coid level in rats of series B. Therefore the fasciculata of their adrenals might respond to stress in a less intensive way than those of series A, where, on the contrary, a lower initial glucocorticoid level could be supposed. The lipid depletion of glomerulosa took place only in the case of intensive stress reaction of fasciculata. Deducing from SELYE's[6] conception of reciprocal function of gluco- and mineralocorticoids, we may suppose the reaction of glomerulosa in series A to compensate the overshooting stress reaction of the fasciculata. The stimulus to the mineralocorticoid secretion probably came from the tissue changes, especially from the changes in their physical chemical state, caused by glucocorticoids. Our view is supported by an observation of a marked swelling of spleen lymphoid tissue after the hydrocortisone injection in adrenalectomized rats[7], which was far more developed than the lymphoid tissue swelling in series B. This would be expected because the supposed abolishing action of mineralocorticoids did not entirely take place in adrenalectomized ones.

The factors determining the neurohumoral state of both series of rats could not be defined more precisely. We consider the influence of the diurnal cycle itself to be almost improbable. Beside it, both the season and the temperature of the surroundings must exercise some influence.

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Zusammenfassung

Zwei Serien Ratten wurden durch Formalininjektion belastet. Die Zona glomerulosa der Nebennierenrinde reagierte durch Lipoidausscheidung nur in jener Serie, die durch hohe Lymphozytenzahl des Blutes, hohen Lipoidgehalt der Fasciculata, kleinere Aktivität der Lymphknötchen der Milz und auffallend intensive Stressreaktion der Fasciculata charakterisiert war. Bei Ratten, deren Glomerulosa ihre Lipoide ausgeschieden hatte, trat weder Schwellung noch Desintegration des lymphatischen Gewebes der Milz auf.

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The Action of Cortisone on the Embryonic Cartilage and Muscle *in vitro*

Cortisone exerts an inhibitory action on the growth of rats[1] and produces marked abnormalities in the newly formed cartilage and bone[2]. These effects of the hormone could be derived from its known suppressing action on the development of all the elements of mammalian connective tissues[3]. Inhibition of growth by cortisone has also been shown in the chick embryo[4] and its anti-inflammatory effect on chorio-allantoic grafts[5]. The question has, therefore, been raised whether such effects could be attributed to a direct action of the hormone on bone growth or else are intermediate through some other endocrines or the general metabolism.

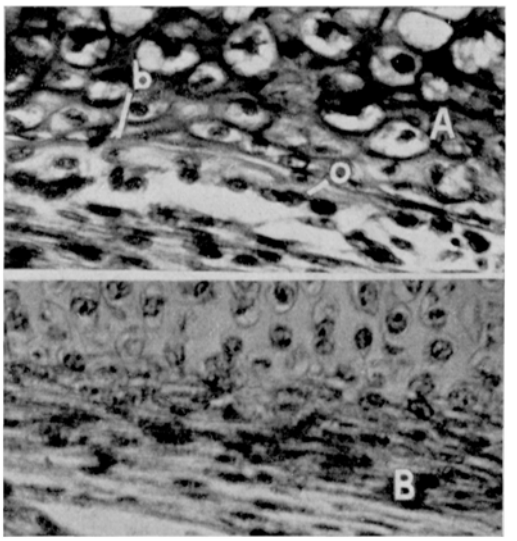

Fig. 1.—Longitudinal sections through femora of 6-day chick embryos, cultivated for 8 days: *A* – on horse serum-ascitic fluid medium and *B* – on a similar medium with cortisone added. H.-E. × 900, *o* = osteoblasts; *b* = bone material.

In the experiments reported here, the effect of cortisone on femora from 6-day chick embryos cultivated by the liquid medium-cellulose membrane procedure on a heterologous medium[6] were studied.

Cortisone* in the amount of 0·02 mg/ml was added to the liquid culture medium. Thus the action of the hormone was direct upon the cartilageneous rudiment of the femur, precluding interjacent factors. In total 32 cultures were grown, 16 on media containing cortisone throughout the whole period of experimentation and 16 without the hormone, as controls. Both femora of one embryo were cultivated in the different media, thus possible individual differences were excluded.

Results. The effects of cortisone were manifested in the retardation of growth of the whole rudiment, and in the bending of the explants which occurred more often in the treated cultures than in the controls. Histologically the untreated explants showed the typical developmental changes of the embryonic cartilage *in vitro* most exactingly described by Fell[7]. After the 8th day of cultivation the diaphyseal cartilage showed a marked hypertrophy (Fig. 1 A), characteristic of the stage preceding the penetration of the cartilage by the connective tissue of the periosteum *in vivo*. The cells were swollen into vesicles and the interstitial substance between them became thin and calcified. On the surface of the diaphysis a continuous layer of cells appeared suggesting a row of osteoblasts associated with the formation of osseous tissue (Fig. 1 A, *o*). A thin but distinct band of bone material was formed around the diaphysis (Fig. 1 A, *b*).

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[5] H. SOBEL, Bull. Res. Counc. Israel *4*, 249 (1954).

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* Cortisone-acetate in dry powder form was kindly supplied by CIBA AG., Basel.

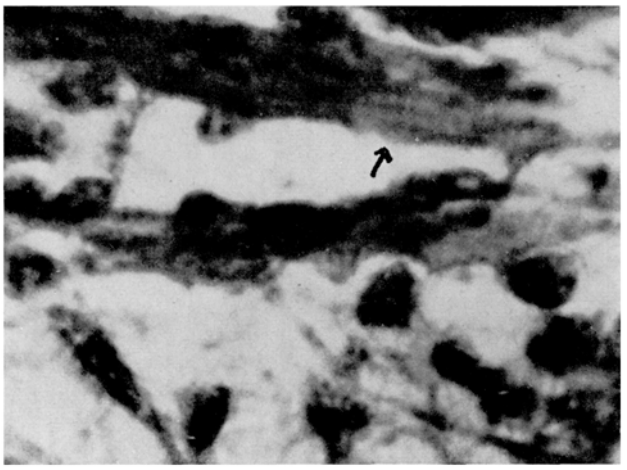

Fig. 2

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].

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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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