EDITORIAL

Serious reactions to penicillin and the later antibiotics now appear to occur more frequently and some fatalities have been recorded. This development must concern the venereologist who daily prescribes antibiotics for a large proportion of his infected patients. Few of these patients are likely to die from their infection and consequently the increasing possibility of serious reactions or actual death from treatment is particularly disturbing. Reactions to penicillin are generally caused by the patient's acquiring a hypersensitivity to the drug. These reactions are usually mild or of moderate severity and consist of either a serum-sickness-like disorder or a skin reaction which is frequently urticarial in type. The severest and fatal reactions to penicillin present suddenly as anaphylactic shock. (Pick and Patterson, 1953). Although a few examples arise from the accidental, intravenous injection of the procaine salts of penicillin (Bell, 1954), most are due to the development in the patient of hypersensitivity to the drug. The latter process probably results from a combination of the drug with serum or tissue protein, forming an antigen which in turn excites the production of antibody. The latter develops after 5 or more days and reaches a maximum soon after 10 days. The antibody leaves the bloodstream and becomes concentrated in or near the tissue cells which thereby become sensitized. With the next injection of antigen (penicillin), an antigen-antibody reaction occurs in the sensitized tissues and the cells are damaged and release histamine. This rough hypothesis of how hypersensitivity to penicillin develops explains most of the observed features: the increasing incidence of reactions in a population that has now been more and more subjected, with and without justification, to penicillin treatment for a wide variety of conditions; the predilection of so many of the reactions for the skin; and the resemblance of the severest and sometimes fatal reactions to the acute fatal anaphylaxis produced in guinea-pigs sensitized to horse serum. Procaine penicillin may be more potent than penicillin alone in producing hypersensitization, because it is not merely procaine plus penicillin but a new compound of greater molecular complexity and has thus a greater antigenic activity than either procaine or penicillin alone. Again, being more slowly absorbed and excreted, procaine penicillin has a longer opportunity of acting antigenically.

Apart from the possibility of danger to the patient, there is also a risk of sensitization in those preparing and administering penicillin and streptomycin. In such cases the sensitization chiefly affects the skin of the hands, arms, and face, and may prevent the subjects, usually nurses, from continuing their occupation as well as exposing them to serious hardship during any future illness in which penicillin or streptomycin would normally be indicated. This problem was the subject of a Memorandum from the Ministry of Health (1953) in which measures were recommended to reduce the risk of sensitization. Successful desensitization has been reported by Crofton (1953) and Russell (1953).

As in the days of arsenotherapy, it now seems that the venereologist prescribing repeated injections of penicillin must once again carefully interrogate his patient before each injection for evidence of any reaction to previous therapy. While the absence of a history of reaction is no safeguard, this precaution may help to prevent the precipitation of fatal anaphylaxis in a patient who has already manifested minor evidence of developing hypersensitivity to the injections (Thompson, 1952). Patch tests, scratch tests, and intracutaneous injection of small amounts of penicillin have been suggested, but these are not by any means infallible safeguards. Faced with the increasing prospect of meeting with hypersensitivity in his patients receiving courses of penicillin and unable to eliminate the risk completely even by careful interrogation of the patient before each injection, the duty of the venereologist is clear. Firstly, he should avoid prescribing penicillin unless the indications for it are unequivocal; and this may be an additional reason of increasing practical importance against the policy of "treatment before diagnosis" which was debated in a recent issue of
Secondly, he should keep a look-out for minor signs of hypersensitivity by carefully questioning the patient before each injection. Finally, he should have immediately on hand the therapeutic measures to combat the emergency without delay. These include adrenaline, nikethamide, oxygen, and the anti-histamine drugs. The last are probably the most effective and must in such emergency be given parenterally. Cortisone or ACTH may be valuable in controlling tissue reaction and especially in preventing continuing antibody-formation from further absorption of a repository penicillin which may otherwise lead to a recurrence of acute anaphylactic symptoms after initial recovery (Kern and Wimberley, 1953). Where it was imperative to resume antibiotic treatment in the presence of hypersensitivity, cortisone and ACTH were found to suppress the reactions (Houghton, 1954).

REFERENCES