

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Smallpox Vaccination after Corticosteroids

Q.—For how long after the end of a three-month course of prednisone of 5 mg. twice daily (5 mg. once daily for the last fortnight) would it be wise to postpone smallpox vaccination?

A.—The effect of corticosteroids on immune reactions depends on many factors, including the type, amount, and potency of the antigen, kind of antibody, the steroid given, and the dosage. In general, high doses will enhance adverse clinical reactions to vaccines and inhibit initiation of the antibody response. They do not appear to affect the survival time of existing serum antibodies, their titres, or their production if initiation of the response occurred prior to the administration of the steroids. The effect on the elimination of circulating antigen is negligible.

Cortisone given several days before an antigen does not impair the antibody response, but it has a marked inhibitory effect if given for two days before and on the day of injection of antigen. Practically all metabolites of prednisone are eliminated within 48 hours, and, since the physiological activity of a steroid is exerted mainly by the portion remaining free and unbound to proteins, antigens given within a few days of cessation of steroid therapy should produce an adequate antibody response. Even 5 mg. prednisone, given twice daily, may not impair the antibody response to normal immunizing doses of a potent antigen such as adsorbed tetanus toxoid.

When a live vaccine is used it should be borne in mind that cortisone enhances the pathogenicity of a number of bacteria viruses and fungi. Impaired handling of the smallpox vaccine virus may result in generalized vaccinia or progressive necrotic vaccinia, and therefore it would be wise to postpone smallpox vaccination for at least a month after cessation of treatment with prednisone.

Autoimmune Reaction

Q.—What is the autoimmune reaction, and what are its manifestations?

A.—Ehrlich postulated that the body would not react against its own tissues. In some way it was able to distinguish between "self" and "not self," and in the latter case an immunological reaction was initiated against the foreign material. It is now thought that in certain circumstances a similar response can be provoked by some of the body's own tissues, and this has been termed the autoimmune reaction.¹

One of the first examples to be recognized was Hashimoto's disease, in which it has been postulated that leakage of thyroglobulin from thyroid acini into the surrounding tissues, where it is not capable of "recognition," sets up a self-perpetuating antigen-antibody response with ultimate destruction of the thyroid. Other diseases believed to have an

autoimmune basis include disseminated lupus erythematosus, pernicious anaemia, and certain cases of Addison's disease and haemolytic anaemia.

The concept of autoimmunity and its manifestations are too complex to be discussed briefly and the questioner is referred to the recent monograph by Glynn and Holborow.² In general terms there is disorganization of the function of the organ or tissues involved, accompanied by constitutional disturbance and hypersensitivity. In many cases it is possible to demonstrate autoantibodies, and corticosteroids or antimetabolic drugs are sometimes able to suppress the autoimmune response.

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- 1 Burnet, M., *Brit. med. J.*, 1959, 2, 645, 720.
- 2 Glynn, L. E., and Holborow, E. J., *Autoimmunity and Disease*, 1965. Blackwell, Oxford.

Infectious Hepatitis Virus

Q.—Is the virus of infectious hepatitis common to man and dog, and could a dog be the vehicle of infection in man?

A.—Despite various reports, the virus of infectious hepatitis in man has not yet been cultivated in the laboratory beyond all doubt.¹ It is impossible, therefore, to be certain whether or not it can be recovered from dogs, but different and unrelated animal species in general have their own distinctive viruses owing to selective growth requirements.

Infectious hepatitis in dogs, or Rubarth's disease, is due to a canine type of adenovirus,² but there is no real evidence that this virus can infect man.³ For these reasons it is extremely unlikely that the dog could be a vehicle of infection in man.

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- 2 Carmichael, L. E., and Barnes, F. D., *Proc. Soc. exp. Biol. (N.Y.)*, 1961, 107, 214.
- 3 Prier, J. E., *Publ. Hlth Rep. (Wash.)*, 1962, 77, 290.

Alternatives to Morphine

Q.—What suitable analgesic is there for a patient in the acute stage of coronary thrombosis who is allergic to morphine, Omnopon, and pethidine?

A.—This question raises a number of points. First, what is meant when it is said the patient is allergic to the drugs? Does it mean the patient has a true allergic response with urticaria, or some other skin rash, pruritus, sneezing, etc.? It is possible, but unlikely, that he might react in this way to all three drugs. If so, the concurrent administration of the antihistamine drug might well be effective in relieving the unwanted effects.

It is more likely, however, that what is meant is that the patient is unduly sensitive to the side-effects of these narcotic analgesics. If this is so it may be the dose and not the drug that is at fault. There is an optimum analgesic dose of all these drugs. For most

patients it is 10 mg. (1/6 gr.) of morphine.¹ Any increase in dosage does not give much increase in relief from pain but does increase the incidence of side-effects.

When the patient is in severe pain in a condition like myocardial infarction, there is a great tendency to think that a large dose of morphine is required and to give doses of 15 to 20 mg., which are likely to cause nausea and vomiting in most patients. The same holds true for Omnopon and pethidine. In a patient sensitive to the effects of these drugs a smaller dose than usual—e.g., 6–8 mg.—of morphine or 50 mg. of pethidine might relieve the pain without inducing unwanted side-effects. The alternative approach is to give the usual therapeutic dose of morphine along with a drug which will counteract the side-effects, and preparations can now be obtained which enable this to be done without the need for two injections—e.g., Cyclimorph ampoules contain either 10 or 15 mg. of morphine and 50 mg. of cyclizine.

For a patient who is genuinely intolerant of these drugs, there are other powerful analgesics which could be tried. Methadone, as recently reported,² is as good an analgesic as morphine when given in a similar dose, but it must be injected intramuscularly because subcutaneous injection is painful. In a double-blind trial in myocardial infarction piminodine in a dose of 10–20 mg. was found to be as good as 10 mg. of morphine, and the incidence of side-effects was low.³ Many would probably consider that this was the sort of situation in which diamorphine (heroin) should be tried.

It must be realized, however, that all these narcotic analgesics have a similar chemical composition and that their action and side-effects are also similar, and therefore a change to a different drug may not solve the problem.

REFERENCES

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- 2 Parbrook, G. D., *Brit. med. J.*, 1966, 2, 616.
- 3 Hoff, H. R., Hotz, M. M., Sperber, R. J., Fisch, S., and DeGraff, A. C., *Amer. J. med. Sci.*, 1955, 249, 495.

Under-water Diving and Fertility

Q.—Is there any evidence that under-water diving diminishes fertility in males?

A.—There is no physiological reason why under-water diving should diminish fertility in males. Professional divers have no shortage of offspring as compared with the rest of the community.

The suggestion may have arisen from the fact that diving itself is a strenuous occupation and the need to breathe air under pressure produces a feeling of tiredness and lassitude for many hours after the dive. Recreational diving, as with other sports, may occupy a great deal of a man's time, thought, and enthusiasm, giving the impression, wrongly, that this is his only interest.

Correction

We regret that the address for obtaining the Gadget Leaflets mentioned in the Appendix to Dr. John Agate's article "Accidents to Old People in their Homes" (1 October, p. 785) was wrongly given. This should have read "Issued by the Central Council for the Disabled, 34 Eccleston Square, London S.W.1."