Fig. 2

In the cortisone treated explants the diaphyseal cartilage is not suggestive of undergoing the hypertrophic changes, characteristic of the preosteogenetic processes. The cells appear small and nonvesicular; the interstitial matrix is abundant, homogeneous and pale staining. In accordance no osteoblasts and no bone material were found in the diaphysis up to the eigth day of cultivation (Fig. 1*B*).

Quite an unexpected result was obtained in the experiments in regard to muscle development. Myoblasts develop in tissue cultures out of the mesenchyme which accompanies sometimes the explanted cartilagineous or procartilagineous anlage[8]. In our experiments in some cultures, cortisone treated as well as controls, a certain amount of undifferentiated mesenchymal tissue was explanted alongside with the cartilagineous rudiments. After 2 to 4 days *in vitro* mononuclear and polynuclear myoblasts appeared in the cultures. The myoblasts formed in separate foci along the cartilage but most frequently they were located around the diaphysis. They appeared first as cylindrical structures but soon they stretched and became spindle-shaped. The formation of the polynucleated myoblasts seems to proceed most often through multiplication of the nuclei not accompanied by division of protoplasm as evidenced by myoblasts in which several nuclei are concentrated in the mid-section of the spindle-shaped cell. On the other hand in some places fusion of several cells occurred indicated by the scattered position of the nuclei in the myoblast.

No differences could be ascertained after the first days of cultivation between the cortisone treated and control cultures in regard to the histogenesis of the muscle cells. But after the 8 h day in the cortisone containing cultures a distinct cross striation, characteristic of skeletal muscle tissues, appeared in some well developed myoblasts (Fig. 2). High power examination revealed that the striation was already double that is to say consisted of the precursors of the 'A' as well as 'Z' disks. Such striation was not found in the controls of similar age.

Comment. Our findings corroborate the results obtained by BUNO & GOYENA[9] on plasma clot cultures as far as the retardation of growth is concerned. In the present experiments, however, different histological changes were observed, in the developing cartilage of the cortisone treated and the control cultures. The typical hypertrophy of the cartilage, preceding the ossification processes, occurred in the control cultures but was retarded or interfered with in the cortisone treated explants. Consequently differentiation of osteoblasts and deposition of bone material was arrested. The results obtained point towards a direct, growth retarding, action of cortisone on developing cartilage and bone. On the other hand the hormone seems to exert a promoting effect on the histotypical differentiation of muscular tissue, since cross striation of the myofibrils appeared in the cortisone treated cultures. This effect of the hormone on embryonic myoblasts could be only partially compared to its known action on differentiated muscles[10].

We wish to thank Mrs. J. KIDRON for some excellent slides and Mr. E. KRISS for microphotograhy.

H. SOBEL and O. FREUND

Department of Zoology, Hebrew University, Jerusalem (Israel), June 12, 1958.

Zusammenfassung

Cortison verzögert das Wachstum von embryonalen Femur-Anlagen und hemmt die hypertrophische Entwicklung des Knorpels *in vitro*, fördert aber die Differenzierung der gestreiften Myoblasten.

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Psychotogenic and Hallucinogenic Properties of Large Doses of Benactyzine

Secondary effects after the administration of Benactyzine have been known in psychiatry for some time[1]. But not even after large doses, were psychoses with hallucinations and impaired consciousness noted[2].

One of us had the opportunity to observe an accidental intoxication with ca. 1400 mg Benactyzine, taking the course of an amental deliriant psychosis with visual hallucinations[3].

As a result of this observation, we tried to evoke an experimental psychosis by means of large doses of Benactyzine, 50–200 mg, in eight volunteers.

In all instances, we investigated the possible effect of Benactyzine on the serotonin metabolism by estimating the 5-hydroxyindolyl acetic acid (5-HIAA) excretion in the urine using the method described by UDENFRIEND *et al.*[4] in specimens of urine collected 24 h before and 24 h after the administration of Benactyzine. In two instances we investigated the 17-ketosteroid excretion using a modification of HENRY and THÉRENET's method[5].

Results. – Seven subjects developed a psychosis lasting 4–12 h. In the forefront there were visual hallucinations, illusions, disturbances of spatial vision, impaired con-

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sciousness, abnormal behaviour with catatonic features, and floccilation. As far as somatic symptoms are concerned, hypodynamia, ataxia, apraxia, dysarthria, and mydriasis were in the forefront.

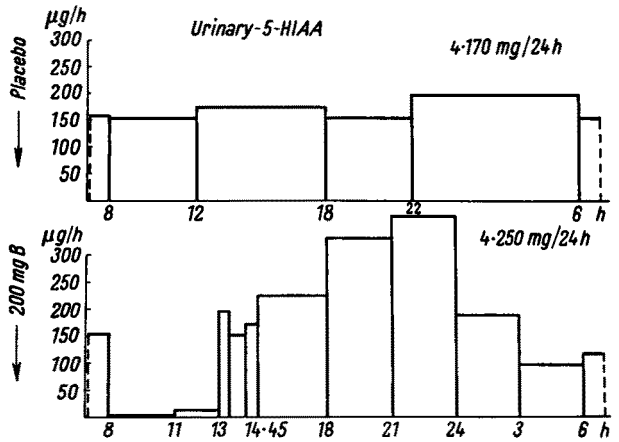

Fig. 1

Changes in the 5-HIAA excretion of one subject are shown in Figure 1. The changes found in the other experimental persons were of similar nature as far as the HIAA excretion and its relation to psychotic changes is concerned. Changes in the 17-ketosteroid excretion are shown in Figure 2.

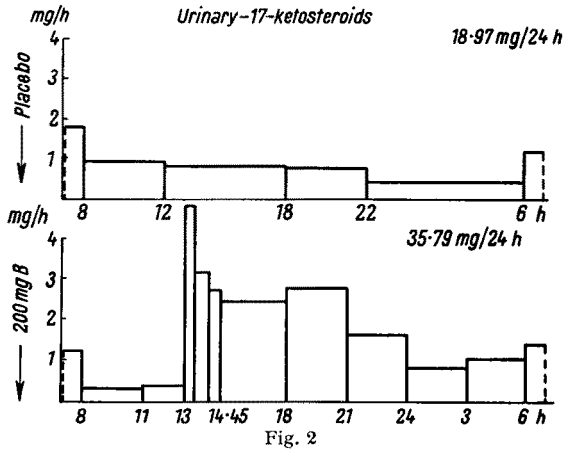

Fig. 2

Discussion.—Doses of 50 mg and 200 mg Benactyzine caused in all instances a symptomatic psychosis of the exogenous type as described by BONHOEFER, with hallucinations, illusions, impaired consciousness, and catatonic features in the behaviour. Motor changes were of a similar type as described in other publications after smaller doses of the drug.

According to the contemporary theory on psychoses[6], the observed psychotogenic effect of Benactyzine may be explained by its interference with the synaptic transmission due to its cholinergic action as well as its interference with serotonin metabolism. Evidence of an impaired serotonin metabolism is provided by the lowered 5-HIAA excretion in the urine and the marked agreement of these changes with the psychotic symptoms. So far it remains hypothetical whether the decarboxylation of 5-hydroxytryptophan is impaired or whether the oxidative deamination of serotonin is blocked. These considerations require further experimental evidence. The total excretion of 5-HIAA in 24 h was, however, not substantially affected. Factors of diuresis do not play any role under our conditions. Our results do not agree with those observed by BERGER *et al.* in animals[7].

The decrease of 17-ketosteroids in the two cases investigated also runs parallel with the maximum of psychotic changes. It can probably be explained by the potent anticholinergic action of Benactyzine. The subsequently increased excretion of 17-ketosteroids is probably due to stress, commonly found also in other experimental psychoses[8].

M. VOJTĚCHOVSKÝ,
and V. VÍTEK, K. RYŠÁNEK, H. BULTASOVÁ

Institute for Human Nutrition Prague (Laboratory for Higher Nervous Activity) and Department for Experimental Therapy of the Chair of Internal Medicine, Institute of Postgraduate Medical Training, Prague, June 5, 1958.

Zusammenfassung

Benactyzin in Dosen 50–200 mg löste bei 7 Versuchspersonen experimentelle Psychose mit gleichzeitiger Herabsetzung von 5-Hydroxyindolylessigsäure im Harn aus. Die psychotogene Wirkung wird mit dem Eingriff in den Serotonin- und Acetylcholinmetabolismus erklärt.

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PRO LABORATORIO

Acceleration of Drying of Biological Material from the Frozen State by the Use of High Frequency Dielectric Heating

In vacuum drying from the frozen state, of either histological specimens or large volumes of biological materials such as plasma proteins, it is necessary to supply the thermal energy needed for the sublimation of ice. Otherwise, the continued removal of heat (more than 600 calories/g of water) lowers the temperature of the material to a point where the vapor pressure of the ice is so low that drying proceeds at an extremely slow rate, possibly lengthening the drying time from a few hours to over a day. Systems of supplying energy that are dependent on the conduction of heat through the material or on the contact of electrodes have the disadvantage of possible local overheating and rapid drying near the origin of the energy, creating a layer of dried material that acts as an insulating barrier which prevents the further penetration of energy. Some of these problems can be overcome by supplying the necessary energy in the form of infra-red radiation[1] which will penetrate the walls of the container without heating them unduly and yet heat the sample, but energy supplied in this way may still heat the already dried material sufficiently to damage it. In theory, an ideal method of supplying energy would be the use of ultra high fre-

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