Tabelle I

Nr.	Kammerwassergewicht 1	Spezifisches Gewicht 2	Proteingehalt 3	Proteingehalt 4	Anorganische Bestandteile in mg% 5
	mg		γ	mg%	mg%
2156	207,6	1,0056	20,5	9,8	950
2158	141,6	1,0060	28,1	19,3	1050
2167	142,5	1,0066	29,0	20,4	1150
2168	121,3	1,0056	22,3	18,4	950
2169	302,9	1,0068	18,1	27,0	1150
2171	110,1	1,0056	19,8	18,0	950
2200	185,4	1,0062	35,1	18,4	1100
2209	239,0	1,0055	21,0	8,8	1000
2210	189,7	1,0065	35,9	18,7	1150
2212	136,8	1,0059	30,1	22,3	1050
2213	267,8	1,0060	24,1	9,0	1050
2214	154,0	1,0060	30,1	20,1	1050
2215	278,3	1,0053	27,1	10,4	950
2218	115,0	1,0060	20,7	17,7	1050
2220	238,4	1,0066	30,9	13,3	1150
2221	216,0	1,0054	21,6	9,8	950
2225	257,2	1,0060	30,8	12,5	1050
2226	280,6	1,0061	26,9	9,8	1050
2145	159,0	1,0051	12,4	7,8	900
2231	219,5	1,0055	19,7	9,1	950
2203	164,7	1,0066	26,2	16,2	1150
2228	160,0	1,0063	19,2	11,7	1100
2216	141,1	1,0063	16,9	12,4	1100
23 Kammerwasser Mittel: 1,0059			24,6 γ	14,9 mg%	1043 mg%
Schwankung: 1,0068–1,0051			35,9–12,4	27,0–7,8	1150–900

gestattet ein Auftrennen nach einzelnen Fraktionen, die in sodaalkalischem 50%igem Methanol eluiert und deren Farbintensitäten im Beckman D.U. auf Wellenlänge 595 mμ bestimmt werden. Der geringe Proteingehalt lässt eine Unterscheidung von α1- und α2-Globulinen nicht zu, die Fehlergrenze der Bestimmung liegt bei $\pm$ 3,2% beim Albumin, bei $\pm$ 5,4% bei den Globulinfraktionen.

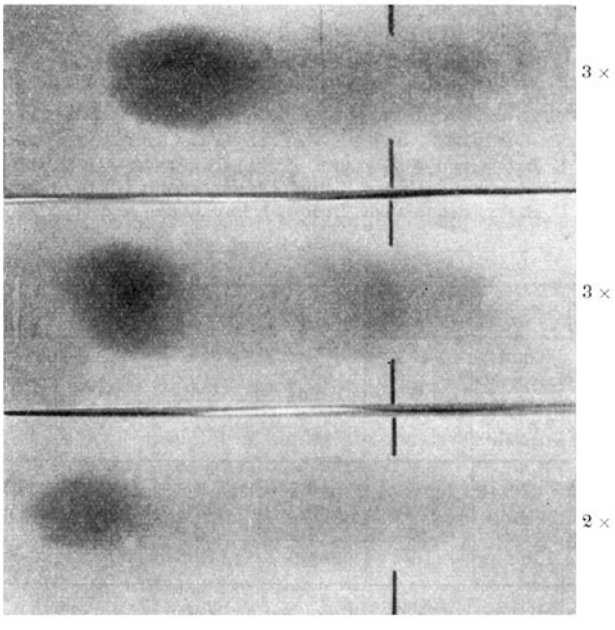

Fig. 2.
Normales Kammerwasser

Tabelle II

	Relative Prozente			
	Albumin	Globuline		
Elektrophoresen von		α	β	γ
2 Kammerwasserpunktaten	63	10	10	17
2 Kammerwasserpunktaten	61	10	12	17
3 Kammerwasserpunktaten	63	10	9	18
3 Kammerwasserpunktaten	66	7	10	17
3 Kammerwasserpunktaten	62	9	11	18
Mittelwerte	62,6	9,2	10,4	17,4
Serum, human, normal[1] . .	59,1	8,8	13,8	18,3
Liquor cerebrospinalis[1] (Lumbalpunktion) . . .	59,6	12,8	19,0	9,8

Gegenüber der Proteinzusammenstellung der von uns früher untersuchten krankheitshalber veränderten Kammerwasser besitzen die normalen durchschnittlich mehr Albumin und weniger α- sowie β-Globuline[2].

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Medizinische Klinik und Augenklinik der Universität Zürich, den 6. April 1954.

Summary

The normal human aequous has a volume of 0·12–0·20 cm^3 and its protein content is from 10 to 20 mg%. We ascertained the specific weight by the falling drop method in a mixture of xylol and brombenzene. In order to estimate the protein content, we placed a series of drops from the human aequous on filter paper with the Agla pipette; they were then tinted with amido-black and the optical density of the eluted spots was read in the Beckman spectrophotometer. The remnants of 2–3 specimens of human aequous were then brought together and concentrated there until the protein concentration is just sufficient to allow a separation into the various fractions by paper-electrophoresis.

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Perfusion Studies Employing α-C^{14} Acetate to Study the Synergistic Effect of Cortisone and Insulin on Lipogenesis

This note reports preliminary observations on the synergistic effect of insulin and cortisone on fatty acid synthesis in the rat liver. A variety of observations on the effect of adrenal cortical hormones[1] and of insulin[2] on lipid metabolism have been reported, however, no information concerning the metabolic interplay of these two hormones has been demonstrated. The unequivocal demonstration that acetate acts as a precursor in the biosynthesis of fatty acids and cholesterol under *in vivo* and *in vitro* conditions[3] makes it possible to study these

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hormonal effects in a quantitative manner. Although liver slices are able to synthesize cholesterol at a fairly rapid rate[1], fatty acid synthesis in this isolated system is considerably slower than in the intact animal, and only small amounts of isotopic material are incorporated under these conditions[2]. To study lipogenesis in a model system (physiological favorable, and yet well controlled), four rat livers[3] from the Wistar strain were perfused for 6 h according to the method of MILLER *et al.*[4] Approximately 200 ml of continually oxygenated heparinized blood which had been diluted with 0·9% saline (1 volume blood, 1/3 volume 0·9% saline), and which had a final red cell hematocrit of 28–33 volume percent was used as the perfusion fluid. In this system a blood flow of about 2 ml per gram wet weight of liver per minute with a pressure head of about 25 cm of blood was maintained throughout the experiment. To this perfusion fluid were added 250 mg sodium α-C^{14}-acetate[5] containing $7{\cdot}3 \times 10^6$ disintegrations per minute and 300 mg glucose, in an effort to keep the glucose level near 300 mg percent. In addition, 40 units of SQUIBB's crystalline zinc insulin (1 ml) and 10 mg of cortisone (Merck) were employed in the experiments indicated in Table I. After the perfusion the livers were lyophilized and the lipids extracted and fractionated by classical methods[6]. Saturated and unsaturated fatty acids from the phospholipid and triglyceride fractions were separated by means of the lead-salt method[7]. Cholesterol was isolated and analyzed as the digitonide. The data summarizing lipid synthesis in four perfusion experiments are presented in Table I.

From Table I, it may be seen that cortisone and insulin, when acting concomitantly, exert a marked effect on fatty acid synthesis while not affecting cholesterol synthesis. The effect is greatest in triglyceride fatty acid synthesis, but also manifests it self in phospholipid fatty acid synthesis. Insulin alone produces a moderate increase in isotope incorporation into fatty acids, thus confirming the reports of other workers using liver slices[1]. The effect of insulin alone differs from the effect of combined cortisone and insulin in a quantitative manner as regards fatty acid synthesis. Furthermore, insulin alone differs quantitatively from the combination cortisone-insulin with respect to glucose utilization, as shown in Table II. It cannot be decided at this time whether the insulin effect observed here and also in liver slices is due to the presence of residual amounts of adrenal cortical hormones in liver and blood rather than an effect referable to insulin *per se*. Since cortisone and insulin when acting simultaneously on this perfusion system affected only the utilization of acetate for fatty acid synthesis, these hormonal regulators might be assumed to influence the utilization of "two-carbon" fragments for fatty acid synthesis in a specific manner without affecting the rate of cholesterol synthesis. It is of interest to note that only in the combined cortisone-insulin experiment is fatty acid synthesis more rapid than cholesterol synthesis. The fact that fatty acid synthesis is more rapid than cholesterol synthesis *in vico*[2] may be referable to the combined hormone action normally existent in the intact animal and strengthens the feeling that the isolated liver, when perfused with blood, approximates this normal behavior when supplemented with insulin and cortisone.

It should be pointed out that the figures in Table I relating C^{14} activity of the lipids to total C^{14} dose added to the perfusion fluid does not represent the total amount of isotope incorporated into lipids since an apprcciable portion of the lipids synthesized are found in the circulating blood. Data regarding the isotope concentration of plasma lipids will be published in full at a later date. It is probable that the addition of extra glucose in these experiments leads to lower specific activities of fatty acids synthesized if one accepts the present view that glucose is converted to fatty acids via the "two-carbon" fragment.

Table II contains data relating the C^{14} activities of residual liver "protein" (after defatting) and carbon dioxide evolved. The findings concerning blood glucose utilization are also shown in this table. The C^{14} is uniformly incorporated into the liver "protein" fraction.

The increase in cholesterol C^{14} activity is two-fold when cortisone alone is added to the perfusing blood. This phenomenon is being examined more closely, par-

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Table I

Hormone additions to perfusing blood		Phospholipid fatty acids: Total fatty acids C^{14} activity*	Phospholipid fatty acids: (% total) (C^{14} dose)	Saturated fatty acids	Unsaturated fatty acids	Triglyceride fatty acids: Total fatty acids C^{14} activity*	Triglyceride fatty acids: (% total) (C^{14} dose)	Saturated fatty acids	Unsaturated fatty acids	Cholesterol: C^{14} activity*	Cholesterol
None	(I)	5·1	(0·1)	6·6	3·6	7·9	(0·1)	9·7	5·5	115	(0·4)
Insulin	(II)	21·5	(0·7)	39·4	8·3	16·9	(0·2)	42·2	8·3	123	(0·4)
Cortisone	(III)	7·0	(0·2)	8·0	3·4	11·3	(0·1)	13·0	6·9	233	(0·7)
Cortisone + Insulin	(IV)	40·0	(1·4)	95·3	36·1	138·5	(1·9)	344·0	118·5	118	(0·4)

* C^{14} activity $\times 10^4$ disintegrations per minute per millimole. In the case of the fatty acids, an average molecular weight of 270 has been assumed. (Mostly palmitic, others range 250–300.) The cholesterol activities are expressed in terms of cholesterol calculated from the digitonide.

Table II

Hormone additions to perfusing blood	$C^{14}O_2$ % of total dose	% of total C^{14} dose per gram residual liver "Protein"	Utilization of glucose* mg
None . . . . . (I)	8·7	1·1	− 79·0
Insulin . . . . . (II)	4·7	0·9	+ 88 − 57
Cortisone . . . . . (III)	3·3	1·0	− 87
Insulin + Cortisone . (IV)	7·0	1·1	+125 −231

* The values given represent the actual cumulated disappearance (shown as —) of glucose from the perfusing blood, corrected for withdrawal of samples during the perfusion. In experiments II and IV an increasing amount of reducing substance was found in the plasma during the first three hours (denoted by +). This increase was followed by a disappearance during the remaining hours of the experiment.

ticularly in the light of recent observations on hypercholesterolemia occuring during cortisone therapy[1].

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Zusammenfassung

Der vorliegende Aufsatz berichtet über Beobachtungen eines synergistischen Effektes von Insulin und Cortison bei der Fettsäuresynthese in der durchströmten Rattenleber.

Dabei wurde Natrium-α^{14}-C-acetat als Tracer verwendet und um Acetat bei der Biosynthese von Cholesterin und Fettsäuren aus dem Zweierbruchstück zu vertreten.

Nach Lyophilisation der Leber, Extraktion und Fraktionierung der Lipide wurde gefunden, dass ins Cholesterin der mit Cortison behandelten Leber mehr radioaktiver Kohlenstoff eingetreten war, bei der Behandlung mit Insulin dagegen mehr in die Fettsäuren und schliesslich in dieselben doppelt soviel als ins Cholesterin bei Behandlung mit Insulin und Cortison zusammen.

Der Anstieg nach Anwendung von Insulin allein dürfte auf Spuren von Nebennierenrindenhormonen zurückzuführen sein, welche noch in Leber und Blut vorhanden waren.

Demnach darf angenommen werden, dass Cortison und Insulin, wenn sie gleichzeitig zur Wirkung kommen, von grossem Einfluss auf die Verwendbarkeit der Zweierbruchstücke sind.

Der Anstieg der Cholesterinsynthese nach Behandlung mit Cortison ist durchaus bedeutungsvoll im Hinblick auf neuere Beobachtungen über Hypercholesterinämien, welche während Cortisontherapie auftreten.

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Factors Involved in Drug-Produced Model Psychoses[1]

The use of fibrous wool protein as a model of the structural surface of receptors, possibly involved in the mechanism producing a model psychosis by drugs, was suggested by three lines of evidence.

First, the strong affinity (sorption) of certain basic compounds to keratins of low sulphur content as shown by the Gram-positiveness of epidermal[2] and nervous[3] tissue.

Second, the accumulating evidence indicating the similarity in behavior between keratins of high sulphur content (e.g. wool) and the protein component of certain cell membranes[1].

Third, some preliminary experiments confirming the role of wool protein as a useful model for simulating some of those receptors for which certain drugs appear to compete[2].

Based on these premises, the affinity for wool[3] of the following four basic compounds was determined at pH 5·2: mescaline hydrochloride, methedrine hydrochloride, lysergic acid monoethylamide (LAE), and lysergic acid diethylamide (LSD), the latter two in form of their methanoltartrates. These drugs when administered to humans in the approximate range of dosage: 500 mg, 100 mg, 1 mg, and 100 γ respectively, cause a model psychosis characterized by hallucinations and related phenomena of similar intensity and duration[4]. The method of determining the affinity for wool used in this study[5] gives only relative values, but these were found to be proportional to the absolute values obtained by another method[6].

The results are presented in the figure. The log. of dosage of each of the four compounds which causes a model psychosis of comparable intensity and duration is plotted against the amount of the compound sorbed by wool.

Affinity, i.e. average millimoles × 10^{-2} of drug sorbed by 1 gm of wool	Single dose of drug	log. of single dose
Mescaline 0	0·5 g	−0·3
Methedrine . . . . 0·6	0·1 g	−1·0
LAE . . . . . 1·1	1 mg	−3·0
LSD . . . . . 2·6	100 γ	−4·0

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