again, nor is there any record of either stillbirths or abortions, except for a single case of abortion in the controls. However, complete ascertainment is extremely difficult and there may well have been a few cases which have not been reported. Our routine procedure is to give the mother a card when she is tested for antibodies six months after the birth of her first baby, and she is told to send it to us when she becomes pregnant again. As a precaution the case sheets of the mothers are also examined at intervals in case there is any indication that the woman has become pregnant

The number of cases in the various trials has increased considerably since I gave my lecture, and the data have been sent to Dr. Murray. Our general experience in Liverpool of the time interval between first and second pregnancies does not suggest that a particularly small percentage of the women in the trial have had second babies.

The anti-Kell experiment gave inconclusive results because of difficulties with the anti-Kell antibody.

Dr. Murray speculates that suppression of D-immunization by anti-D gammaglobulin may be accompanied by some impairment of general immunity to infection. Not only have we followed up both our volunteers and trial women and found nothing to suggest this, but the gammaglobulin we inject differs from preparations used for other purposes only in that 1/500th part is anti-D, and I cannot see that its effect on general immunity can be different from that of the more usual preparations.

We have now tested for anti-Gm antibodies 62 treated women and have found positives in four, giving an incidence of 6.3%. The controls are still being studied, but we do not think that the formation of anti-Gm antibodies is likely to be damaging, for, if it were, it would make the giving of blood transfusions a most dangerous procedure, since incompatible Gm antigens must often be injected in large quantities in transfusions of whole blood.

Although in our first experiments, in about 1960, there was enhancement of immunization by IgM, which has never been satisfactorily explained, yet since that time we had not used IgM but always IgG both in our experiments and the clinical trials.

We do not understand the relevance of Dr. Murray's questions about the "ultimate relationship of anti-Gm in rheumatoid arthritis" to our work. The four women with the anti-Gm are entirely well and there is no suggestion that they have or are developing rheumatoid arthritis. Furthermore, there is no evidence that Gm antibodies, either natural or induced by immunization, predispose to rheumatoid arthritis, and the distribution of the Gm groups is normal in patients with this disease.

While agreeing that more research is needed, the most important point to us seems to be to find the smallest effective dose, and an M.R.C. working party is organizing trials to determine this. There is some very recent evidence on the subject from New York.[1] Four groups of 10 Rh-negative men were given 10 ml. of group O Rh-positive whole blood intravenously at monthly intervals for a total of three injections. Twenty-four hours following the administration of blood three of the four groups were given 1.0 ml., 0.5 ml., or 0.25 ml. respectively of an ortho preparation containing 1,200 μg. of anti-Rh$_o$ (D) antibody per ml. Blood samples were obtained thereafter at monthly intervals for nine months and examined for the presence of anti-Rh. The results are summarized in the Table.

Group	Dose of Ortho Anti-D Gamma-globulin	Number With Anti-Rh at 9 Months	% With Antibody
I	0	6 of 10 men	60
II	1,200 μg	0 „ 10 „	0
III	600 „	0 „ 10 „	0
IV	300 „	0 „ 10 „	0

Pollack *et al.* (1967).[1]

It therefore looks as though 300 μg. of ortho anti-D (approximately the amount being used in our current 1-ml. trial) is effective in protecting against a fairly large volume of injected Rh-positive blood.

Whether the treatment is "unquestionably right for national use" is a decision for the Ministry of Health, which has set up a subcommittee of its Standing Medical Advisory Committee to consider the whole matter.—I am, etc.,

C. A. CLARKE.

Department of Medicine,
The University,
Liverpool.

REFERENCE

1 Pollack, W., Singher, H. O., Gorman, J. G., and Freda, V. J., Scientific Exhibit, American Association of Blood Banks Meeting, October 1967, New York.

Allergic Alveolitis

SIR,—In your leading article (16 September, p. 691) the term "extrinsic allergic alveolitis" was suggested as the appropriate general description for a group of conditions resulting from the inhalation of antigenic material and occurring in farmers, mushroom-pickers, bird-fanciers, pituitary snuff-takers, bagasse handlers, etc.

We would accept this term as appropriate if the pathology were confined to inflammatory changes in the interalveolar septa with or without an exudate into alveolar spaces, but this is not so, because at one stage a salient feature is the presence of numerous "sarcoid-like granulomata" which induced Dickie and Rankin,[1] who first described the histology in farmer's lung, to use the term "acute granulomatous interstitial pneumonitis." Another frequent feature, as indeed is pointed out in the leading article, is a bronchiolitis, the exudate of which may become organized. Further, as is to be expected in a pulmonary Arthus or Type III reaction, vasculitis occurs. Organization of the inflammatory damage often occurs in this group of diseases, leading to a chronic stage characterized by pulmonary fibrosis.

The term "extrinsic alveolitis" invites the suggestion that this fibrosis is to be compared with diffuse idiopathic fibrosing alveolitis, now apparently the term replacing idiopathic diffuse interstitial pulmonary fibrosis or "chronic Hamman–Rich disease," where the end result produces a fine interstitial fibrosis with a respiratory function profile of transfer factor defect.

In the group of diseases now under consideration, however, this is only one of the possible end-results. In many patients there is much fibrosis involving terminal conducting airways—for example, an obstructive airways disease profile is seen in about one-third of sufferers from chronic farmer's lung.[2] Reporting on lung-function studies in bagassosis, Weill and others[3] concluded that some dyspnoeic patients in the chronic stage had obstructive airways disease which they considered was causally related to bagasse exposure.

We therefore feel that "extrinsic allergic pneumonia" is less specific and more appropriate than "extrinsic allergic alveolitis."

One of the difficulties in interpreting the published work on farmer's lung is that authors seldom make it clear whether they are discussing the acute potentially reversible stage or the chronic stage of irreversible fibrosis. In order to obviate this situation it is suggested that the acute stage be referred to as "acute extrinsic allergic pneumonia," and the fibrotic end-result as "chronic extrinsic allergic pneumonia." The term used should describe clearly the whole clinico-pathological entity.—We are, etc.,

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REFERENCES

1 Dickie, H. A., and Rankin, J., *J. Amer. med. Ass.*, 1958, **167**, 1069.
2 Hapke, E., Thomas, G. O., Seal, R. M. E., Meek, J., and Hayes, M., to be published.
3 Weill, H., Buechner, H. A., Gonzalez, E., Herbert, S. J., Aucoin, E., and Ziskind, M. M., *Ann. intern. Med.*, 1966, **64**, 737.

Demonstration Aerosol Inhalers

SIR,—Dr. A. Herxheimer (28 October, p. 236) suggested that manufacturers of pressurized aerosol preparations should provide "demonstration" inhalers so that prescribing doctors could instruct their patients more effectively.

It has been our practice to provide doctors with inert aerosol inhalers from time to time, through our representatives. Our object has been to stress the desirability of correct administration, and encourage doctors to supplement the instructions in the patient's leaflet with a practical demonstration.

As part of our current efforts to avoid misuse and abuse of pressurized aerosols, our representatives are now offering inert inhalers to all doctors on whom they call. The co-operation of all prescribers is being sought in ensuring that patients are using the right technique, and thereby obtaining maximum response from minimum dosage.—I am, etc.,

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Medical Adviser,
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Loughborough,
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Purpura in a Patient Taking Chlordiazepoxide

SIR,—Non-thrombocytopenic purpura occurring following chlordiazepoxide (Librium) administration has been seen recently in this hospital.

The patient, a 65-year-old well-nourished Jewish woman, was investigated for a generalized purpuric rash. She had been receiving protamine zinc insulin for many years, and for at least 12 months had been receiving irregular courses of chlordiazepoxide (10 mg. twice daily) at approximately monthly intervals, each course lasting approximately a week. On admission the chlordiazepoxide was discontinued. The routine blood investigations were all normal.

The tourniquet test was positive, clot retraction was 45% (normal 48–64%), and the platelet count varied between 114,000 to 245,000/cu. mm. A peripheral blood film showed normal platelet morphology with perhaps occasional large forms. No lupus erythematosus cells were seen. The urine contained 130 mg./100 ml. protein, sugar at times, and an occasional granular cast. Serum proteins were 7.6 g./100 ml. (albumin

3.6 g./100 ml.). Protein electrophoresis showed an increase in all the globulin fractions with mild decrease of the albumin fraction.

The most likely abnormality was therefore an increase in capillary fragility, although a qualitative defect could not be outruled. The pupura gradually faded; and on discharge four weeks later the tourniquet test, though still positive, was less marked. During her hospitalization she was transferred from insulin to chlorpropamide (Diabinese) 500 mg. daily, with good control of her diabetes and no deterioration in her purpura.

She was readmitted three weeks later with right hemiparesis due to cerebral thrombosis. Chlordiazepoxide 10 mg. was given on admission. The following morning the tourniquet test was negative and the platelet count was 200,000/cu. mm. The blood urea was 44 mg./100 ml., and urinalysis showed 60 mg./100 ml. protein only. Five days after admission she was noted to be depressed, and chlordiazepoxide 10 mg. t.i.d. was prescribed. Within 48 hours the purpura reappeared and the tourniquet test was strongly positive. The platelet count was 190,000/cu. mm. The chlordiazepoxide was discontinued; the purpura gradually faded, and the tourniquet test became steadily weaker. Nine weeks later it was negative and the platelet count was 162,000/cu. mm. It was found difficult to control her diabetes with chlorpropamide and insulin therapy was recommenced, with good control and no recurrence of the purpura. She was discharged with residual hemiparesis, has remained well, and has had no further episodes of purpura.

The only reported case of purpura occurring with chlordiazepoxide administration was at a clinicopathological conference,[1] at which concurrent chloramphenicol administration was considered responsible for the purpura. Thirty-four suspected cases have been reported to the manufacturers, but no cases have been reported in the literature. It is interesting to note that the purpura did not appear when 10 mg. was administered on the evening of her second admission, and only appeared when 30 mg. per day was given later. It seems, therefore, that there is a minimum dose needed to manifest the purpura.—I am, etc.,

Mercer's Hospital, Dublin 2. ISAAC J. COPPERMAN.

REFERENCE
[1] *Amer. J. Med.*, 1965, **39**, 260.

Salmonella in Tortoises

SIR,—I was most interested to read Dr. L. T. Newman's letter on the problem of salmonella in tortoises (4 November, p. 296). It is a well-known fact that tortoises and related terrapins are excreters and carriers of salmonellas, and, as such, are a constant hazard to their owners and handlers, in particular young children.

In 1966, in conjunction with Dr. C. D. Plows, of the Sheffield Public Health Laboratory Service, we were able to identify an Arizona strain from a case of gastroenteritis in a 3-year-old Sheffield girl. A symptomless excreter of the organism (her 5-year-old brother) was also found in the same family. The source of infection was traced to a pet terrapin—a type of small turtle (genus: *Graptenys*)—purchased by the family from a pet shop in Sheffield. Full details of this investigation are to be reported in the *Journal of Hygiene* (in press).

Terrapins, like tortoises and turtles, are excreters of both salmonellas and Arizona. If the habit of keeping terrapins as pets increases, then these small innocuous animals may well become an important source of human salmonella infection. This is especially so in young children. Terrapins are more likely to act as a source of human infection than tortoises for the following reasons: terrapins are smaller and therefore easier and more tempting for young children to handle; they are usually kept indoors and in a tank of water; it has been observed that children do play with them and are in the habit of transferring them in and out of the tank at frequent intervals. If the terrapins are excreters then the water in the tank will become infected, so increasing the possibility of spread to humans or to other pets.—I am, etc.,

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Paraquat Poisoning

SIR,—The recent report of Dr. Ch. Almog and Dr. E. Tal (16 September, p. 721) of the result of a subcutaneous injection of paraquat (Gramoxone), with the development of a right facial paresis, prompts me to record another case of facial palsy associated with Gramoxone.

This was in a male horticultural worker of 49 who presented in May this year. He had rolled a cigarette with unwashed hands after washing spray nozzles contaminated with Gramoxone. He developed a burning sensation of the tongue and examination four days later revealed nothing abnormal. Two days later, he awoke with headache and nausea, sore throat, fever, aching of the limbs, and general malaise, and by mid-afternoon had marked muscular weakness and nearly collapsed. His temperature was 101.5° F. (38.5° C). Neck stiffness was present, and there was a thin line of vesicles on the right fauces. There was a horizontal nystagmus which the patient claimed had been present for years.

He was admitted under the care of Dr. J. Campbell, and four days later developed a right lower motor neurone facial palsy with no other neurological findings. The chest, skull, and mastoid *x* rays were normal. The cerebral spinal fluid the day after admission showed R.B.C.s 41/cu.mm., W.B.C.s 5/cu.mm. protein 110 mg./100 ml., sugar 100 mg./100 ml. chlorides 760 mg./100 ml. A repeat lumbar puncture one week later showed R.B.C.s 8/cu. mm., W.B.C.s 39/cu.mm. neutrophils 11%, lymphocytes 89%, protein 40 mg./100 ml., chlorides 750 mg./100 ml., sugar 104 mg./100 ml; the pressure was 150 mm. with a free rise and fall Blood count, E.S.R., blood urea, liver function tests, aspartate transaminase, and alanine transaminase were normal; the urine contained a trace of protein, many pus cells, and follow-up intravenous pyelogram suggested old right-sided pyelitis.

A follow-up chest *x* ray five months later showed no evidence of any active pathology in the lungs, and the heart was of normal size (Dr. Maxwell).

This sequence of contact with paraquat (Gramoxone) and facial palsy may be entirely coincidental; the minute dose of paraquat involved might suggest a hypersensitivity response in this case. It would be interesting to know of facial or other palsies occurring in others using or manufacturing paraquat.—I am, etc.,

K. A. MOURIN.
Dereham, Norfolk.

Low Back Pain

SIR,—"Medicine Today" (11 November, p. 341) presents what is presumably a résumé of eminent authoritative exposition of the symptoms, signs, diagnosis, and treatment of this most common of complaints. Reading this, for I have not yet seen the film, it truly amazes me that these are the practices still in vogue.

What is new? What does "Medicine Today" have to offer? Let us be reasoned, and, if you like, be with it. Let us read, learn, digest, and practise, if not all, some of the teachings of Dr. James Cyriax. He after all (and a great number of his enlightened colleagues) has been thundering out for 20 years or more the signs, symptoms, and treatment of derangement of intervertebral joints (D.I.J.).

Whether you like it or not, his whole concept works—and very well at that. The problem is for the average doctor to grasp, interpret, and treat the condition.

The essence of treatment of D.I.J., no matter how severe, is immediate manipulation (apart from S.4). The acute severely immobilized patient with lumbago or sciatica is gently manipulated, not once, but daily, on alternate days, or every third day. This, together with a rigid bed, trunk extension exercises (as soon as the patient can start them), and no lumbar flexion when up and about, has been constantly found to get the patient back to work within a week or two.

Lying doggo in bed, swallowing hundreds of painkilling tablets, sweltering under a heat-tunnel, etc., is just not good enough when immediate reduction of the D.I.J. and mobilization is all that is required.—I am, etc.,

T. HAMBLY.
Pondwell, Ryde, Isle of Wight.

Intestinal Spirochaetosis

SIR,—Lieutenant-Colonel C. O. Burdick (11 November, p. 357) asserts that we have "misinterpreted normal intestinal microvilli cut tangentially as spirochaetes." He presumably bases this view on the single low-powered electronmicrograph published with our paper.

We wish categorically to deny this suggestion. There can be no doubt that the condition we described (16 September, p. 718) is an infestation of the colonic mucosa by small, spiral micro-organisms. These are much larger than microvilli but smaller than bacteria. Axial filaments are clearly visible in our own material and in negatively stained preparation of the organisms prepared by Dr. J. Gordon. The organisms are motile on dark-ground microscopy.

It is of interest that this condition is quite common and can be diagnosed from routine histological preparations. The lesions must have been seen frequently by pathologists, but it seems the appearances have not been interpreted correctly in the past.—We are, etc.,

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SIR,—Dr. S. C. Dyke (21 October, p. 176) has referred to my work on intestinal spirochaetosis in terms which I deeply appreciate.