depletion is not convincingly supported by their data. The incidence of hypersegmented neutrophils in the blood can hardly be used as a criterion of folic-acid deficiency, since many of their patients with hypersegmented neutrophils had normoblastic marrows, and, conversely, only 10 of 15 cases with megaloblastosis showed an excess of hypersegmented neutrophils in the peripheral blood.

If iron deficiency did initiate or exacerbate folic-acid deficiency one would expect fewer and less severe cases of megaloblastic anaemia in pregnant women who have received prophylactic iron. In our experience, which extends over the past nine years, this is not the case. On the contrary, the most florid megaloblastic marrow picture is seen in women who have taken regular supplements of iron in pregnancy. Several of our patients who had received no iron prophylaxis up to about the 30th week of pregnancy were found to have an equivocal or frankly normoblastic marrow, but after two to three weeks' iron therapy marrow aspiration yielded a florid megaloblastic marrow.

It is not really surprising that many pregnant women should be both iron and folic-acid deficient when one inquires into the diet of these patients. There is also evidence that a state of malabsorption, which is probably reversible, develops in many patients in late pregnancy. This is reflected in the relatively high faecal fat output of women with megaloblastic anaemia in pregnancy.¹ Megaloblastic anaemia in pregnancy, therefore, resembles intestinal malabsorption rather than the post-gastrectomy syndrome.

Finally, we do not share Dr. Chanarin's disappointment with the diagnostic value of the serum-folate assay. Four years' experience of this test has taught us that, once the technique is mastered, folate assay can detect at least 75% of cases of megaloblastic anaemia in pregnant women. If the labile folate factor is estimated² a 96% correlation can be obtained with marrow findings in pregnant women.—We are, etc.,

C. GILES.
E. W. BALL.

Stoke-on-Trent.

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Reactions to Intravenous Iron Dextran

SIR,—Total dose intravenous infusion of iron dextran (Imferon) may be followed by a number of reactions varying from local phlebitis to the severe complications of shock, dyspnoea, or cyanosis described by Dr. Barbara Clay and her colleagues (2 January, p. 29). I have recently treated four patients by this method and two of them developed thrombosis of veins remote from the site of infusion.

The circumstances in the two cases were very similar. Both were African females, aged 39 and 47 years, and both presented with iron-deficiency anaemia caused by menorrhagia from fibroid uteri. The haemoglobin levels were about 9 g./100 ml., and iron-deficiency was evidenced by hypochromia of the red cells, low serum-iron values, and the absence of stainable iron on marrow biopsy. The patient aged 47 had varicose veins of the right calf. These were mild, had been present for "years," and had

never troubled her. The history and physical examination were otherwise negative in the two cases. Both were ambulant up to the time of the infusion, and neither had received parenteral iron previously.

One patient was given 35 ml. of iron dextran dissolved in 1 litre of normal saline at the rate of 40 drops per minute, and the other 40 ml. in 1 litre of saline at the rate of 15 drops per minute. In both cases a superficial arm vein was used for the infusion, during the course of which no local or systemic reactions were observed. The infusion was given during the afternoon and evening, and the patients were discharged the following morning.

Both patients presented with pain and swelling of one leg two days after the infusion. On examining the affected limb the calf was found to be warm and tender, and both the calf and foot were considerably oedematous. In the 47-year-old patient the deep-vein thrombosis involved the right leg. The condition was treated in the usual way and both cases responded satisfactorily.

I have no proof that the infusion of iron dextran caused the venous thrombosis in these patients, but the circumstances suggest that the association is more than coincidence. Its mechanism is obscure, but in one of the patients it is possible that the pre-existing venous abnormality acted as a predisposing factor. Perhaps some of your readers have encountered similar cases.—I am, etc.,

Non-European Hospital,
Johannesburg, S. Africa.

H. C. SEFTEL.

Management of Acute Iron Poisoning

SIR,—With reference to the commentary on desferrioxamine B mesylate in "To-day's Drugs" (6 February, p. 366), we should like to make some further observations on the management of acute iron poisoning.

During the third phase evidence of hepatic insufficiency tends to appear. This has been well documented in the past,^{1,2} and we have recent experience of one such child who died in liver failure and at necropsy showed massive hepatic necrosis. It would seem that in this context great caution should be applied in the use of the sedatives phenobarbitone, paraldehyde, and chlorpromazine which you mention.

There may be potential danger in advocating very large doses of chelating agent by mouth (e.g., 5–10 g. is suggested). Where the mucosa is damaged can the absorption of soluble iron chelate in fact increase the overall accumulation of iron in the body? In severe poisoning the patient may become oliguric,³ and our fatal case passed only 20 ml. of urine. In this circumstance the question of possible tissue toxicity from the ferrioxamine complex itself arises. Where excretion is minimal, chelation should perhaps be combined with other means of removal, such as exchange transfusion.

In addition to the fatal case mentioned above we have three further patients who have been followed with respect to serum and urinary iron, and an account of these is in preparation for publication. In the case of a girl aged 2½ years who was mildly affected as judged by her clinical state and an initial serum iron of 500 µg./100 ml., uninterrupted recovery followed the use of a considerably reduced chelating regimen. We should agree, therefore, with the comment stressing the tentative nature of any dosage schedule for desferrioxamine at present, and the need

for further well-documented case reports.—We are, etc.,

Royal Hospital for Sick Children,
D. G. D. BARR.
D. K. B. FRASER.
Western General Hospital,
Edinburgh.

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Disinfectants in Hospitals

SIR,—I refer to the article "Disinfectants in Hospitals" (13 February, p. 408) and to statements about ampholytic surface-active agents.

It is stated that the compounds are not sporicidal. We have ample independent evidence to show that these compounds will kill the spores of *Bacillus globigii*, *B. anthracis*, *Clostridium sporogenes*, and *Cl. welchii* at room temperature with a contact time of 30 minutes. It is also stated that the compounds are expensive. On a price-per-gallon basis this may appear to be so at first sight, but the cost of disinfecting 1 sq. yd. (0.28 sq. metre) of surface is 0.06 pence. In fact, the rational use of these compounds has turned out to be less expensive than the indiscriminate and sometimes unnecessary use of compounds the price per gallon of which may be somewhat less.—I am, etc.,

COLIN HARRIS.

Tego Division,
Hough, Hosason & Company Ltd.,
Manchester 19.

SIR,—The article entitled "Disinfectants in Hospitals" (13 February, p. 408) gave much useful guidance on the use of disinfectants in hospitals. However, the difficulties in choosing effective disinfectants within their class still remain.

The general disinfectant in use in this hospital was stated by the suppliers to be such that "bactericidal activity" was "maintained in the presence of blood and other organic matter." It was on this written claim that the preparation was retained. However, when the suppliers were asked for definite bacteriological data to support their claim they were unable to provide it immediately. It was only after a delay of two months, and after a further letter to them, that they were able to supply the required details. Their letter revealed a Chick Martin coefficient of 0.2 and repudiated their former claim. This clearly shows that this product is unsuitable for the purpose for which we require it, and we are discontinuing its use.

It may be that other hospitals are also using disinfectants which are equally unsuitable and for which the suppliers make equally unjustified claims.—I am, etc.,

Battersea General Hospital, D. P. MORGAN.
London S.W.11.

Medical Survey of Tristan da Cunha

SIR,—In 1963 we reported the results of a medical survey of the entire population

of Tristan da Cunha.¹ Our findings were based on general clinical examinations of the islanders carried out during the first three months of their period of involuntary exile in England.

Some of the findings of a specialized psychiatric and sociological inquiry have now been published by Rawnsley and Loudon.² We should like to draw attention to certain important discrepancies between these findings and our own impressions of the mental state of the Tristan people. We reported that they were "... noticeably free, with very few exceptions, of anxieties and worries. . . ." Rawnsley and Loudon had the opportunity to make an intensive study over the subsequent months. It was found that there were four current cases (2.1%) of psychotic disorder, and that 24% of the adults suffered from headache precipitated by anxiety and worry. This symptom was endemic both on Tristan and in England. There was also shown to be a most interesting association between the occurrence of headache at the present day and the occurrence of an epidemic of hysteria which affected over 10% of the population in 1937.

When they arrived here their polite friendliness in a new and strange environment, together with mounting nostalgia, led them to present an idealized picture of themselves and their life on Tristan which more detailed study has corrected.—I am, etc.,

H. E. LEWIS,

Secretary,

Tristan da Cunha Working Party.
Medical Research Council,
National Institute for Medical Research,
Division of Human Physiology,
Holly Hill,
London N.W.3.

REFERENCES

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Cystic Disease and Carcinoma of the Breast

SIR,—There is one important piece of evidence, which you do not mention, which would strengthen the conclusion of your leading article (20 February, p. 469) that "these patients wish for reassurance, and in our present state of knowledge they should receive it." I refer to the experience, for the most part unrecorded, of large numbers of surgeons all over the world who for several decades now have been treating cysts of the breast by aspiration, and who have not seen any particular tendency to carcinoma in these patients. Nurick and I some years ago¹ pointed out a fallacy which is present in most series purporting to show that cysts of the breast predispose to carcinoma—namely, that the authors do not exclude from their figures the small group of cysts of the breast in which intraductal papillary carcinomas by a combination of some irritant action and the effusion of varying amounts of blood actually cause a cyst. The much more common simple cysts of the breast have quite different clinical features, and, if one may extrapolate from the work of Hayward and Parks which you mention,² are best regarded as chance temporary upsets of normal secretory-absorptive processes during the phase of breast involution. Finally, may I make a plea that, since the condition is paraphysio-

logical rather than pathological, the reassurance which you rightly say these patients should receive would be strengthened if, instead of using the term "cystic disease," we referred to the condition as either "simple cysts" or "involution cysts"?—I am, etc.,

London W.1.

DAVID H. PATEY.

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- ² Hayward, J. L., and Parks, A. G., *Endocrine Aspects of Breast Cancer*, 1958, p. 133, ed. by A. R. Luwrie. Livingstone, Edinburgh.

Pleural Effusion and Breast Cancer

SIR,—The observation by Dr. E. H. Porter (23 January, p. 251) that pleural effusions secondary to cancer of the breast are more commonly ipsilateral than contralateral is, of course, not new. This point was mentioned in the columns of your journal in 1953 in a paper written by me in collaboration with Dr. Frank Ellis,¹ and I have little doubt that it was made by others before us.

Out of 159 cases of breast cancer with pleural effusion who died between 1954 and 1960 at the Peter MacCallum Clinic, Melbourne, 95 effusions were ipsilateral, 41 contralateral, and 23 bilateral in their onset. Like the Christie Hospital, Manchester, figures, our larger series showed that the excess of ipsilateral over contralateral effusions is seen in all years of follow-up after the first treatment, even after five years (see Table I). It is seen in the primarily operated cases (Stages 1 and 2), and in the primarily irradiated cases (Stages 3 and 4). It is seen in operated cases, both when the scar was irradiated post-operatively and when it was not (see Table II). This latter observation does not exclude the likelihood that the incidence of pleural effusion may be decreased by

TABLE I

Years	1	2	3	4	5	5+
Stages 1 and 2 { Ipsilat. . .	22	12	13	5	5	13
{ Contralat. .	7	9	6	4	4	6
Stages 3 and 4 { Ipsilat. . .	13	7	3	1	0	1
{ Contralat. .	1	3	—	—	—	1

TABLE II

Years	1	2	3	4	5	5+
Surgery alone { Ipsilat. . .	14	6	9	3	4	8
{ Contralat. .	5	8	3	3	2	6
Surgery and R/T scar { Ipsilat. . .	8	6	4	2	1	5
{ Contralat. .	2	1	3	1	2	—

irradiation of the scar post-operatively, but it would require a randomly selected series to establish this point, and ours is not.

I agree with Dr. Porter that clinical evidence suggests that the development of a malignant pleural effusion in breast cancer is more likely to be due to lymphatic permeation than to haematogenous spread. This is supported by my observation that in the 106 cases developing an effusion post-operatively there was associated evidence of local recurrence in 74—a proportion of 69% (skin nodules in 53, ipsilateral supraclavicular nodes in 39, opposite breast invasion in 12, opposite axillary-node involvement in 9, and ipsilateral axillary-node recurrence in 2 cases). These local recurrences were usually closely associated in time with the pleural effusion and actually appeared simultaneously with the effusion in 22 of the 73 cases. The

development of a pleural effusion following mastectomy may suggest, therefore, as does the development of local recurrence, injudicious selection for radical surgery.—I am, etc.,

Peter MacCallum Clinic, BASIL A. STOLL.
Melbourne, Australia.

REFERENCE

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Hepatic Coma Due to Liver Metastases

SIR,—Dr. A. Paton (30 January, p. 316) and Dr. N. R. Pal and his colleagues (16 January, p. 168) discuss coma due to hepatocellular failure when liver tissue is extensively replaced by metastases. Another cause of coma in such patients may be hypoglycaemia resulting from severe depletion of glycogen stores in the liver. The rarity of this is pointed out by Professor Sheila Sherlock.¹ Woodward and Fry² found that patients with carcinoma had an average blood sugar of 20 mg./100 ml. higher than that of normal controls, so it is reasonable to suppose when hypoglycaemia occurs in the presence of liver secondaries that it is due to disturbance of hepatic function.

The following brief case report will further emphasize this.

The patient, a widow aged 68, whose husband died six years previously with carcinoma of the stomach, presented with a short history of anorexia, upper abdominal pain, and weight loss. She was found to have a hard, nodular, enlarged liver, and carcinoma of the stomach with hepatic metastases was suspected. Investigations showed serum bilirubin 0.3 mg./100 ml. and alkaline phosphatase of 31.5 K-A units. She was fasted prior to a barium-meal examination and collapsed in the radiology department, at the same time becoming pale, sweating, and aphasic. The right plantar response was equivocal, and it was thought possible that she had sustained a cerebrovascular accident. Lumbar puncture, however, revealed a cerebrospinal fluid sugar content of 17 mg./100 ml., and shortly afterwards the blood sugar was 30 mg./100 ml. She improved rapidly following intravenous infusion of 50% glucose, and one week later was fit for a laparotomy (Mr. L. Lancaster) which confirmed an inoperable carcinoma of the stomach with extensive hepatic infiltration. Two weeks later she again became comatose in the early hours of the morning, improving after glucose water was given into the stomach by Ryle's tube, but half an hour later she relapsed and died.

Post-mortem examination revealed a large fungating carcinoma of the fundus with extensive replacement of liver tissue by secondary deposits.

—I am, etc.,

GARETH HUGHES.

Caernarvon & Anglesey Hospital,
Bangor, Caernarvonshire.

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Inaccuracies of Statistics

SIR,—It was encouraging to see from your leading article (13 February, p. 401) recognition of the inaccuracies of hospital statistics. Unfortunately, although technically more accurate, the same analysis could also be applied to the returns of the Registrar