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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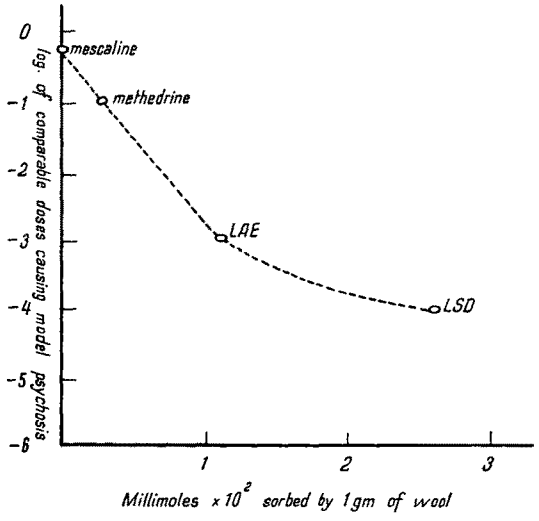
The results indicate that the higher the affinity of a drug for wool, the lower the amount of that drug required to cause a model psychosis.

We are inclined to attribute the increasing affinity of the drugs in question for wool to their different degrees of specificity thus simulating a reversible inhibition of an equilibrium involved in the production of model psychoses.



We included only these four drugs in our Table and Figure because it is not easy to find other drugs which precipitate a reversible model psychosis with hallucinatory experience of comparable duration and intensity after administration of a *single* dose. Atabrine e.g., which is known to produce hallucinations and catatonic excitement, requires prolonged daily administration[1]. Its affinity was found to be 0·9 millimoles $\times 10^{-2}$/g of wool. Another antimalarial of similar structure and action, Pentaquine, displays an affinity of 3·6 millimoles $\times 10^{-2}$/g of wool. If Pentaquine is administered daily at a dosage four times higher than usual (0·12–0·24 g/day), it acts as an adrenergic blocking agent[2]. This feature seems to be, among others, a common characteristic of drugs capable of precipitating a model psychosis.

LIDDELL and WEIL-MALHERBE[3] have shown that methedrine as well as LSD seem to block adrenergic activity by lowering the blood-epinephrine level after short initial increase during the model psychosis; so might LAE since it belongs to the family of ergot alkaloids, which are presumed to inhibit sympathetic vasomotor tone[4]; however, it should be noted that the peripheral adrenolytic effects of LAE and LSD are about 300–2000 times weaker than that of dihydroergotamine[5].

Surgical (sympathectomy)[6] or chemical (Dibenamine)[7] adrenergic blockage, also produce psychotic experiences in certain subjects, possessing high epinephrine and norepinephrine[1] levels[2] to which they apparently are not adapted.

Hence it appears (a) that sympathetic stimulation followed by (peripheral) adrenergic blockage are factors involved in the production of model psychoses and (b) that drugs which exhibit their adrenergic blocking activity in smaller doses than e.g. Dibenamine and simultaneously display a high affinity for (wool) protein, are able to cause model psychosis in very small doses. Further aspects of the problem are to be considered in a more detailed report[3].

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Zusammenfassung

Mezkalin, Methedrine (Pervitin), Lysergsäuremonoäthylamid und Lysergsäurediäthylamid weisen eine steigende Affinität zu Wollprotein auf. – Es scheint, dass zwischen der Dosis, welche von diesen Substanzen benötigt wird, um beim gesunden Menschen nach einmaliger Verabreichung Modellpsychosen ungefähr vergleichbarer Intensität und Dauer hervorzurufen, einerseits und der Affinität derselben Substanzen zu Wollprotein andererseits eine umgekehrte Korrelation besteht.

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The Differentiation of Optic Lobes Neurons in a Blind Cave Teleost

The structure of the most specialised neurons of the optic lobes of Ichthyopsida (except for Cyclostomata and Selachians) and Sauropsida is well known from the work of RAMON, CAJAL, VAN GEUCHTEN, and others. They are mono- or bipolar spindle cells with one (sometimes two) "recurrent" branch emerging from the prolongment of the cell directed to the external surface of the lobe. These recurrent branches, considered as axons, after a narrow curve, run almost parallel to the cell down to the deepest layers of the lobe wall.

This very peculiar orientation of fibres was related by LEGHISSA (1946) to neurobiotactic antagonist effects created during development by the activation of two functional fields, a superficial one of optical nature and a deep one of general sensitivity (spino- and bulbotectal tracts).

It has also been demonstrated by many authors (KRAUSE, DÜRKEN, LARSELL, and others, and, more recently, FILOGAMO (1948), KOLLROS (1947, 1948), PFLUGFELDER (1952) that the enucleation of one or both eyes determines an hypoplasia of one or both optic lobes. This phenomenon has been related, in Amphibians, to