whom had received cephaloridine. We used a Levinthal agar-dilution technique with an inoculum of 0.004 ml. of a 1:250 dilution of an overnight broth culture (10^4 organisms).

The Table shows that for 27 of the 52 strains the M.I.C. was above the level likely to be obtained with the recommended dose.

M.I.C. (μ g./ml.)	40	20	10	5	4	3	2	1	Total
No. of strains	6	21	13	1	3	6	1	1	52

If this drug is used for the treatment of respiratory infections due to *H. influenzae* it is possible that it may not always be effective.—We are, etc.,

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D. M. JONES.
P. DAVIS.

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Uricosuric Drugs in Gout

SIR,—Your correspondent in "To-day's Drugs" on the treatment of gout (16 January, p. 174) probably passes over the place of sodium salicylate in modern treatment because in these days of slick tablet therapy it has been out-moded, but it was the first uricosuric drug to be used and as it has been a therapeutic agent for over ninety years the statement that "uricosuric drugs have been in use for fourteen years" reads rather strangely. Moreover, it has a very effective uricosuric action in doses of 4–6 grammes daily,^{1–3} a dose which is much less irritant to the gastric mucosa than the same amount of aspirin daily, the only form of salicylate treatment of gout mentioned by your writer. I do not suggest that this form of therapy is preferable to modern drugs, but it is of interest to remember that nearly thirty years ago a more recent drug, cinchophen, had to give way to the oldest salicylate therapy when cases of liver poisoning had resulted from it. I feel sure that your writer, who has not forgotten his colchicine and local lead and opium applications, will not object to this brief excursion into the past.—I am, etc.,

G. H. JENNINGS.

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Reactions to Intravenous Iron Dextran

SIR,—The article by Dr. Barbara E. M. Clay and her colleagues concerning reactions to the total-dose infusion of iron dextran (2 January, p. 29) is most interesting. However, the results are somewhat exceptional compared with ours and we would like to comment on them.

The incidence of acute reactions is 4.5%, while in our series one case occurred in 150 infusions to gynaecological patients; no acute reactions were noted in 50 obstetric cases.

Dr. K. N. Varde¹ reports one acute reaction in over 300 obstetrical infusions and the manufacturers have submitted to us on request the details of 1,807 fully documented cases of iron-dextran infusion from all over the country. Excluding the Hull series, the anaphylactic reaction rate is 0.28%. We all recognize the need to explain this difference, and the following suggestions may be helpful.

In our gynaecological patients the acute reaction and other minor reactions occurred early in the series, coincidental with the use of old stock iron dextran in use before intramuscular administration temporarily ceased in 1960. Change was made to currently manufactured Imferon, and since then the reaction rate has become negligible. It is interesting to note that Dr. Varde met with reactions at the outset of his trial, although he attributed this to a high concentration of iron dextran.

The incidence of folic-acid deficiency in pregnancy has risen—Hibbard² quotes 4.2% in the Liverpool area, Glasgow being 4%. Indeed 64% of pregnant patients infused here were folic-acid deficient and received folic acid prior to infusion. All Dr. Varde's cases received folic acid, but Dr. Clay and her colleagues do not refer to the folic-acid status of their patients, apart from stating that cases remaining resistant to oral iron appeared to be those with a folic-acid deficiency—a point which may be pertinent in view of our experience with the following case.

A para 6+1, age 31 years, gave a history of gross facial oedema, rash, and malaise developing to oral iron administered in another hospital in her previous pregnancy. She was warned to refuse iron thereafter. In her current pregnancy she was found to have a severe iron and folic-acid deficiency anaemia. Folic acid was given two weeks before commencing oral iron, and this time no reaction occurred.

Thus it is possible that in unsuspected folic-acid deficiency pre-treatment with oral iron prior to infusion, as in the Hull series, may trigger off a sensitivity reaction on occasions. This problem of hypersensitivity to drugs in pregnancy is a difficult one. Whilst the reactions here do not histologically resemble the Schwartzman phenomenon the reaction time after commencement of infusion might suggest some similar mechanism.

Though the points raised are debatable they merit investigation because the iron-dextran infusion is a valuable method of treatment and the causes of acute reactions need to be defined in order to minimize them.—We are, etc.,

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REFERENCES

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Iodophors

SIR,—Your article in "To-day's Drugs" (12 December, p. 1513) was an informative critical evaluation of currently used anti-septics. In the section on iodophors, however, the writer stated that they are "inactivated by blood and serum and are probably of no value in the treatment of wounds." While this statement might be valid for some iodophors, published evidence indicates the contrary in the case of povidone iodine

(P.V.P.-I). The cultures of a variety of micro-organisms were killed within fifteen seconds by P.V.P.-I in dilutions up to 1:10, even when human blood or serum (5%) was added to a 4 mm. loopful inoculum.¹ P.V.P.-I was found to be effective in clinical cases of infected or bleeding wounds.² A study of 125 patients with infected wounds or ulcers and 70 with infected burn wounds has shown that P.V.P.-I (Betadine) markedly reduced the bacterial flora in 86% and 84% of the respective groups. The authors also pointed out that when necrotic tissue was present this had to be removed in order to obtain optimal effect.³

Thus, following the criteria of an ideal antiseptic postulated in your article, P.V.P.-I seems to be one that fulfils all of the requirements—i.e., rapid action, lack of toxicity, and resistance to blood, pus, and tissue fluids.—I am, etc.,

British Drug Houses
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Toronto, Ontario,
Canada.

M. NADASDI.

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Clofibrate and Androsterone in Hypercholesterolaemic Xanthomatosis

SIR,—Dr. Bernard Mason and Professor C. Bruce Perry in their article (9 January, p. 102) state, "A much less marked effect on the serum cholesterol was observed in two patients with hypercholesterolaemia and xanthelasma palpebrarum, but there was no change in the xanthelasma." The following case would support their findings:

A male patient aged 54 attended at Outpatients in March 1961 suffering from ischaemic heart disease. He had the characteristic yellow plaques on both upper eyelids. The result of his serum cholesterol was as follows:

Date	Serum cholesterol (mg./100 ml.)	
March 1961	536	
21 April 1961	564	
25 May 1961	446	
18 August 1961	444	
9 December 1961	478	
2 March 1962	458	
19 April 1962	410	
23 August 1962	486	
13 December 1962	512	
10 January 1963	492	} on Atromid
7 February 1963	442	
4 April 1963	417	
13 June 1963	424	
4 September 1963	446	
10 December 1963	388	
4 June 1964	554	

Eight capsules of Atromid daily was started on 13 December 1962 and continued for 12 months. There was no appreciable change in the level and no effect on the xanthelasma palpebrarum.

—I am, etc.,

Dorchester, Dorset.

EDWARD J. JARRETT.

Chlorhexidine and Suture Materials

SIR,—May I, through the courtesy of your journal, reply to Mr. A. W. Fowler's letter (23 January, p. 252) in which he recommends

that all suture materials be steeped in a 1/2,000 solution of Chlorhexidine?

I would like to point out that all surgical catgut supplied by British manufacturers is sterile and preconditioned for use, and that immersion in chlorhexidine, particularly if it is an aqueous solution, could have an effect on the plybonding leading to separation of the plies and perhaps to premature or delayed absorption—not to mention loss of strength, since most catgut has an affinity for moisture and will absorb it until a peak saturation point is reached with subsequent loss of tensile strength.

Some non-absorbable sutures like silk are serum-proofed by the manufacturers for partly obvious reasons, and one of these is to reduce intercellular reaction when implanted. What will happen to this proofing after immersion in chlorhexidine, or indeed what will happen to the silk? Will it continue to fragment after due period of implantation and be absorbed by inclusion into the mononuclear phagocyte, or remain unencapsulated—a mechanical irritating body?

Investigation studies on the use of chemicals when used in connexion with suture materials have been regrettably inadequate and in my opinion detailed histological studies in animals are necessary to determine the effect that Chlorhexidine could have on them and wound healing before the acceptance of Mr. Fowler's recommendations.—I am, etc.,

J. J. F. HOWELL,
Product Director,
Ethicon Ltd.

Edinburgh 11.

Iron Content of Infant Milk Foods

SIR,—As an interested party, I was pleased to read Dr. James Grant's letter (16 January, p. 193), advocating the fortification with iron of dried milks for infant feeding. Dr. Grant states that he is informed "that the official attitude is against adding iron to national dried milk because the healthy baby is provided with sufficient iron at birth to last until weaning." But this generalization often proves false. It is not true of the "healthy infant" who, for example, was born of a mother seriously anaemic during pregnancy, or who was of low birth weight, or had lost blood after birth (perhaps into a cephalohaematoma or from the cord), or who, though now growing rapidly, suffered from early infections, sometimes even seemingly mild ones. Such infants make up a not inconsiderable number of the infant population. Fortunately many of them are now ordered iron, though the regularity of its giving by the mother is a different matter. There is no doubt that prophylactic administration of iron is best secured for an artificially fed infant by incorporating the iron in his food; and it seems unfortunate that none of the national dried milk is fortified with iron. Surely such milk might be supplied both fortified and unfortified without increase in cost since it is supplied on such a vast scale. Personally I would give the fortified milk as a routine, using the unfortified milk only temporarily.

In 1932 there was no national dried milk, but I think it is clear that the "official attitude" then was that iron-fortified milk should be available and used in welfare centres. The Ministry of Health set forth the Minister's views in Circular 1290, dated

27 October 1932, which was sent to all Maternity and Child Welfare Authorities. I give below extracts from this circular:

"I am directed by the Minister of Health to state that he has received the following recommendations from the Advisory Committee on Nutrition after their review of recent research work on this subject: Having regard to the cogency of the evidence that nutritional anaemia of infants can be greatly reduced by the administration of iron and ammonium citrate, it would be proper for the Ministry of Health to give practical advice on the matter to the Medical Officers of Authorities responsible for the feeding of infants. . . .

"There appears to be ample evidence to justify the conclusion that the administration of iron and ammonium citrate to infants, or the feeding of infants with milk to which iron has been added, considerably reduces the incidence of nutritional anaemia, raises the resistance to infections, thereby reducing the morbidity rate, and improves growth. . . .

"It is understood that dried milk preparations containing added iron are already on the market, and it is suggested that those Authorities who supply dried milk for the feeding of infants should consider the desirability of obtaining supplies of the medicated kinds for use in suitable cases."

The incidence of nutritional anaemia in infants has been much reduced during the last 30-odd years largely as a result of the recognition of the frequency and the effects of such anaemia. Contributing factors to the lowering of the incidence have been: a higher standard of living and widespread treatment of anaemia in pregnant women; much earlier weaning of infants on to a diet containing meat, eggs, etc., thus providing more iron; the availability of antibiotics for the treatment of infections; earlier recognition of anaemia in individual babies; and far more administration of iron to infants.

Dr. Grant finds that anaemia is still "not uncommon." If preventible, why not prevented? A Whitehall official once observed in my hearing that "he wasn't willing to face the lion's jaws" by telling the dried-milk firms that iron was to be added to national dried milk. Perhaps the Ministry may yet re-read their Circular 1290 and supply iron-fortified national dried milk in the interests of child health.—I am, etc.,

London N.W.7. HELEN M. M. MACKAY.

Alcohol-withdrawal Syndrome

SIR,—The interesting clinical evaluation of chlordiazepoxide and promazine in the treatment of alcohol-withdrawal syndrome, reported by Dr. G. Sereny and Dr. H. Kalant from the Alcoholism and Drug Addiction Research Foundation in Toronto (9 January, p. 92), reaches similar conclusions to those of my colleagues and I and described at the International Conference on Alcoholism in Vienna in 1962.^{1,2} It also compares with a study of the use of promazine, chlorpromazine, and chlordiazepoxide in the withdrawal of alcohol from 68 patients reported by me at the International Conference on Alcoholism in London last year.^{3,4} In our series, however, we used the drugs by injection. The doses of promazine and chlorpromazine were of the order of 50 and 100 mg., which correspond to the oral dose of 50 and 100 mg. of promazine used by Sereny and Kalant. With the chlordiazepoxide, however, we used injections of 100 mg. two

hourly to a total of 600–800 mg. per day as compared with the oral dose of 25–50 mg. to a total daily dose of 200–400 mg. used in Toronto. We had no untoward result using the chlordiazepoxide in this dosage but we encountered, both with promazine and chlorpromazine, several alarming episodes of prolonged hypotension when these drugs were used in conjunction with a recent preceding period of heavy drinking. In none of these patients was there any definite evidence of liver damage.

In terms of sleep, blood-pressure, pulse-rate, tremor, hallucinations, and delirium tremens (the criteria used by Sereny and Kalant) we had no doubt as to the advantage of using chlordiazepoxide as compared with the other two drugs or a placebo injection.—I am, etc.,

London S.W.3.

NOEL H. MOYNIHAN.

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- ⁴ Moynihan, N. H., 1965, in press.

Toxic Insecticides

SIR,—A possible toxic effect of insecticides which has not attracted much attention is anosmia.

I have seen a nursing sister who used an insecticide spray in September 1962 for the first time. The main active constituent of the spray was pyrethrum, which does have some slight neurotoxic properties. Whilst using the spray the patient developed an attack of sneezing with watery rhinorrhoea, nasal obstruction, and anosmia. An allergic rhinitis had evidently developed, and skin tests showed a strongly positive reaction to pyrethrum. No other allergens were found. The allergic rhinitis was completely controlled by antihistamines, and the nasal airway returned to normal. Despite this, however, the anosmia has persisted. Full rhinological examination has been negative apart from the anosmia, and the patient was admitted to a neurosurgical unit for investigation, but no intracranial cause for the anosmia was found. It would seem probable that the pyrethrum has damaged the olfactory nerve endings in the nasal mucosa.

Although the allergic properties of pyrethrum are well known, I have been unable to find any reference to its toxic action on the olfactory nerve endings. It would be interesting to know if any of your readers have encountered similar cases.—I am, etc.,

Birmingham 15.

D. J. BRAIN.

Reasons for Emigration

SIR,—Dr. John Seale (12 December, p. 1522) is continuing to attack the National Health Service over the problem of emigration of doctors, using parts of the recent monograph by Abel-Smith and Gales¹ to support his conclusion that the Health Service is responsible for the high emigration rate. When all of the facts presented by Abel-Smith are considered, it can be seen that this conclusion is unjustified.

Of Abel-Smith's conclusions Seale says: "Although few doctors [living abroad who answered a questionnaire] expressed general objections to the principle of a National Health Service, the findings . . . confirm my