1952, in an unpublished lecture, I described how I obtained a 26% increase in the positive isolations of *Sh. sonnei* from post-acute cases by using this medium to supplement Leifson's deoxycholate citrate agar medium. Since then Armstrong (1954) has published results demonstrating similar advantages (21–31%) in the use of the selenite medium. Cultural improvements of this order make it probable that, were a fresh comparison to be undertaken, swabs would show little if any advantage over the faeces for the isolation of *Sh. sonnei* even if the swabs were correctly taken and cultured without delay.

Conclusion

Faeces and not rectal swabs should be the specimens of choice in the diagnosis of diarrhoea. For this purpose swabs are not adequate. The swab has a place in the investigation of outbreaks of known bacillary dysentery in institutions with laboratory facilities on the spot, but should be regarded as a preliminary to be followed, if possible, by a fuller examination of the faeces.

When considering arguments of convenience it should be remembered that the onus of collecting faeces can be placed on the patient's family, whereas rectal swabbing requires the time and skill of a qualified person.

My thanks are due to Colonel H. J. Bensted for his help during the preparation of this paper.

REFERENCES

- Anderson, D. E. W., and Cruickshank, R. (1941). *British Medical Journal*, 2, 497.
 Armstrong, E. C. (1954). *Monthly Bull. Minist. Hlth, London*, 13, 70.
 Brodie, J. (1942). *J. Path. Bact.*, 54, 499.
 — (1953). *British Medical Journal*, 2, 1095.
 Cruickshank, R., and Swyer, B. (1940). *Lancet*, 2, 803.
 Fairley, N. H., and Boyd, J. S. K. (1943). *Trans. roy. Soc. trop. Med. Hyg.*, 36, 253.
 Ferris, A. A., and Fortune, C. (1944). *Med. J. Aust.*, 2, 430.
 Fortune, C., and Ferris, A. A. (1945). *Ibid.*, 1, 337.
 Hardy, A. V., Watt, J., and De Capito, T. M. (1942). *Publ. Hlth Rep., Wash.*, 57, 521.
 Hobbs, E. C., and Allison, V. D. (1945). *Monthly Bull. Minist. Hlth, Lond.*, 4, 12, 40, and 63.
 Humphreys, R. M. (1944). *Lancet*, 2, 548.
 Hynes, M. (1953). *British Medical Journal*, 2, 876.
 Irons, J. V., et al. (1939). *J. Lab. clin. Med.*, 25, 81.
 Jamieson, W. M., Brodie, J., and Stiven, D. (1944). *British Medical Journal*, 1, 322.
 Kroger, E. (1951). *Arch. Hyg., Berl.*, 135, 215.
 Leifson, E. (1935). *J. Path. Bact.*, 40, 581.
 — (1936). *Amer. J. Hyg.*, 24, 423.
 Moffett, M., Young, J. L., and Stuart, R. D. (1948). *British Medical Journal*, 2, 421.
 Parker, M. T. (1953). *Ibid.*, 2, 823.
 Shaughnessy, H. J., Frierwer, F., and Snyder, A. (1948). *Amer. J. publ. Hlth*, 38, 670.
 Wright, J., and Roden, A. T. (1953). *Amer. J. Hyg.*, 58, 133.
 Yannet, H., Deutsch, J. V., and Lieberman, R. (1944). *Yale J. Biol. Med.*, 16, 443.
 —, Leibovitz, A., and Deutsch, J. V. (1942). *J. Amer. med. Ass.*, 120, 184.

The World Health Organization has published a booklet giving interpretations and instructions for coding causes of death, supplementary to those contained in the *International Statistical Classification of Diseases, Injuries, and Causes of Death*, 1948. This booklet is Addendum 1 (H.M.S.O., 1s.). Its aim is to interpret and clarify rather than to amend the classification, and in so doing to keep to what is believed to have been the original intention of the classification, avoiding changes in meaning or assignment except where they were necessitated by inconsistencies between notes or instructions or between the tabular list and the index. The booklet contains: (1) Lists of amendments to the tabular list and the index in relation to specific code numbers. (2) Supplementary rules for selection of causes of death where the certificate is not clear about which of several stated causes is the underlying cause. (3) Amendments to the intermediate and abbreviated lists. (4) Corrections of typographical errors in Volume 1 of the classification. The 1948 classification is to undergo next year a restricted revision containing these amendments, but it is not intended that the revised classification should come into use before 1958, and it is unlikely to be published for some time.

SEVERE LOCAL AND GENERAL REACTION TO INSULIN ZINC SUSPENSION AND SOLUBLE INSULIN

BY

C. N. ARMSTRONG, M.D., F.R.C.P., D.P.H.

AND

W. H. LLOYD, M.B., M.R.C.P.Ed.

From the Royal Victoria Infirmary, Newcastle-upon-Tyne

A man aged 47 suffering from diabetes mellitus with ketonuria was admitted to hospital on March 31, 1954, for stabilization. He had never before been treated for this condition and there was no significant past or family history. Physical examination revealed only moderate obesity, although he had lost 17 lb. (7.7 kg.) in weight in the preceding four months. Treatment was started on January 31, 1954, with insulin zinc suspension and a diet containing 140 g. of carbohydrate. On February 5 a change to soluble insulin was made as his glycosuria and ketonuria persisted. By February 10 he was satisfactorily controlled by 30 units of soluble insulin morning and evening. All injections of insulin were given subcutaneously into his right upper arm.

During the morning of February 11 he complained of a tender irritant lump in his right upper arm together with general malaise, nausea, anorexia, and heartburn. He had vomited once during the night and had slept badly. He was not feverish, and examination showed an area, approximately 5 by 3 cm., of reddening of the skin on the outer side of his right upper arm with induration of the subcutaneous tissues. On the 12th a change to insulin zinc suspension, 60 units, was made and a single injection was given into the left upper arm. By the early afternoon a local reaction had developed at the site of injection which was similar in size to that observed in the right upper arm on the preceding day. The next day insulin zinc suspension, 60 units, was injected into the left thigh and was followed later that day by a similar local reaction. On February 14 soluble insulin, 30 units, was injected subcutaneously into the left thigh, morning and evening; local reactions of great severity followed—the entire left thigh became greatly swollen and tender, and bullae, the largest of which measured 4.5 by 2.5 cm., appeared at the site of the injections (see photograph). At the same time the patient experienced an exacerbation in his symptoms of general malaise.

Bullae at site of injections.

Treatment with promethazine hydrochloride, 25 mg. six-hourly, was started, and further injections of soluble insulin were given into the subcutaneous tissues of the anterior abdominal wall. The initial injections were followed by local reactions of little severity, and by February 18 injections of soluble insulin were unattended by any reaction and he again felt well. Treatment with promethazine hydrochloride was discontinued on the 17th, and on the 19th injections of insulin zinc suspension were started again, and have continued to the time of writing without incident.

Comment

General reactions to insulin are not common. Jorpes (1949) quotes Allan and Scherer (1932) as stating that only

1 to 2% of all patients sensitive to insulin exhibit general manifestations. There can be little doubt that this patient's symptoms of general malaise, nausea, anorexia, and heartburn, with irregular vomiting, coinciding in onset and offset with the cutaneous reactions, were part of a general allergic reaction. This case is also interesting for the severity of the local cutaneous reaction (there does not appear to be a record of a local cutaneous reaction with bulla formation following subcutaneous injections of insulin) and the very short period of hypersensitivity.

Gastineau and Leavitt (1946) reported a case of allergy to insulin with a generalized reaction which was improved by treatment with diphenhydramine hydrochloride. In their case the reaction recurred when that drug was discontinued. In our case spontaneous desensitization probably occurred, as promethazine hydrochloride was given for only three days, and there was no recurrence when it was discontinued.

Wilder, in the discussion of the case of Gastineau and Leavitt (1946), draws attention to insensitivity to the anti-diabetic activity of insulin as a form of allergy to insulin. In this case no increase in the dose of insulin was necessary during the period of allergy.

In most of the reported instances of allergic reactions to insulin it has been shown that the reactions are diminished or abolished by the use of insulin recrystallized several times, and it has been suggested that minute traces of secondary protein contaminating the purified insulin are responsible. This was probably the mechanism in our case, as a comparison of the two insulin solutions used has shown that crystalline insulin is the only substance common to both.

REFERENCES

- Allan, F. N., and Scherer, L. R. (1932). *Proc. Mayo Clin.*, 7, 204.
Gastineau, C. F., and Leavitt, M. D. (1946). *Ibid.*, 21, 316.
Jorpes, J. E. (1949). *Arch. Intern. Med.*, 83, 363.

TREATMENT OF ANOGENITAL WARTS WITH PODOPHYLLIN

BY

RONALD SCUTT, M.B., M.R.C.P.Ed.

Surgeon Lieutenant-Commander, R.N.

The treatment of soft warts in the anogenital region with podophyllin was first described by Kaplan (1942), who wrote: "The treatment . . . consists of the application of 25% podophyllin in mineral oil to all the condylomatous masses, care being taken not to make the application too liberal. Within 6 to 8 hours after the application the patient begins to experience pain over the area of application and usually requires codeine sulphate or even morphine for relief. During the next 12 hours there is a marked local reaction, with inflammation and oedema throughout the tissues near the site of application. On the second and third days the condylomata begin to slough off and the pain eases. On the fourth or fifth day the tissues return to normal. . . . A weaker solution requires repeated applications and the pain is almost as severe."

Review of Literature

Eleven years have elapsed since that paper was published, and numerous reports have confirmed the efficacy of the treatment but stressed the frequency of reactions. Culp *et al.* (1944) treated 100 cases in the U.S. Army and 13 developed balanitis or proctitis, three of them severe enough to necessitate a dorsal slit or circumcision. Macgregor (1945) reported 25 cases in which the excess podophyllin was cleaned off with soap and water after six to eight hours,

the area dried, and a dusting powder applied. In his opinion, this greatly reduced the incidence of severe reactions. Lipman Cohen (1946) treated 30 Service cases, all as in-patients. In some there was much swelling and discharge under the foreskin, which could not be retracted. This subsided with baths and 12.5% aqueous sodium sulphate dressings. The scrotum became superficially ulcerated if left for long in contact with the podophyllin. A dorsal slit and later circumcision were required in one case. In a further small series, in which the Macgregor technique was used, Cohen reported that the reactions were rather less, and remarked that "this method . . . is much less painful than Kaplan found originally, but more so than Macgregor stated."

Sullivan and King (1946) followed a similar routine, and reported that "balanitis and phimosis occur in some patients. . . . The frequency of this complication depends on the amount of podophyllin which comes into contact with the glans penis and foreskin, and also probably on individual sensitivity to the drug. The balanitis and phimosis subside in a few days if the preputial sac is irrigated daily with a mixture of equal parts of distilled water and 3% hydrogen peroxide. It is not necessary to perform a dorsal slit or circumcision except in extreme cases." Flagg and Powell (1947) experimented with various strengths of podophyllin, and recommended the use of the 25% suspension for meatal lesions, 10-15% for lesions on the glans or prepuce without phimosis or a redundant foreskin, and 5-10% for lesions under a redundant phimotic prepuce. They reported reactions in 27% of cases (non-meatal) treated with the 25% suspension. Nobis (1948) tried the effect of suspension in 96% alcohol instead of liquid paraffin, in an attempt to localize the applications to the warts and avoid the seeping which is inevitable with the oily base. Ronchese (1949) stressed the importance of ringing the area with soft paraffin, while Willcox (1948) suggested that more harm than good may result from this manoeuvre.

It will be seen from this review that, although the efficacy of podophyllin has been established beyond doubt, local reactions from its use are far from negligible. Cases of severe conjunctivitis have been caused by accidental transfer of the irritant material to the eyes. There is a considerable risk that the patient who attends as an out-patient will forget or be unable to report again six to eight hours later for the removal of the podophyllin. It may perhaps be possible to avoid severe reactions by careful in-patient supervision, such as was reported by Cohen (1946). A stay in hospital, however, of between 4 and 29 days (average 12 days) seems hardly justified in the management of a comparatively minor complaint, and in civilian practice would be quite impracticable.

New Method

It is for these reasons that the development of a safer method of treatment seems imperative. Wurm (1950) described a method in which he used a much weaker preparation, 1.5% podophyllin being dissolved in hexaethylene polyglycol, in order to get better penetration. A modification of this method has been used for the past 18 months on over 100 cases in the skin and venereological out-patient departments attached to the Royal Naval Barracks at Portsmouth.

To start with, 1.5% podophyllin in propylene glycol was used, but it has since been found that a 3% concentration is more effective, and does not cause any inflammatory reaction. The area is first cleaned with 1% cetrimide, and dried. The application is then made with an orange stick and cotton-wool, followed by profuse powdering with talc. The prepuce, if present, is then adjusted to cover the glans penis and the patient warned not to interfere with it. After 24 hours the procedure is repeated, and again on subsequent days. By the second, third, or fourth application the lesions start to melt away, and it is very seldom that more than four or five applications are required. If there is the slightest reaction, the treatment is not carried out until