

Insulin

The insulin era opened dramatically with the isolation of the hormone by F. G. Banting and C. H. Best.¹ The next major event was long in coming and was provided by F. Sanger and his colleagues,² who determined the exact structure of the insulin molecule—the amino-acid composition of the A and B chains and the disulphide linkage between them. This work, together with the rapid advances in protein chemistry, led to the synthesis of insulin, an almost simultaneous achievement in three different countries.³⁻⁵ The next event provided something of a surprise. Previously, the biosynthesis of insulin had been thought to occur by fusion of the two, separately manufactured, A and B chains. The discovery⁶ of “proinsulin” and subsequent studies strongly support the alternative hypothesis that proinsulin is formed as a single polypeptide, from which part is cleaved off to leave the familiar insulin molecule. This proinsulin has since been found both in blood and in urine,⁷ so that it may have both biological and clinical significance.

The latest achievement is the elucidation of the crystalline structure of insulin by Dr. Dorothy Hodgkin and her colleagues at the Laboratory of Molecular Biophysics in Oxford,⁸ an achievement, it seems, not only of x-ray crystallographic skill but of tenacity of purpose. Dr. Hodgkin first worked on the problem in 1934, and in 1966 she described⁹ the difficulties which at that time still obscured the three-dimensional configuration of crystalline insulin—difficulties which now, happily, seem to have been overcome.

The overall effects of insulin are anabolic, promoting the synthesis of protein, fat, and glycogen. It also increases the disposal and oxidation of glucose. A number of theories have been proposed to explain the actions of insulin, with most attempting a unitary hypothesis. However, to understand how the responsive cells recognize the message delivered by the hormone, it is really necessary to know, or at least to have some inkling of, the chemical state and the three-dimensional configuration of the hormone as it is at the cell receptor. One of the puzzles provided by insulin is that, though the kind and degree of biological activity of insulins derived from various species is similar, there are considerable differences in the amino-acids comprising the two chains. Thus it is difficult to determine which part or parts of the insulin molecule are responsible for the biological activity, and it is in this context that the synthesis of insulin—and of insulin analogues—is important, rather than as a possible replacement for insulin extracted from animal pancreas. Studies with hormone analogues have yielded valuable information in other branches of endocrinology and may be expected to do so in the case of insulin. It is also in this

context that Dr. Hodgkin's achievement may be viewed, for it may be that it is the conformation of some part of the insulin molecule rather than a particular amino-acid sequence which confers the unique biological activity. Thus knowledge of the architecture of the insulin molecule will provide a further basis for theoretical and experimental studies upon the problem of its mode of action.

Ammonia in the Eyes

The policeman injured on Dartmoor on 13 August is the latest victim of an assault with ammonia. Increasingly, violent criminals are using ammonia sprays as a quick means of incapacitating those who stand in their way. Alkaline burns of the eye have always been among the most serious of chemical injuries, since the alkali penetrates the tissues readily. The diffuse keratitis that is caused is made worse by contractures beneath the conjunctiva which restrict closure of the lid. Of all the alkalis ammonia is the most penetrating, and the blindness that it causes is all too often permanent.

Last year A. H. Osmond and C. J. Tallents¹ reported one such victim of a bank raid. He nearly died from the glottal oedema that developed some hours later, and one of his eyes was destroyed by the intense kerato-uveitis that followed the attack. Six months later V. N. Highman² reported two further cases (out of seven that had been treated at the Western Ophthalmic Hospital, London) in which an acute congestive glaucoma developed within a few hours of the ammonia injury. In both of these cases the sight was essentially lost, partly through the coincident uveitis and secondary cataracts. Subsequently R. McGuinness³ described a further victim of a jewellery raid, both of whose eyes were left with band-shaped keratopathy, heterochromia, and lens opacities. And three such patients seen at East Grinstead all developed cataracts in addition to gross corneal oedema.⁴

The particular dangers of ammonia sprays should be more widely appreciated. Unlike most other alkaline burns the gross corneal damage is augmented by damage to the lens and uvea, provoking cataract, uveitis, and sometimes an acute congestive glaucoma. The essential treatment is simply to wash the ammonia off the surface of the eye as quickly as possible, and speed is the only thing that counts. The nature of the irrigating fluid and the techniques of irrigating barely matter. Tap-water is nearly always immediately available, and immersion of the face in a basin or bucket is usually the quickest method. The only other point is that the lids should be opened, and blinkings and eye-movements encouraged, in order to help the lavage. Other measures that ought to be adopted are largely prophylactic—educating the public in the need for immediate and urgent lavage and protecting those who are most vulnerable, such as bank clerks and carriers of wage-packets. For the former a transparent shield should be fitted above the counter and behind the grille (as many banks have already introduced); and carriers should be equipped with protective goggles.

¹ Osmond, A. H., and Tallents, C. J., *British Medical Journal*, 1968, **3**, 740.

² Highman, V. N., *British Medical Journal*, 1969, **1**, 359.

³ McGuinness, R., *British Medical Journal*, 1969, **1**, 575.

⁴ Casey, T. A., unpublished.

¹ Banting, F. G., and Best, C. H., *Journal of Laboratory and Clinical Medicine*, 1922, **7**, 251.

² Sanger, F., *Science*, 1959, **129**, 1340.

³ Katsoyannis, P. G., Fukuda, K., Tometsko, A., Suzuki, K., and Tilak, M., *Journal of the American Chemical Society*, 1964, **86**, 930.

⁴ Zahn, H., Bremer, H., and Zabel, R., *Zeitschrift für Naturforschung*, 1965, **20B**, 653.

⁵ Kung Yueh-ting, et al., *Scientia Sinica*, 1965, **14**, 1710.

⁶ Steiner, D. F., *Transactions of the New York Academy of Sciences*, 1967, **30**, 60.

⁷ Rubenstein, A. H., Cho, S., and Steiner, D. F., *Lancet*, 1968, **1**, 353.

⁸ *The Guardian*, 14 August 1969.

⁹ Adam, M. G., Collier, L., Hodgkin, D. C., and Dodson, G. G., *American Journal of Medicine*, 1966, **40**, 667.