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-Rho (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.,

R. M. E. SEAL.
J. C. WAGNER.

Sully Hospital and
Medical Research Council's
Pneumoconiosis Research Unit,
Penarth, nr. Cardiff.

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.,

H. E. LEWIS,
Medical Adviser,
Riker Laboratories.

Loughborough,
Leicestershire.

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