leagues from these experiments that no growth-inhibitory effect of sodium fluoride was seen must be regarded as meaningless.

The data of Albright,³ however, are significantly different from ours; mouse-leukaemia cells grown in suspension were not affected in their growth by higher NaF concentrations than the 0.1–10 p.p.m. used by us. The attachment to a glass surface which is a *sine qua non* for the growth of HeLa and the strain L fibroblasts is not required by Albright's mouse-leukaemia cells, and this attachment may be the step at which the cell is most sensitive to the action of fluoride. We demonstrated that although growth rate was decreased in cultures containing 0.1–10 p.p.m. NaF, the absolute reproductive capacity (ability of single isolated cells to grow into macroscopic clones) was unaffected unless much higher fluoride concentrations were used.

Finally, we have never interpreted our results in respect of the safety or hazard of public-water fluoridation; despite the flurry of press and scientific comment upon our work, we have merely presented a biological observation, not refuted by subsequent studies, which remains to be confirmed and explained or validly refuted.—We are, etc.,

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REFERENCES

- Berry, R. J., and Trillwood, W., *Brit. med. J.*, 1963, **2**, 1064.
- Elkind, M. M., Han, A., and Volz, K. W., *J. nat. Cancer Inst.*, 1963, **30**, 705.
- Albright, J. A., *Nature (Lond.)*, 1964, **203**, 976.

Efficacy of Intra-articular Steroids

SIR,—In the *Annals of the Rheumatic Diseases*^{1–3} several articles have appeared by the group at Leeds and Harrogate in which they apparently “prove” that intra-articular corticosteroid injection has no more beneficial effect in osteoarthritic knees than placebo injections. Their papers are studded with “controls” and statistical analyses. I have recently gone over them in revising my chapter on intra-articular corticosteroid therapy, wondering why this group alone could be so completely out of line with all other reports. I have found the answer, and have checked it in our clinic.

Hartfall and his colleagues have used the technique of injecting knees with the patient sitting up, knees bent, and attempting to inject through or beside the patellar tendon. We had never used this approach, discarding it years ago as completely inadequate. They describe no fluid obtained by this technique, and the reason is because no fluid can be obtained with this method from any osteoarthritic knees—i.e., the joint space has not been entered, and injections were only made into the infrapatellar fat pad, not into the joint. We checked this on 12 patients with osteoarthritis, could obtain no fluid by this approach, but obtained it easily by our method. They have therefore proved that, no matter what is injected into a knee, it will have no palliative effect unless it enters the joint space, and nothing more. Rheumatoid arthritic knees, of course, usually contain large effusions, and fluid can be obtained

even by this method in them, so their rheumatoid injections could have been effective as described.

In earlier papers published in the *Lancet*⁴ and the *British Medical Journal*⁵ the group claimed that half the patients showed marked destruction of joints from such therapy, including even “Charcot joints.” They used large doses of steroids; repeated them frequently; and do not say that they cautioned the patients to moderate activity. Our own incidence of such joint destruction has been less than 1% of patients.

I am grateful to those who place “dangerous curve” signs on the roads I drive, but I am not grateful for “detours” when a mere warning would be adequate. Physicians should be warned of dangers from abuse of any therapy, but this group seems to suggest that intra-articular steroid therapy is not palliative in osteoarthritis, and is so dangerous in rheumatoid arthritis that it should be abandoned. I have had more experience than they, having administered more than 150,000 intrasynovial steroid injections to more than 5,000 patients in our clinic since 1951. No other therapy has given so much relief to so many for so long.—I am, etc.,

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REFERENCES

- Wright, V., Chandler, G. N., Morison, R. A. H., and Hartfall, S. S., *Ann. rheum. Dis.*, 1960, **19**, 257.
- Morison, R. A. H., Woodmansey, A., and Young, A. J., *ibid.*, 1961, **20**, 179.
- Wright, V., *ibid.*, 1964, **23**, 389.
- Chandler, G. N., and Wright, V., *Lancet*, 1958, **2**, 661.
- , Jones, D. T., Wright, V., and Hartfall, S. J., *Brit. med. J.*, 1959, **1**, 952.

Reactions to Intravenous Iron Dextran

SIR,—I too was interested in the article by Dr. Barbara E. M. Clay and her colleagues (2 January, p. 29) and also in the comments by Drs. R. S. Lane and Jean M. Scott (13 February p. 449), who suggest that folic-acid deficiency may trigger the sensitivity reaction.

Recently I have infused 101 cases with iron by this method with two severe reactions of the anaphylactoid type but without collapse. All the cases were associated with pregnancy but the reactions were both in puerperal patients. I have fairly detailed information concerning the folic-acid status of one of these two women. It is shown in Table I.

The serum-folic-acid activity (S.F.A.A.) is suspiciously low, but the marrow was normo-

TABLE I.—Serum Folic-acid Activity in Patient Reacting to Iron Dextran

Gestation (weeks)	27	31	35	38 (Delivery)	7th Day Puerperium
Hb (%)	78	79	84	83	55
Total serum folic-acid activity (m μ g./100 ml.)	2.8	3.0	3.3	1.6	2.6

TABLE II.—Serum Folic-acid Activity in Patient Not Reacting to Iron Dextran

Gestation (weeks)	25	29	38	39 (Delivery)	7th Day Puerperium	6th Week Puerperium
Hb (%)	74	65	77	87	83	84
Total serum-folic-acid activity (m μ g./100 ml.)	2.4	1.7	1.2	1.4	1.2	1.8

blastic on the seventh puerperal day, that of the infusion. Neither folic acid nor any iron therapy had been administered.

In contrast, five of twenty cases showed low S.F.A.A. levels throughout pregnancy. Of thirty readings from these five patients in the second and third trimesters, only two were greater than 2.0 m μ g./100 ml. The following case serves as an example (Table II).

The S.F.A.A. was consistently low and megaloblastic anaemia was excluded. Infusion took place at 30 weeks. Based on the 6th-week post-delivery level this woman, even in the non-pregnant state, has a low serum folate.

Of the other four cases mentioned, three were normoblastic and the fourth, a twin pregnancy, subsequently developed a megaloblastic marrow at full term. None had the slightest reaction to infusion.

Thus on the basis of the S.F.A.A. it becomes apparent that a deficiency is not necessarily a trigger or even predisposing factor. Once again one is confronted by that age-old problem—individual idiosyncrasy.—I am, etc.,

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I. W. MANSON.

Drug Advertisements

SIR,—May I congratulate Professor O. L. Wade on his letter (27 February, p. 585)?

This is a most important subject. I have amused myself from time to time collecting advertisements relating to conditions in my specialty which are not only misleading but devoid of any scientific basis. Surely if the printing of such clap-trap is worth while we cannot be such a learned profession as we would like to think. Many must be mere tradesmen recommending advertised remedies.

It is a pleasure to read such a well-thought-out letter with constructive ideas.—I am, etc.,

Tunbridge Wells,
Kent.

W. H. GERVIS.

Booster Tetanus Toxoid

SIR,—Authorities offer different advice on the timing of a booster dose of tetanus toxoid following the completion of a standard course of three injections. Reinforcement is variously advised after three years or five years. A report by Goldsmith, Rosenberg, and Pollaczek (*New Engl. J. Med.*, 1962, **267**, 485) suggested that this period could be extended to 18 years.

We have under our care 17,000 to 18,000 workers who occasionally suffer injuries requiring first aid at the medical centre. As many are ex-Servicemen it seemed interesting to find out how many of those who had been immunized in the Forces show evidence of active immunity. We therefore gave a small dose of tetanus toxoid to a random sample of workers who had previously been immunized against tetanus, to determine the type of antibody response (primary or secondary). We

are at present also studying the antitoxin response following tetanus toxoid injections in various other circumstances. These studies will be reported in full in due course.

Our preliminary results show that in over 80 cases who had had standard courses of tetanus toxoid in the past high (i.e., protective) antitoxin titres were present one week after a boosting dose of tetanus toxoid (fluid or adsorbed). In 72 cases the last tetanus toxoid injection had been given over five years previously, and in 25 of these the interval varied from 15 to 20 years after injection. We would suggest, therefore, that with adequate evidence of a past course of three or more injections of tetanus toxoid a booster dose in the form of 0.2 ml. of adsorbed tetanus toxoid given parenterally is all that is required even though 20 years may have elapsed since that course.

We realize that adequate evidence may not always be easy to obtain, but consider that the search is justified if prolonged protection can be so easily renewed and the use of anti-tetanus serum avoided.

It may not be widely known that tetanus toxoid was discontinued at the end of the war in 1945, in both the Army and Royal Navy. It was started again in 1949 in the Army and 1958 in the Royal Navy. Only in the Royal Air Force has it been continued without interruption since 1939.—We are, etc.,

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G. M. BARNES.
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Training of Radiographers

SIR,—There is a surprising omission in your leading article (27 February, p. 542). You nowhere refer to the Radiographers Board or to the Council for Professions Supplementary to Medicine.

The omission is the more surprising because you hint that the present proposals of the Society of Radiographers may have been influenced by the fact that the Society is both an examining and a negotiating body. The Society is well able to answer these criticisms itself, but it is not the body which will finally decide what the training for radiographers should be; that will be decided by the Radiographers Board and the Council, subject to the overriding jurisdiction of the Privy Council.

One of the purposes of State Registration for the Professions Supplementary to Medicine is to relieve professional associations from the responsibility of taking decisions in matters where they can be accused, however inaccurately, of allowing irrelevant factors to influence them. Such matters are now dealt with by an objective body uninfluenced by these factors.

I have not commented on the merits of the Society's proposals because they have not yet been submitted to the Radiographers Board; when they are considered, the Board, no doubt, will study them realistically and bear in mind their influence both on the recruitment of students and their fitness for the work they will perform.—I am, etc.,

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Efficacy of Oral Contraceptives

SIR,—Although doubts are frequently expressed about the safety of the oral contraceptives their effectiveness is not questioned. The following case suggests that 100% efficiency ought not to be taken for granted.

A married woman, age 24, has two children aged 6 years and 3 years. She had an abortion at 12 weeks in 1960. In February 1964 she started taking Anovlar (norethisterone 4 mg., ethinyloestradiol 0.05 mg.) as a contraceptive. The tablets were taken exactly as instructed, the patient keeping a written record of the dates of her menses. She is quite certain that she never missed a single tablet except in May 1964, when she decided to omit the tablets for a complete cycle. In October 1964 her expected menstruation failed to appear, but she recommenced the tablets on the fifth day after the expected date as instructed. When menstruation did not occur in November she decided that she must be pregnant and took no further tablets. Examination on 26 January 1965 revealed that the uterus was enlarged to a size which conformed to the 18 weeks of amenorrhoea since her last period started on 20 September 1964, and she had already felt foetal movements.

Oral contraceptives are now very extensively prescribed without the careful observation and follow-up procedure which were a feature of the initial trials. One wonders whether other failures are occurring which have not been reported.—I am, etc.,

Manchester 20.

CLIFFORD R. KAY.

Foetal Malformation and Cortisone Therapy

SIR,—Two cases encountered recently of deformed children born to women under cortisone therapy would seem to warrant a suspicion that the cortisone was responsible. One patient, a primigravida, had had cortisone for many years for an ulcerative colitis. Its administration was continued throughout the pregnancy, which proceeded quite normally, the only abnormal appearance noted being a diffuse and uniform cyanosis of her legs. Labour was normal. The child had a severe gastroschisis, one of the rarer malformations. The second case was that of a primigravida who had been under cortisone treatment for years for a severe asthma. Her child had a hydrocephalus.

Quite possibly the association between the cortisone therapy and these malformations was accidental, many negative instances occurring to support such a view. On the other hand, two considerations lend some force to the supposition that a causal relation may exist, one of the inhibitory effects of cortisone on tissue response, the other the adrenal hypoplasia which is such a feature of the most common lethal malformation, anencephaly. And certainly human teratogenesis is so complex a problem that negative instances do not have the force they may possess in other types of inquiry. At all events it would seem wiser to discontinue cortisone therapy at the start of any pregnancy unless there is some overriding need for its continuance.—I am, etc.,

Liverpool 1.

PERCY MALPAS.

Disinfectants in Hospitals

SIR,—I would like to comment on certain points relating to the recent report by the

Public Health Laboratory Service Committee on the use of disinfectants in hospitals (13 February, p. 408), with particular reference to the use of iodophors.

It has been recently shown by W. B. Hugo and J. M. Newton^{1,2} that an iodine-non-ionic surface active agent complex was more stable than a weak iodine solution *B.P.*, in that it retained its availability and stability over a wider pH range. They showed that the addition of 10% serum required an increase in the concentration of iodine to kill the bacteria. There was a slight reduction in the "all or none" effect of a concentration producing killing, but killing still occurred rapidly. The antibacterial effect was related to inoculum size, for with inocula ranging from 10^6 – 10^9 organisms/ml. it was found that a much lower iodine concentration was required to kill the smaller inoculum. The controlling feature of the killing of both *Escherichia coli* and *Staphylococcus aureus* was found to be the relationship between the dry weight of the bacterial suspension and the concentration of iodine, and that this value of the dry weight increases as an approximately linear function of the iodine concentration. It is therefore evident that the effectiveness of an iodophor solution depends on its content of available iodine, and a concentration of only 150 parts per million is adequate for routine surface disinfection.

The Committee recommends hypochlorites for surface disinfection, as approved by the Ministry of Agriculture, at a concentration of 200–250 p.p.m. of available chlorine. An omission was made in respect of iodophors which are also approved by the Ministry of Agriculture at a concentration of 25 p.p.m. of available iodine for dairy sterilization.

Iodophors can be adapted to a specific function and one such iodine-non-ionic detergent complex (Wescodyne Surgical) contains 150 p.p.m. available iodine at its commonly used dilution of 1:160.

It is surprising that the Committee should dismiss the disinfectant-evaluation method devised by Hare and his colleagues.³ A technique which is rapid, economical, and simple and which furthermore can be adapted to any current infecting organism is surely more satisfactory than a comparison with phenol.—I am, etc.,

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REFERENCES

- ¹ Hugo, W. B., and Newton, J. M., *J. Pharm. Pharmacol.*, 1964, **16**, 273.
- ² ——— *ibid.*, 1964, **16**, 189.
- ³ Hare, R., Raik, E., and Gash, S., *Brit. med. J.*, 1963, **1**, 496.

Improving Ambulance Services

SIR,—Your correspondent Dr. E. F. D. Gawne (23 January, p. 247) will be reassured to know that the West Riding of Yorkshire's Ambulance Service has recently held its first training course for professional ambulance personnel.

The two weeks' course was a residential one held at the splendid new training centre at Birkenshaw whose facilities are shared with the fire service. I had the pleasure of spending the last day at the course and was most impressed by the keenness of the 20 students who attended. Their experience in ambulance work varied from a few months to