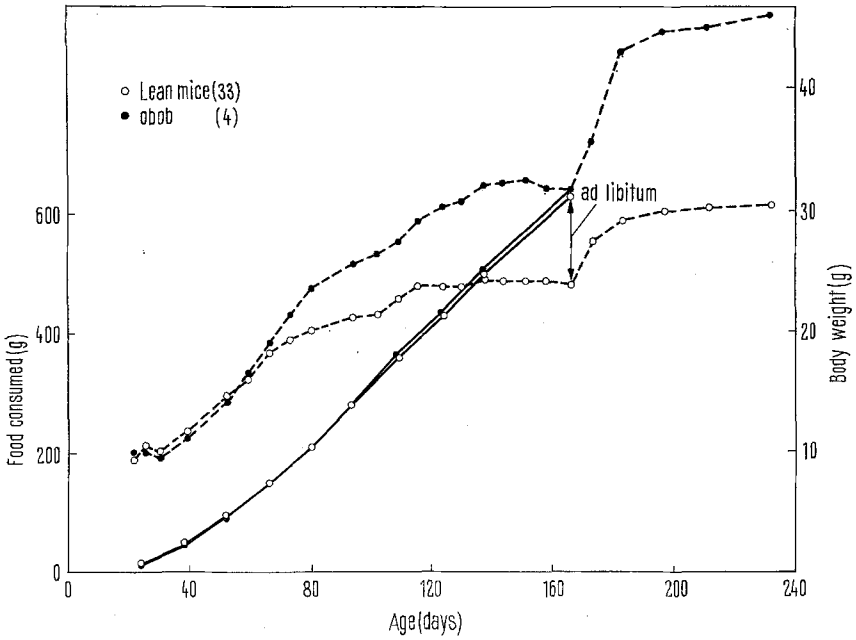

Mean food intake (continuous lines) and body weight (interrupted lines) of growing lean mice and *obob* (for details of experiment see text).

of phenotypically normal mice (*ObOb* or *Obob*) are significantly different even when their food intake is identical. The fact that *obob* can become obese even in the absence of excessive food intake suggests that the hyperphagia of the *obob* cannot account entirely for their obesity. Other contributing factors could be an increase in the useful energy of food captured, a decrease in the energy expenditure, or both.

But if *obob* can become obese by such means and with normal food intake, why are they hyperphagic? An answer to this question is difficult unless one postulates a genetically predetermined level of stored energy or adipose tissue mass, i.e., the Lipostatic theory of obesity[6]. In this context, the hyperphagia of the *obob* is only one means by which the animal may achieve the genetically determined mass of adipose tissue. It is conceivable that the muscle resistance[3,4] and the hyperinsulinism[7,8] of these animals are further means to the same end.

The data of VAN PUTTEN, VAN BEKKUM and QUERIDO[9] and those of HAN[10], showing greater than normal deposition of fat in animals with hypothalamic lesions despite normal food intake, are in keeping with the present findings. Also, LIEBELT[11], working with goldthioglucose-injected rats, concluded that the dispersed fat organs are integrated into 'the adipose tissue mass' and the latter influences the regulation of food intake[11].

Thus, in both the obese hyperglycaemic mice (metabolic obesity) and in animals with hypothalamic lesions (regulatory obesity), hyperphagia might be secondary to an alteration of the homoeostatic level of 'adipose tissue mass'.

Zusammenfassung. Nachweis, dass bei einem Mäusestamm, welcher eine genetisch bedingte Fettsucht aufweist, die Fettsucht auch bei Nahrungseinschränkung auftritt, wenn diese Tiere homozygot sind, dies im Gegensatz zu heterozygoten Tieren. Daraus wird der Schluss gezogen, dass diese Fettsucht nicht primär alimentär, sondern durch einen genetischen, metabolischen Defekt bedingt ist.

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[6] G. C. KENNEDY, Proc. R. Soc. Series B, *140*, 578 (1952).
[7] G. A. WRENSHALL, S. B. ANDRUS and J. MAYER, Endocrinology *56*, 535 (1955).
[8] J. L. CHRISTOPHE and J. MAYER, Nature *184*, 61 (1959).
[9] L. M. VAN PUTTEN, D. W. VAN BEKKUS and A. QUERIDO, Metabolism *4*, 68 (1955).
[10] P. W. HAN, Trans. N.Y. Acad. Sci. *30*, 229 (1967).
[11] R. A. LIEBELT, S. ICHINOE and N. NICHOLSON, Ann. N.Y. Acad. Sci. *131*, 559 (1965).
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Inhibition of Ovarian Compensatory Hypertrophy by Implants of Atropine in the Hypothalamus

The inhibition of ovulation in the rat by systemic injections of atropine[1] as well as hypothalamic local implantation[2] suggest the participation in the control of folliculotrophic release of a midbrain hypothalamic cholinergic system related to the control of different vegetative functions[3].

Knowing that hemicastration in the rat gives rise to ovarian hypertrophy as a result of increased gonadotrophic release, we used this procedure in order to study the inhibitory action of atropine.

The experiments were carried out on albino rats of our strain weighing 150–200 g and having had at least 3

regular 4–5 day estral cycle. The animals were kept on a 14-hour light and 10-hour dark schedule and water and food were available ad libitum.

Atropine sulphate (150–250 μg) was tamped into capillary tubes (O.D. 300 micra-ID 150 micra), the tips of the tubes being sealed with a thin layer of sucrose. The animals were anesthetized with sodium penthobarbital (30 mg/kg) and the tubes were implanted stereotaxically, according to the DE GROOT atlas, in the lateral anterior hypothalamus. The tubes were fastened to the skull surface with dental acrylic. In a control group, tubes containing paraffin were implanted in the same zone.

Daily vaginal smears were taken during the post-operative period.

Hemicastration was accomplished by the lumbar route simultaneously with the implantation of atropine or paraffin. The excized ovaries were used as a control of the weight of the remaining ovary in each animal.

In a group of animals regarded as absolute controls, only hemicastration was carried out.

At the end of the experiment the animals were killed under ether and the remaining ovary, the uterus, adrenals, thyroids and pituitary were carefully dissected and weighed on a torsion balance. Histological sections of both ovaries and uteri were performed. The brains were fixed in 10% formalin and serial sections were made and examined to determine the precise location of the implant.

In the hemicastrated atropine-implant animals there was no change in the remaining ovary (Table). In those animals hemicastrated and implanted with tubes containing paraffin in the same area and with the same evolution in time, compensatory hypertrophy developed (Table).

In the controls, the increase in ovarian weight was greater than in the paraffin-implanted animals, although the difference was not significant. Some other hemicastrated atropine-implanted animals, allowed a longer evolution (28 days) and exhibited the type of ovarian compensatory response seen in the controls.

The vaginal smear showed no difference in length or in number of days of cornification in any of the groups, neither was there a significant change in the weight of the other endocrine organs. In the hemicastrated atropine-implanted animals, the prolonged dioestrus seen in whole animals was not observed.

It is known that the appearance of an ovarian compensatory hypertrophy is permanently inhibited by lesions of various hypothalamic areas. Animals allowed to live longer demonstrated that the atropine-induced inhibition of gonadotrophin release was a transient occurence.

The same dose of atropine found to arrest ovulation, temporarily inhibits the appearance of ovarian hypertrophy in the hemicastrated animals. Since the cholinergic inhibition is different in whole and hemicastrated animals, we assume this to be related to the type and amount of folliculotrophic hormones released[4].

Group	No. of animals	Evolution (days)	Increment of ovary weight mg/100 g body weight	
			Mean	Range
Atropine	10	12–14	0.80	—2.6–3.5
Paraffin	10	12–14	6.55	2.9–11.3
Control	10	12–14	10.37	4.0–23.1

Résumé. Des injections d'atropine dans l'hypothalamus antérieur et latéral de la rate font disparaître l'hypertrophie compensatrice de l'ovaire qui suit l'hémicastration. On conclut que dans ces conditions, l'atropine agit par des voies cholinergiques en relation avec la sécrétion des gonadotrophines.

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[1] J. W. EVERETT, Physiol. Rev. *44*, 373 (1964).
[2] W. L. BENEDETTI, R. LOZDZIEJSKY, M. A. SALA, J. M. MONTI and E. GRIÑÓ, Experientia *25*, 1158 (1969).
[3] T. BAN, Progr. Brain Res. *21*, 1 (1966).
[4] This work was presented in part at the 'Segundas Jornadas Rioplatenses de Endocrinología y Metabolismo', Salta (Argentina), 23–27 September 1969.

Peritoneal Fluid Cytodifferential Changes Associated with the Administration of Cortisone

Cytodifferential changes in the cellular composition of abdominal fluid offers a unique opportunity for studying endocrine influences on the peritoneal cavity[1–7]. We observed that the relative proportion of cells in aspirated cytologic specimens were characteristically altered during the estrous and menstrual cycles[1,2,5,7]. Furthermore, estrogen administration increased polymorphonuclear leukocyte counts and reduced mesothelial cell distributions whereas male hormone had an opposite effect. Since cortisone administration produced no increase in mononuclear cells in peritoneal fluid[7–9] we find it difficult to explain the decrease in blood lymphocytes by a movement of cells from blood into peritoneal fluid following glucocorticoid injection. Possibly, cells originate locally and cortisone inhibits mitosis as well as the release of these cells into body fluids[9]. However, physiologic saline administration markedly changed the normal cellular content of peritoneal fluid[10]. In the present study, we investigated the influence of cortisone in saline administered s.c. on the cellular distribution of peritoneal fluid in adult female mice.

Method. We injected micronized cortisone in 0.5 ml physiologic saline (0.9%) s.c. for 21 days at daily doses of 0.025, 0.1, 0.5, 1.5 or 5.0 mg to adult female mice (CF-1 strain; 20–25 g; 6–38 animals/group). One group of mice received no injections (untreated control) while another group (saline control) was given 0.5 ml physiologic saline daily without steroid. We weighed the animals on day 1 and day 22, immediately before autopsy, we aspirated each animal for abdominal serous fluid and then removed and weighed the adrenals and thymuses. The average weight of these organs was expressed as mg/100 g body weight.

Serous abdominal fluid was aspirated by a 27 guage needle from the animal's ventral surface. We spread the aspirated specimen on an albumin-coated slide, stained