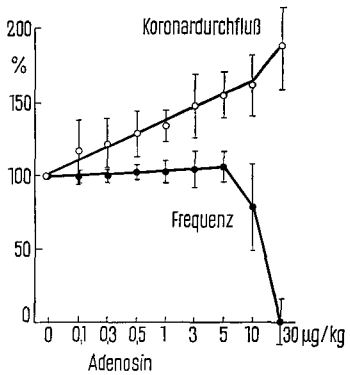
Tieres, von dem das isolierte Herz stammte. Die für die Versuche verwendeten Meerschweinchen wogen 400–500 g. Die zeitlichen Abstände zwischen den einzelnen Adenosingaben betrugen jeweils 4 min. Die Adenosinwirkung auf Frequenz und Koronardurchfluss war bereits nach 2 min wieder abgeklungen.

Die Registrierung des EKG erfolgte mit einem Direktschreiber der Firma Grass, Quincy, Mass., USA. Durch Auszählen der QRS-Komplexe wurde die Herzfrequenz ermittelt.

Von der 15. bis 45. Sekunde nach Adnosingabe wurde die aus dem Herzen austretende Perfusionsflüssigkeit in einem Messzylinder aufgefangen. Aus dem gemessenen Wert wurde das Durchflussvolumen pro Minute errechnet.



Der Einfluss steigender Adenosindosen auf Koronardurchfluss und Herzfrequenz. Koronardurchfluss und Herzfrequenz von Adenosin = 100%.

Ergebnisse und Besprechung. Die Ausgangsfrequenz betrug 188 ± 22 Schläge/min, der Koronardurchfluss vor der Adenosingabe $10{,}4 \pm 1{,}22$ ml/min. Wie die Figur zeigt, erhöhen bereits Adenosingaben von 0,1 µg/kg den Koronardurchfluss um 20%. Bei weiterer Erhöhung der Adenosindosis nimmt der Koronardurchfluss linear zu. Bei 10 µg/kg Körpergewicht Adenosin wird eine Durchströmungszunahme von 160% gemessen. Bei dieser Adenosindosis, die etwa das Hundertfache der gerade wirksamen Dosis beträgt, tritt erstmals eine Abnahme der Herzfrequenz in Erscheinung. Eine weitere Erhöhung der Adenosindosis führt zu einem totalen Herzstillstand, dabei steigt der Koronardurchfluss noch weiter auf 180% an.

Die Versuche zeigen, dass zwischen der Adenosindosis, die die Koronardurchblutung sicher erhöht, und der Dosis, die die Frequenz verlangsamt, eine Sicherheitsbreite liegt, die mit dem Faktor 100 gekennzeichnet ist.

Summary. In the isolated guinea-pig heart, it has been found that the amount of adenosine which slows the heart rate is about 100 times greater than the amount which increases coronary flow.

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The Degree of Lipolysis of Isolated Fat Cells from Rats of Different Ages in Relation to the Triglyceride and Nitrogen Content

The amount of active protoplasm in an organism decreases with age, and conversely the content of inactive matter increases[1]. The fat content increases in the organism with increasing age, both in animals and man. This increased fat content in the organism could be conditioned either by increased lipogenesis or by decreased lipolysis. In previous experiments in rats[2], we found a decreased free fatty acid response in the serum and fatty tissue to lipomobilizing substances, e.g. adrenaline, with increasing age. In old people, decreased lipomobilization was also found after injecting adrenaline[3]. Decreased lipolysis was demonstrated in old rats also on incubating fatty tissue with adrenaline in vitro, in accord with the findings of other authors[2,4,5].

Morphological and biochemical studies of fatty tissue showed that aging affected the character of fatty tissue itself. Thus, for example, it was found that the indices of active protoplasm (nucleic acids, nitrogen, enzyme systems: lipoprotein lipase and hormone-sensitive lipase) decreased with aging, whereas triglyceride values increased[4–6]. However, changes in nitrogen cells and nucleic acid values are not necessarily due to changes in fat cells alone, but also in different cells, for example in mast cells[7]. In order to exclude other possible factors, isolated fat cells were used for the direct study of lipolysis in relation to age.

Fatty tissue from 2- and 14-month-old rats of the Wistar strain was incubated with collagenase (Calbiochem, grade B) and the fat cells obtained[8] were then incubated with 2.5 µg adrenalin/ml at 37 °C. Before and after 60 min incubation, determinations were made of the amount of free fatty acids liberated into the medium[9].

The nitrogen content was estimated in the suspension of isolated fat cells in addition to the estimation of the

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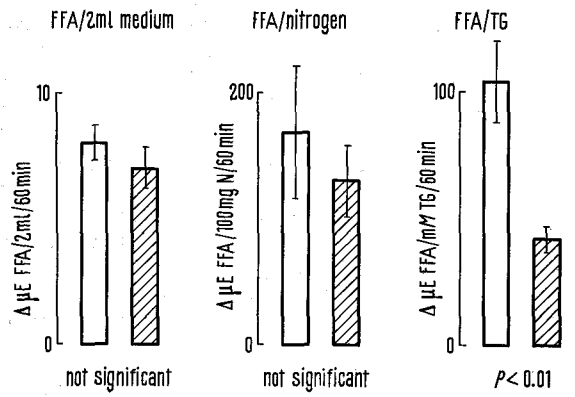
triglyceride[10] content usually carried out to determine the approximate amount of isolated fat cells. The results obtained showed that an approximately equal number of fat cells was obtained from the isolated fatty tissue in older rats (nitrogen in 2-month-old rats 0.237 mgN/ml ± 0.029, in 14-month-old rats 0.266 mgN/ml ± 0.0154; P = not significant) with a higher triglyceride (TG) content (in 2-month-old rats 39 μM/ml ± 4.11, in 14-month-old rats 84 μM/ml ± 3.52; $P < 0.01$). This ratio of nitrogen to triglycerides is in accord with data on the general composition of fatty tissue showing that there was a decrease in nucleic acids and a relative increase in the amount of triglycerides/U weight in older rats (μg P_{NA}/100 mg in 2 month: 8 ± 0.477 month: 5.34 ± 0.578; $P < 0.05$; μM TG/100 mg in 2-month-old rats: 88.3 ± 9.5; in 14-month-old rats: 107 ± 6.22; P = not significant).

The increment of free fatty acids found in the medium was then evaluated both in relation to the volume of the incubation medium and to the nitrogen and triglyceride content (Figure). This showed in the first place that the age difference in the amount of free fatty acids liberated is only significant in relation to triglyceride values. When the amount of liberated free fatty acids was related to nitrogen content or total volume of the medium, it certainly had a falling trend with increasing age, but the differences are not statistically significant.

Yet another experiment was made with the same set-up, using noradrenaline concentrations of 2.5 μg/ml as lipomobilizing substance. Exactly the same relationships were found, i.e. the amount of free fatty acids liberated calculated to the volume of the medium and to nitrogen content is not significantly lower in 14-month-old rats, whereas when calculated to triglyceride content lipolysis was strikingly lower in older rats ($P < 0.001$).

It would seem that the decreased lipolysis of fatty tissue in older rats is caused by alterations in the character of fatty tissue itself. The triglyceride content is increased in the fat cells so that the relative amount of active protoplasm is decreased both in relation to volume and weight; this means a relative decrease in the enzymatic equipment of the cell[6]. This is not a case of absolute decreased response (activity) of hormone-sensitive lipase which is responsible for lipolysis. Aging alters the morphological character of fatty tissue and this is the basis of the altered metabolic activity found in older rats. It is, therefore, necessary, and we consider this to be the main conclusion from our present work, to revise the other findings relating to the metabolism of fatty tissue in rats of different age from this point of view.

In addition, the question remains of what is the immediate cause of the accumulation of triglycerides in fat cells with increasing age. Since the incorporation of acetate and palmitate into triglycerides of fatty tissue is decreased[5], there is no question of an increased synthesis of triglycerides with age. We cannot, of course, exclude a long-continued but not significant decrease in lipolysis in the course of aging being a factor. One piece of evidence for this hypothesis is perhaps the finding that lipolysis of isolated fat cells in relation to the same amount of nitrogen as metabolically active unit is slightly decreased in older rats (even if non-significantly) as compared with young rats.



Free fatty acids (FFA) released by free fat cells in response to epinephrine 2.5 g/ml in relation to the volume of the medium, to the nitrogen content and to the triglyceride (TG) content of isolated fat cells. ■ rats aged 2 months, ▨ 14 months.

Zusammenfassung. Die Freigabe unesterifizierter Fettsäuren in ein Medium aus isolierten Fettgewebezellen älterer Ratten (14 Monate) ist im Vergleich mit jüngeren Ratten (2 Monate) kleiner im Verhältnis zu den Triglyzeriden und nur unbedeutend in der Relation zum Stickstoff oder zum Volumen des Mediums.

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Pressor Response to Angiotensin I During Cardio-Pulmonary Bypass

The lungs must play an important role in the activation of the decapeptide angiotensin I since the administration of a given amount into the right heart gives rise to twice as much musculotropic[1,2] and pressor[3,4] activity as a similar dose introduced into the left heart. Conversion into the octapeptide angiotensin II in whole blood circulating extracorporeally was reported to be of only 14% after 15 sec of contact[1] and is therefore too slow to be physiologically significant. It is of importance to determine whether the lungs are the exclusive site of activation for angiotensin I; such a possibility would force a revision of current concepts[5,6] of the intrarenal role of juxtaglomerular renin by making it impossible for the kidney to generate angiotensin II within its own circulation. This question of the exact contribution of the lung could best be approached by studying angiotensin I activation following total removal of that organ. In 2 dogs, the systemic pressor responses to intra-arterially injected angiotensin I