitis. Hb was 60% and W.B.C. 750/c.mm.; no neutrophil polymorphs were present, practically all of the cells being lymphocytes; platelets were plentiful. A specimen of bone-marrow showed granulocytic hypoplasia, and the case was regarded as one of drug agranulocytosis. She was treated intensively from the outset with large doses of penicillin, erythromycin, prednisolone, and also packed cells from two pints of fresh blood. During the following two weeks there was remarkably little change in her general condition, although the W.B.C. count remained at around 500/c.mm., with continued complete absence of polymorphs. During her third week in hospital there appeared signs of widespread consolidation of the left lung, and at the end of that week there occurred a remarkable and sudden rise in the W.B.C. count to 3,000, 15,000, and 56,000/c.mm. respectively, on successive days (the last count comprising neutrophil polymorphs 21%, metamyelocytes 41%, myelocytes 30%, and pre-myelocytes 2%). Bone-marrow now showed very active haemopoiesis. By the end of the fourth week, however, the patient was rapidly losing ground with high swinging temperature. Repeated blood-cultures were sterile and the W.B.C. count had rapidly fallen to 2,000/c.mm., containing 56% neutrophil polymorphs. She became extremely exhausted and breathless, and died five weeks after admission. The only significant finding at necropsy was a large left-sided empyema. Examination of the sternum showed active marrow substance.

Novalgin is a pyrimidone compound containing amidopyrine in the sulphonated form—one of a group of similar analgesic-antipyretic drugs capable of producing severe and often fatal agranulocytosis by causing maturation arrest at the stem stage in the bone-marrow. Once a patient has been sensitized, a very small dose may precipitate an attack of agranulocytic angina. Thus, in the present case, although the drug had been taken in the past with apparent impunity, the severe sore throat and fever appear to have developed almost immediately after its further use after a long interval.

Although the dangers of amidopyrine have been fully recognized for almost 30 years, it is astonishing that such a drug continues to be produced. It is even more disturbing that the drug—in one form or another—is still being prescribed, particularly when a number of alternative and safer mild analgesic drugs are now available. One suspects that the drug is often used unwittingly—by the indiscriminating acceptance of a proprietary name, which gives no indication of its potentially deadly content.—I am, etc.,

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