The introduction of glibenclamide inaugurated a new era in the oral treatment of diabetes with sulphonylurea compounds. The drug is active already in doses of milligrams, exerting a rapid and long-lasting hypoglycemic effect; it is practically devoid of toxicity and antigenic properties and is well tolerated and suitable for combination therapy with insulin; it therefore takes the first place among presently available oral hypoglycemic agents. Another important property of this preparation is its beta-cytotrophic action, which was demonstrated by LOUBATIÈRES et al. in the experimental animal.

In 1969 in the II Medical Clinic of LFHKU we started the clinical experiment of glibenclamide. This preparation gave good results. In 50 patients a good hypoglycemic effect was found, with no untoward hypoglycemic reactions. An advantage was that combination therapy in some diabetic patients of middle and old age was possible with insulin, where the insulin dose administered up to that time could be reduced.

Key-words: Combined therapy with glibenclamide and insulin, beta-cytotrophic action; Combined therapy with glibenclamide and insulin, regeneration of Langerhans islets.
CASE REPORT

As a demonstration of the beta-cytotrophic action of glibenclamide, we report three cases that have come to our attention.

The first of these, a 70-years-old woman, F. D., case no. 14607/69 had been suffering from diabetes for 4 years.

The patient was transferred to our clinic from the dermatological clinic, where she was treated for a lichen ruber verrucous, in a precomatous state. Since the discovery of her diabetes, she had been treated with insulin, lately the dose amounting to 20 IU and 28 IU of a depot insulin preparation.

On admission to our clinic on October 24, 1969, in the evening the patient was unconscious, the blood glucose level was 680 mg %, acetone was found in the urine. She was treated with infusions and 56 IU of regular insulin daily. The patient did not exhibit a family history of diabetes, the usual personal anamnesis was devoid of any particular sign.

Laboratory findings: blood sedimentation 25/51, 23/36; urine: albumin opalescence, glucose +++; urinary sediment: crystal layer Addis sediment: E. 200,000, L. 600,000; bacteriological examination of the urine: E. coli; blood urea nitrogen: 24.8 mg %; serum bilirubin 0.6 mg %; proteinuria; Weltmann coagulation band: +4; thymol turbidity test: 2.6 U; serum bilirubin 0.6 mg %; blood diastasis: 64 U; normal hemogram. Fundus of the eye: hypertonic retinopathy I; normal perimeter; X-ray examination of the sella: clearly defined, normal dimensions.

The skin eruption of lichen worsened clearly after the passage to regular insulin. This induced us to attempt a combination treatment with glibenclamide and depot insulin, which the patient tolerated better, as concerns the skin eruption. The skin eruption in the course of some days was considerably subdued and also the metabolic situation improved remarkably. The patient was dismissed on 12-13-69. Glibenclamide was further administered in the dose of 5 mg twice daily with 28 IU of depot insulin, afterwards with 24 IU of depot insulin.

In January 1970 (15-1-70) our patient died suddenly during the influenza epidemic, due to a grippal pulmonary inflammation. At the autopsy in our institute of pathological anatomy a clearly atrophic pancreas was found, its weight being 20 g. Since the autopsy was carried out 24 hrs after death, at the histological examination of the pancreas in many

CASISTICA

A dimostrazione dell’azione beta-citotrofica della glibenclamide, riportiamo la descrizione di tre casi clinici di nostra personale osservazione.

Il primo di essi riguarda la paziente F. D., di 70 anni, cartella clinica n. 14607/69, affetta da diabete da 4 anni.

La paziente venne trasferita nel nostro Reparto della clinica dermatologica, ove si trovava in cura per un lichen ruber verrucous, in stato precomatoso. Fin dall’epoca della comparsa del diabete, essa era stata trattata con insulinina (negli ultimi tempi con 20 UI e 28 UI di un preparato di insulina-ritardo).

All’ingresso nella nostra clinica, la sera del 24-10-1969, la paziente era in stato di incoerenza, con glicemia di 680 mg % e acetonuria. Venne praticato trattamento infusivo e la si passò a 56 UI/die di insulina pronta. La paziente non aveva storia familiare di diabete e nell’anamnesi personale non vi erano elementi di particolare rilievo.

I reperti di laboratorio: VES 25/51, 23/36; velocità di albumin urinaria, +++; sedimentazione del sedimento; conta sec. Addis: E. 200,000, L. 600,000; esame batteriologico delle urine: presenza di E. coli; azotemia 24,8 mg %; prove di eucolloidità sierica: Takata negativa, Weltmann +4, McLagan 2 U; bili-rubinemia 0,6 mg %; diastasiemia 16 U; diastasuria 64 U; emogramma normale. Fondo oculare: retinopatia vasopertonica di grado I; campimetria normale; esame RXgrafico della sella turcica: sella nettamente delimitata, di normali dimensioni.

L’eruzione cutanea a tipo lichen subì un evidente peggioramento dopo il passaggio all’insulina pronta. Per tale motivo fummo indotti a tentare un trattamento combinato con glibenclamide ed insulina-deposito che, da questo punto di vista, risultò meglio tollerato dalla paziente. Nel corso di alcuni giorni l’affezione cutanea si attenuò sensibilmente, ed anche la situazione metabolica migliorò notevolmente. La paziente venne dimessa il 15-12-69. La somministrazione di glibenclamide venne continuata, alla dose di 5 mg due volte al giorno, associata all’iniezione di 28 UI (in seguito 24 UI) di un preparato di insulina-deposito.

Nel gennaio 1970 (15-1-70) la nostra paziente morì improvvisamente per polmonite grippale, nel corso dell’epidemia influenzale. All’esame necropsico, eseguito presso l’Istituto di Anatomia Patologica, venne riscontrata la presenza di un pancreas nettamente atrofico, del peso di 20 g. Poiché l’autopsia fu praticata 24 h dopo il decesso, in numerose zone