The authors did not discuss the reason why gonococcal dermatitis was more common in women than in men. It may be because gonococcaemia is apt to follow damage to the genitourinary tract after abortion, childbirth, or surgical procedures such as dilatation and curettage. But probably other factors are involved, and efforts should be made to elucidate them so that septicaemia can be prevented.

Taken together the published reports show this complication of gonorrhoea to follow in about 2% of cases. If this figure is applied to cases of gonorrhoea at present reporting at the clinics in the United Kingdom, at least 900 cases of septic dermatitis may be occurring per year. As with the Swedish experience, cases may be labelled as "benign bacteriaemia," "allergic rash," "virus intection," or "benign rheumatic fever." Few patients will present initially to the venereologist, but will be seen by general practitioners or in hospital by physicians, dermatologists, or orthopaedic surgeons. In most cases penicillin or some other antibiotic will probably be given as empirical treatment without the correct diagnosis being reached. It is therefore appropriate that the attention of all doctors in general and specialist practice should be drawn to this metastatic complication of gonorrhoea.

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Glibenclamide for Diabetes

The hypoglycaemic properties of the sulphonamide *p*-amino-benzene-sulfamido-isopropyl-thiodiazole were first reported in 1944 by A. Loubatières[1] after the unexplained death of three patients suffering from typhoid fever who were treated with the drug. Other patients treated with it had convulsions, and still others had a fall in blood sugar. Typhoid fever had been considered to predispose to hypoglycaemia, but Loubatières showed that the drug was hypoglycaemic in the normal, fasting dog.

In 1954 the sulphonamide derivative 1-butyl-3-sulphonyl-urea (carbutamide) was under clinical test for antibacterial activity and found to cause neurological disturbances. During a study of these side effects the drug was observed to cause hypoglycaemia.[2] Carbutamide became the first of a number of sulphonylurea derivatives to be used in the treatment of diabetes. Though no longer used in Britain, its successors tolbutamide, chlorpropamide, tolazamide, and acetohexamide have been and are widely prescribed and have largely replaced insulin in the treatment of those maturity-onset diabetics not controlled by dietary restriction alone. A relative newcomer to this class of drugs is glibenclamide.[3 4]

A striking feature of glibenclamide is its potency. Most of the direct comparisons have been made with tolbutamide, and the relative potency of the two drugs varies somewhat, depending on the method of testing. The difference can best be seen in the maximum daily dose usual in treating diabetics, which is 20 mg for glibenclamide and 3 g for tolbutamide. Given by mouth to healthy volunteers, about 45% of the drug was absorbed. The maximum concentration in the blood was 2-4 hours after administration, and the biological half-life was five hours.[5] Virtually all the drug was metabolized to two predominant, hydroxylated derivatives, which were excreted via urine and bile. The metabolic effects of glibenclamide resemble those of the other sulphonylureas. Both in vivo and in vitro the release of insulin from the pancreatic beta cells is increased, and a fall in blood glucose depends on the presence of some functioning pancreatic tissue.[6] Glibenclamide differs from tolbutamide in its qualitative as well as quantitative effects on insulin release, but these differences may be due to distribution rather than mode of action of the drugs.[7]

In clinical use a single daily dose of glibenclamide is sufficient, and there is usually no advantage in increasing the frequency of administration. As 2·5 mg (half a tablet) has caused hypoglycaemia in some patients[8] caution is necessary in instituting therapy with glibenclamide. The range of dosage is from 2·5 to 20 mg/day, with most patients requiring 5-10 mg. Untoward effects reported so far have been mainly attacks of hypoglycaemia, attributable to potency rather than toxicity. Because of this potent hypoglycaemic effect it has been suggested that the drug should be used only in patients who have failed to respond to treatment with diet and one of the other sulphonylureas,[9] and this advice appears to be wise. In relation to hypoglycaemia it should also be remembered that, like the other sulphonylureas, the effects of glibenclamide are probably potentiated by certain other drugs, including sulphaphenazole, phenylbutazone, and dicoumarol. For those patients under treatment with chlorpropamide who experience facial flushing, headache, and palpitations after even small quantities of alcohol glibenclamide comes as a potential relief, for not only is intolerance to alcohol rare among patients on glibenclamide but cases have been reported of the intolerance disappearing on changing to that drug from chlorpropamide.[10 11]

Glibenclamide thus appears to be a useful addition to the range of oral hypoglycaemic sulphonylureas, but because of its potency (and its expense) it is probably best used as a second or third line of attack in patients whose blood-glucose control is inadequate with other therapy.

No discussion of the use of oral hypoglycaemic drugs is now complete without reference to the study of the American University Group Diabetes Programme, now published[12] and the subject of previous comment in these columns.[13] On the results of the long-term use of tolbutamide reported in this study the U.S. Food and Drug Administration issued a warning about oral hypoglycaemic drugs and recommended much more stringent limitations on their use than were applied previously. Opinion in Britain has not gone all the way with this condemnation. But it may be accepted that the long-term effects of all forms of treatment—dietary, oral drugs, and insulin—in diabetes of maturity onset require further evaluation.

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