larly of the head, the minimal action being seen with doses of 1 to 2 μg (15 to 30 mμg/kg). (2) Definite arterial hypotension and spinal fluid hypertension have been produced in sensitive individuals with doses ranging between 1/10 and 1/5 of a μg (1,5 to 3 mμg/kg). (3) Intolerance may be shown when 15 to 30 μg (200 to 300mμg/kg) are injected. With such doses the subject will have hot flushes of the face, throbbing headache, palpitations, nausea, intestinal hyperperistalsis, intense polypnea, conjunctival redness, marked fall of the arterial blood pressure lasting between 10 and 20 min and spinal fluid hypertension. (4) Arterial hypertension induced by 3 to 5 μg of synthetic hypertensin or by 10 to 15 μg of norepinephrine is inhibited or reversed by 1 to 2 μg of eledoisin injected 5 sec previously (Figure 1). (5) The stimulation of eledoisin on the respiration is very intense and definitely greater than that elicited by serotonin, bradykinin, norepinephrine and hypertensin when used at equal doses as eledoisin. In some instances very small doses of of eledoisin (100 mμg) do not change the arterial blood pressure and pulse rate; in such cases a definite increase of the respiration rate would indicate the effect of the drug. (6) Hypertensive subjects are particularly prone to the hypotensive effect of eledoisin. A fall of the systolic blood pressure ranging between 80 and 100 mm of Hg and of the diastolic between 30 to 60 mm of Hg may be induced by 1 to 2 μg in these patients. However, with these doses, the blood pressure regains its normal levels within 5 to 10 min. (7) At comparable doses eledoisin is 3 to 5 times more active than histamine and 5 to 10 times more powerful than bradykinin when evaluated for 'threshold' effects on blood and spinal fluid pressure (Figure 2). Compared with these two substances hypotension from eledoisin is much more prolonged, the recovery time being 3 to 4 times longer with equal pressure changes. (8) Eledoisin incubated with human plasma (5 μg/ml) will partially lose its hypotensive effects depending on the time of incubation. In fact 2 h of incubation induce about a 20% decrease, 12 h a 50% decrease; after 24 h of incubation the hypotensive effect will be 70% of the original value. Comparatively synthetic bradykinin incubated with human plasma (20 μg/ml) will reduce its effects more than 50% after 30 min. The hypotensive effect of this drug is practically nil after 2 h of incubation. (9) No tachyphylaxis was found.

Comment. These first experiments of ours performed in man show that the synthetic endecapeptide 'Eledoisin' is the most powerful hypotensive agent ever tried, having effects many times greater than those of Histamine and Bradykinin. Remarkable is the longer hypotensive effect of eledoisin when compared with that of these two substances. The more intense and prolonged effect may be related to the fact that eledoisin is produced by an animal of quite different species to man. This raises the possibility that, when this organic compound is injected, no inactivation by a specific enzyme takes place as is conversely the case for histamine or bradykinin.

The vasodilating action of eledoisin seems to be greater and shows mainly in the upper part of the body, as indicated by the intense vasodilatation of the skin of the face, the conjunctival redness and the spinal fluid hypertension.

Particularly interesting is the intense stimulation of the respiration under eledoisin treatment. In fact, our first observations seem to show that this drug causes hyperpnea most likely with a direct action on the respiratory centre and does not depend solely on arterial hypotension. We may state that, starting with very low doses, hyperpnea appears first and precedes the hypotensive effect.

It is possible that eledoisin will find an important place in the clinical and therapeutical armamentarium once the marked hypotensive, vasodilating and hyperpneic properties have been thoroughly assessed.

Riassunto. Gli autori segnalano le prime osservazioni sugli effetti circolatori e respiratori della eledoisina nell'uomo. L'eledoisina, rappresenta il principio più potente in senso ipotensivo, vasodilatatorio e iperpneizzante.

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Fig. 2. In this Figure the effects of Eledoisin, Histamine and Bradykinin on the cerebral spinal fluid pressure are compared. Top record: Eledoisin 0.25 μg. Middle record: Histamine 5 μg. Bottom record: Bradykinin 80 μg. Each record in the figures inscribes tachographic tracing of the respiration, timer markings 5 sec apart and cerebral spinal fluid pressure which has been electromanometrically measured at high sensitivity and without dumping.

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Influence of Previous Feeding with a High-Fat Diet on Liver Steatosis Produced by Acute Starvation or Growth Hormone in Mice

Acute starvation or a single dose of growth hormone (STH) in mice cause a marked fatty infiltration of the liver, which is a manifestation of enhanced mobilization of depot fat[1]. It is known that a high ratio of dietary fat leads to metabolic adaptation involving preferential fat utilization[2].

In female albino mice (H strain, 25–28 g body weight), fed for 12–22 days with a sufficiently supplemented high-fat diet[3] we investigated the occurrence of liver steatosis after a 25–36 h fast and/or the intravenous administration of STH (0.6 mg/animal). The results are summarized in the Table. Fasting, as well as STH, or a combination of both stimuli, lead to a substantial rise of liver fat in mice previously fed a control diet. On the other hand, in parallel groups fed a high-fat diet, liver steatosis does not develop either after a 24 h fast or in fed animals after STH administration. If 36 h fasting was combined

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Total liver fat[a] (mg/100 g body-weight) in mice previously fed a high-fat and control diet respectively (mean ± S.E.; figures in parantheses indicate the number of animals)

Diet[b]	Fed	Fed STH (3 h)[c]	Fed STH (6 h)[c]	Fasted 24 h	Fasted 24 h STH (30 min)[c]	Fed	Fasted 36 h	Fasted 36 h STH (6 h)[c]
Control	340 ± 29.8 (8)	388 ± 20.7 (9)	433 ± 22.4 (8)	526 ± 56.8 (7)	717 ± 74.0 (8)	268 ± 16.6 (10)	887 ± 54.3 (10)	1229 ± 155.3 (10)
High-fat	282 ± 13.0 (11)	210 ± 22.5 (10)	290 ± 25.9 (10)	297 ± 17.2 (7)	309 ± 20.4 (7)	360 ± 20.9 (8)	452 ± 77.0 (9)	604 ± 106.0 (9)
P	>0.05	<0.05	<0.001	<0.01	<0.001	<0.01	<0.001	<0.01
Duration of experimental feeding		12 days			12 days		22 days	

[a] Estimated gravimetrically after extraction with chloroform-methanol (2:1). [b] Composition[3] (in cal.%): *Control diet:* 20 protein, 60 carbohydrate (starch), 20 fat. *High-fat diet:* 20 protein, 8 carbohydrate, 72 fat (beef tallow). [c] Interval between subsequent STH injection (Somatotropin SPOFA, 0.6 mg/animal) and killing of mice.

with an injection of STH, the resulting fatty infiltration of the liver is considerably less marked in mice fed a high-fat diet than in animals receiving a control diet.

Previous feeding with a high-fat diet thus prevents the development of liver steatosis or substantially reduces the fatty infiltration of the liver caused by acute starvation or STH. It is not probable that this is a consequence of a decrease in the mobilization of depot fat. In an *in vitro* experiment we did not reveal any significant difference in the rate of free fatty acid release from mesenteric fat pads of mice fasting 24 h, regardless of whether they were previously fed a control or a high-fat diet (208 ± 26 and 225 ± 37 μE/100 mg tissue nitrogen/90 min respectively). The absence or a lower degree of liver steatosis induced by fat mobilizing stimuli in animals fed a high-fat diet may thus be considered a consequence of a nutritionally induced metabolic adaptation manifesting itself by an increased ability of the organism to utilize fat, in our case the endogenous fat mobilized from depots.

Zusammenfassung. Bei 12–22 Tage mit einer ausreichend ergänzten Fettdiät gefütterten Mäusen, tritt die durch akuten Hunger oder einmalige Verabfolgung von STH ausgelöste Lebersteatose, wenn überhaupt, nur in abgeschwächter Form auf. Dieser Effekt kann als Folgeerscheinung einer Stoffwechseladaptation an die hohe Fettzufuhr gedeutet werden, die durch eine gesteigerte Verwertungskapazität von exogenem und endogenem Fett in Erscheinung tritt.

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PRO EXPERIMENTIS

Nouvelle méthode de préparation de la préalbumine sérique et principales caractéristiques physico-chimiques

Mise en évidence par SCHULTZE, SCHÖNENBERGER et SCHWICK[1], la préalbumine du sérum a parfois été considérée comme un artéfact dû à certaines conditions d'électrophorèse. Par une nouvelle méthode de préparation, nous avons pu obtenir cette protéine à l'état pur, montrant ainsi qu'il s'agissait d'une entité dont les principales caractéristiques physico-chimiques ont été déterminées.

Le premier temps de la préparation est l'application de la méthode de fractionnement du sérum par le phénol[2]: 200 g de ClNa sont dissous dans un litre de sérum; un volume d'une solution à 5% de phénol est alors ajouté, goutte à goutte avec agitation; un important précipité se produit, que l'on élimine par centrifugation. Le surnageant est dialysé contre eau courante, puis lyophilisé: il contient essentiellement une α_1-globuline (l'orosomucoïde) et, en proportion plus faible, la préalbumine. Dans le deuxième temps, le lyophilisat est repris par du sérum physiologique, un insoluble est éliminé par centrifugation, et le surnageant est ajusté à pH 4,3 et amené à 66% de saturation en sulfate d'ammonium. Le précipité obtenu est dialysé et lyophilisé: il est constitué par la préalbumine et des traces d'orosomucoïde. Une électrophorèse de zone sur colonne d'amidon, à pH 8,6 selon la technique de BOURRILLON et GOT[3] permet de séparer l'α_1-globuline et d'obtenir la préalbumine pure.

L'immunoélectrophorèse et l'électrophorèse en gel d'amidon (Figure 1b) montrent que cette préalbumine est homogène. De plus, l'électrophorèse en gel d'amidon d'un sérum enrichit en préalbumine (Figure 1b) met en évidence l'augmentation de la bande correspondant à la protéine riche en tryptophane, à laquelle cette préalbumine est identifiée.

L'étude électrophorétique en veine liquide, de pH 8,6 (Figure 1c) à pH 4,6, confirme l'homogénéité de cette protéine et permet de tracer la courbe de mobilité en fonction du pH (Figure 2): son point isoélectrique est à pH 4,7 et sa mobilité à pH 8,6: $-7{,}6 \times 10^{-5}\,cm^2\,V^{-1}\,sec^{-1}$.

La courbe de précipitation par le sulfate d'ammonium montre qu'elle précipite entre les concentrations 2,4 *M* et 2,8 *M* à pH 7. La vitesse de sédimentation à dilution in-

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