tion was incubated for half an hour with catalytic amounts of catalase ($7 \times 10^{-10} M$) before mixing with the enzyme solution, no inhibition of the rabbit muscle dehydrogenase was observed. These results, which are in close agreement with those obtained when the inhibiting effect of irradiated protein solutions was studied, are clearly consistent with the proposed peroxide mechanism. The transient inhibition of catalase is also compatible with this mechanism, as a transient formation of inactive catalase-peroxide complexes is observed when catalase is added to an excess of perodixes (*7*).

It appears that, irrespective of the underlying mechanism, the present finding that tobacco smoke inhibits various enzymes, and that inhalation apparently removes or destroys the inhibitor, may be of biological interest (*8*).

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Response of Condylar Growth Cartilage to Induced Stresses

Abstract. The endochondral growth apparatus of the mandibular condyles, in contrast to epiphyseal plates of long bones, reacts positively to mechanical stimulation. Roentgenographic and histologic analyses of the joint structures of two experimental rhesus monkeys, when compared with untreated controls, showed obvious morphologic and structural transformations of the condylar heads as the result of the instituted treatment. Corollary differences were found in the ontogenetic and histogenetic pattern, as well as in the hormonal control, of these condylar growth centers.

Experiments by Strobino *et al.* on calf tibias (*1*) and the clinical experiences of Blount and Zeier (*2*) with unsuccessfully splinted long bones of children indicated that, contrary to Wolff's law and Roux's principle of functional bone transformation, epiphyseal cartilage plates remain highly unresponsive to mechanical stimuli. Fell (*3*) concluded from findings in tissue cultures that the "gross morphology of bone tissue depends much more upon environmental influences than does that of cartilage." On the other hand, we have presented histologic evidence that in an infant with micrognathia (Robin's syndrome) the condylar cartilage responded to functional treatment with a corrective growth spurt (*4*).

In view of reports of self-corrections of this condition (*5*), an experiment in three rhesus monkeys aged 44 to 50 mo was designed to assess condylar response to induced stresses.

Monkey I served as untreated control, and monkeys II and III as the experimental animals. Inclined bite planes were cemented on the upper and lower dental arches so that the mandible upon occlusion was guided into a forward position. The forces applied thus were physiologic but parafunctional. Monkey II was killed after 2½ mo of treatment; monkey III was autopsied after 4½ mo of the experiment.

Both experimental monkeys show obvious changes in the gross morphologic and roentgenographic appearance of the condylar head (Fig. 1). Histologically the structural arrangement of the condylar head, compared with the normal control (Fig. 2), shows increased cartilage proliferation in a backward and upward direction; endochondral ossification is most active in the posterior portion (Fig. 3). Since modeling resorption at the anterior surface lagged behind proliferation at the posterior surface, the condyles assumed a bilobed shape (Fig. 4). These growth processes result in a bend of the condyles toward the fossa as if they were returning to the position before treatment.

Thus, concrete evidence is obtained which shows that the condylar growth center responds to functional therapy. This unique behavior of condylar cartilage is accompanied by some peculiarities in development, histologic structure, endochondral ossification, and its hormonal control, which differ from the pattern of epiphyseal growth centers:

1) All epiphyseal plates of long bones are derivatives of the primordial cartilage skeleton; the condylar cartilage develops independently from it as a so-called secondary cartilage "grafted" upon the mandibular membrane bone (*6*).

2) Epiphyseal plates grow interstitially; condylar cartilage accrues by surface apposition in a peripheral fibrocartilage layer.

3) In contrast to other cartilage bones, no secondary ossification centers are formed in the condyles. Maturation

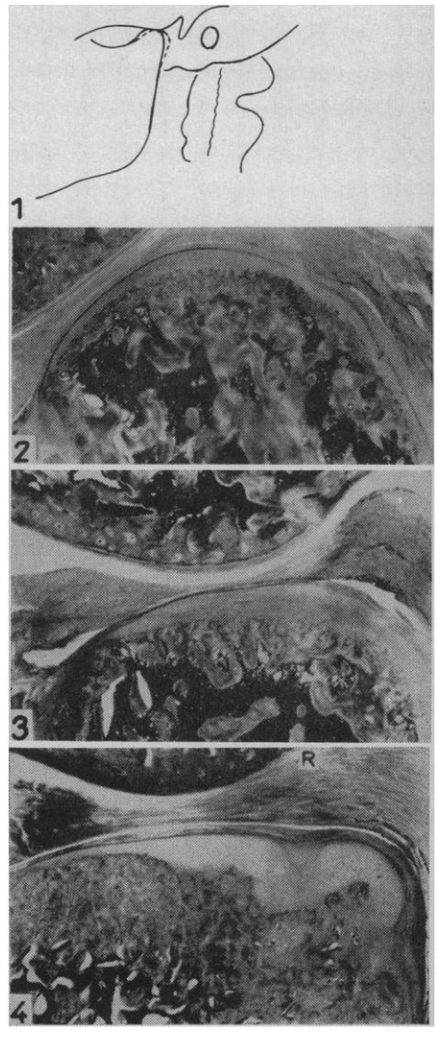

Fig. 1. Superposed tracings of the roentgenocephalograms of the temporomandibular joint structures of experimental monkey III at the beginning of experiment upon insertion of a fixed mandibular protractor appliance, and after 4½ mo of treatment (stippled), reveal that upon treatment the condyle has assumed an oviform shape and is dorsally more prominent with respect to the posterior border of the ramus. The circumferences of the mandibular angle and temporal joint structures are unchanged. Fig. 2. Sagittal section of joint structure of control monkey I. (Alizarin-S vital-staining had unfavourable effect upon histodifferentiation.) Fig. 3. The condyle of experimental monkey II after 2½ mo of treatment shows increased size through cartilage proliferation in a caudal direction. Fig. 4. The condyle of experimental monkey III after 4½ mo of treatment exhibits a prolonged, bilobed shape. *R*, resorbtion.

never occurs; the cartilage persists through life, and it is never completely eroded nor sealed off as are the epiphyseal plates.

4) Endocrine experiments in rats have revealed differences in the hormonal control of growth activity between the epiphyseal plates and the condylar heads. After thyroidectomy, growth hormone elicited a greater response in the condyles than in long bones, while the latter responded better to thyroxin (*7*).

The condylar cartilage holds a unique position among endochondral growth centers.

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23 January 1961

Blood Trehalose and Flight Metabolism in the Blowfly

Abstract. The concentration of trehalose in the blood of *Phormia regina* was found to determine the rate of energy expenditure during flight as reflected in measurements of the wing-beat frequency. Fat body was found to be the source of blood trehalose; either endogenous or exogenous substrates are used for its synthesis.

The function of the nonreducing disaccharide, trehalose, in insect blood has been the subject of a number of studies (*1*). In the adult blowfly, *Phormia regina* (Meig.), it has been found previously that trehalose is the main carbohydrate in the blood (up to 3 g/lit.), that glucose also is present but at much lesser concentrations, that both sugar concentrations are a function of nutrition, and that trehalose concentration falls during flight (*2*). We have since examined this last point in more detail and have sought the source of blood trehalose.

For flight, males were maintained on 1*M* glucose for 4 to 5 days after eclosion and then mounted by a thin support glued to the dorsum of the abdomen. To promote flight, the tarsi were removed (*3*). About 60 percent of such flies flew regularly for long periods; these flies were selected for study. The wing-beat frequency, shown to be a reliable measure of the rate of energy expenditure (*4*), was measured stroboscopically. Blood carbohydrates were assayed chromatographically and colorimetrically as before (*2*).

The wing-beat frequency fell during prolonged flight, as reported by others (*5*, *6*), and blood trehalose fell with it (Fig. 1); blood glucose did not change significantly. The duration of flight to exhaustion was 2 to 3 hr. These results suggested that substrate availability might directly determine the wing-beat frequency, since it has been shown that, after flight to exhaustion, feeding of suitable carbohydrates can bring about almost immediate resumption of flight for long periods (*7*). Accordingly, the effect of trehalose injections on the wing-beat frequency was measured over the physiological range of the frequency.

Flies were flown to complete exhaustion (*7*), and the wing-beat frequency at which they stopped was designated as the "exhausted wing-beat frequency." Each fly was then injected serially with 52, 105, and 210 μg of trehalose dissolved in saline. In all cases 0.524 μl (standard error, $\pm$0.008) was injected through a fine glass needle on a microinjection apparatus. After each injection, the fly was rested for a 3-min equilibration period and then flown. The wing-beat frequency was recorded every 10 sec for the first minute of flight; then these values were averaged and designated as the wing-beat frequency after injection. The flies were again flown to exhaustion after each injection. After the last injection, each fly was fed 2*M* glucose to repletion, rested for 30 min and flown again. The wing-beat frequency thus obtained was designated as the wing-beat frequency after feeding. This value may be considered as the maximum for a given fly.

Table 1 summarizes the results of these experiments. Clearly, the injections of trehalose did increase the wing-beat frequency, and the amount of the increase over the level at exhaustion was directly related to the amount of trehalose injected. The greatest amount (210 μg) restored the wing-beat frequency to the level found after feeding. These results indicate that the wing-beat frequency under these conditions was determined by the concentration of trehalose available to the flight muscles. Glycogen in flight muscle undoubtedly is also an important energy source, and its concentration has been related to the wing-beat frequency in *Drosophila* (*5*).

Table 1. Wing-beat frequency (WBF) as a function of blood trehalose administered by injection. Each exhausted fly was serially injected with the three quantities of trehalose, in the same volume of saline, and re-exhausted between injections. The "fed" value was obtained from the same flies after the last injection by feeding to satiation and resting for 30 min.

Treatment	Mean WBF (cy/min)	%
Exhausted	7,460	67
Injected		
52 μg	8,800	79
105 μg	9,750	88
210 μg	10,950	99
Fed	11,020	100

Phormia regina has been estimated to expend carbohydrate during flight at a rate of about 15 μg/min (*8*). At this rate the total amount of trehalose in the blood (about 200 μg maximum) could support flight for only a few minutes unless it was continually being replaced. The origin of blood trehalose was therefore a question of considerable interest. Fuel for the flight of Diptera comes in large part from glycogen stored in the fat body (*7*,

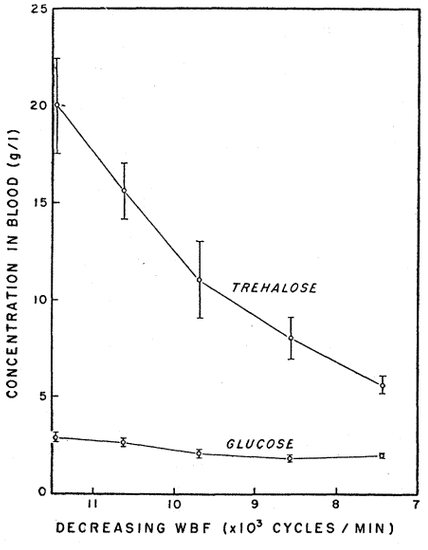

Fig. 1. Relationship between the wing-beat frequency (WBF) and the concentration of blood glucose and trehalose. The data were grouped by averaging observations of wing-beat frequency (at least 10 individual ones per point) made over intervals of 1000 cy/min from 12,000 to 7000 cy/min (which is approximately the exhausted frequency). The standard error of the mean (bars) was calculated for the sugar concentrations.