Aus der in der Tabelle II enthaltenen Zusammenstellung lassen sich folgende Ergebnisse ableiten:

1. Von 18 bei der Komplementbindungsreaktion als Kuhmilch-Antikörper positiv erkannten Seren reagierten sämtliche im Hämagglutinationstest eindeutig, und zwar so, dass in einer Reihe von Fällen die Seren bis zu einer Verdünnung von 1:200 mit Kuhmilch reagierten.

2. Von 14 Seren, welche bei der Prüfung mittels der Komplementbindungsreaktion als frei von Antikörpern gegen Kuhmilch gefunden wurden, erwiesen sich 12 auch im Hämagglutinationstest als negativ, während zwei (Nr. 6 und 14) positiv reagierten. Demnach besteht zwischen den beiden Proben nicht eine völlige Parallelität. Auf Grund unseres allerdings nicht sehr reichen Materials scheint jedoch der Hämagglutinationstest die empfindlichere Probe zu sein, da sie auch bei negativer Komplementbindungsreaktion positiv ausfiel.

3. In diesem Sinne spricht auch die Tatsache, dass die drei bei der Komplementbindungsreaktion auf Kuhmilch-Antikörper als fraglich bezeichneten Proben im Hämagglutinationstest deutlich positiv mit einem Titer von 1:20 ausfielen.

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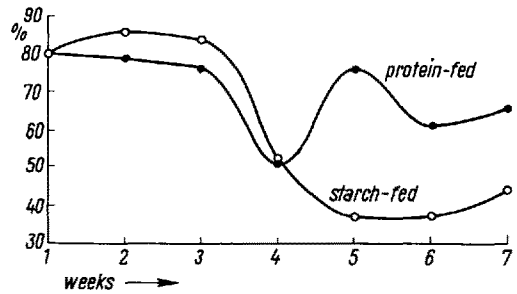
Summary

By means of a *haemo-agglutination test* using erythrocytes sensitised with tannic acid, we were able to demonstrate the presence of cow's milk antibodies in humans. The use of the haemo-agglutination test enables us now to give exact information on the titer value of the antibody in human serum. Previously this was limitately possible using the method of antibody demonstration by means of the complement-compound reaction.

We have well-established reasons to assume that other antibodies caused by various antigens, can be determined by means of the haemo-agglutination test.

The Effect of Diets on the Utilization of the Food by the African Giant Snail, *Achatina fulica* Bowdich

Lately the problem, whether a particular individual can change its digestive enzyme production to a changed diet, or in other words: to what extent an *adaptation* in its enzyme production can occur, has come more and more to the front. In mammals a few observations seem to point into this direction[1,2,3], although such an adaptation apparently needs some time before it is established[4]. In invertebrates the reports are more confusing. A positive correlation was reported in one case[5], but in another one the opposite was found[6]. This problem was investigated again in *Achatina fulica*, the results of which were rather confusing[7]. To get a better idea of whether an adaptation to special diets does occur in this snail, the utilization of the food presented was studied. For this purpose 2 batches of 4 mature snails were isolated and fed daily with boiled potato (starch diet), and with horse meat (protein diet). It was assumed that, if an adaptation did occur, this might show in an increased resorption of carbohydrates by the first group ('starch' snails), an increased resorption of proteins by the second one ('protein' snails). At the end of each week the snails were fed with a known amount of potato or meat. After 24 h the faeces (and eventually not eaten food rests) were collected and processed. Of the fresh meat and potato a control sample was taken at the same time of feeding, weighed and processed. Thus the contents of carbohydrates and protein-N of the food could easily be computed. From these values those of the 'faeces' were subtracted and the amount resorbed was thus known. This amount was expressed as a percentage of the food given.



To determine the carbohydrate contents of the potato and faeces, the samples were hydrolized in 10 ml of 0·1 *N* HCl on a water bath for 24 h, after which the volume was readjusted to the original 10 ml by adding distilled water. This was neutralized with 10 ml of 0·1 *N* NaOH and filtered. 5 ml was pipetted off and the amount of reducing sugar was determined with Schoorl's sugar titration[8] in mg glucose. The protein-N content of sample and faeces of the protein snails was determined with Kjeldahl's method.

The results of the experiments are given in the Figure. From this it is obvious that the starch snails do not show an increase in utilization. Although the curve does show a slight increase during the first 3 weeks, it is questionable from these data alone whether this increase is significant. We must keep in mind that the wet-weight determinations include an error which may easily be of the order of 5 to 10%. A definite drop occurs after 3 weeks and only after 6 weeks a slow rise of the curve appears. This curve therefore does certainly not suggest an adaptation to the diet in the sense that more carbohydrates are resorbed.

The protein utilization curve shows the same dip after 3 weeks (the steady but very slow decrease during the first 3 weeks needs not be significant for the same reason as given above). A definite rise seems to occur after the fourth week, again followed by a decrease (6 weeks) and a second slow rise (7 weeks). The increase from the fourth to fifth week appears large enough to be acceptable. Apparently there is a tendency to utilize more of the meat after a certain period of adaptation, but this 'adaptation', if it is real, is small. In any case there does not seem to exist a clear adaptation of the resorption, when the snails are fed on a special diet of either starch or protein in the

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sense that a definitely increased utilization occurs over that found at the start of the experiment.

One cannot conclude from these results that the same holds true for the digestive enzyme production by the mid-gut gland. This is an entirely different process. We can only say that the *resorption* of digested material is apparently decreased in the snails (particularly in the starch snails). It may be possible that the initial rate of resorption may be reached again, provided a long period (more than 7 weeks) of adaptation is allowed. The slow rise of both curves at the end of the experimental period indicates such a possibility. The low metabolism of these sluggish animals may also support this.

What causes this decrease in utilization of the food, when put on a special diet, must be left undecided for the time being. It is quite possible that certain important substances, present in the natural food (these snails are notorious scavangers and their natural diet therefore consists of many different materials), are missing. This lack may affect the rate of resorption, but nothing definite is known of this in snails. In any case the results of this investigation do not support the hypothesis of a true adaptation (in 7 weeks) by the individual snail to a special diet. On the contrary, if there is a correlation between utilization and diet, this seems to be a negative one.

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Zusammenfassung

Eine spezielle Diät (Stärke oder Fleisch) induziert keine Adaptation in *Achatina fulica* in dem Sinn, dass mehr Kohlehydrate, bzw. Proteine resorbiert werden als mit normalem Futter.

Metabolites of LSD and Ergometrine[1]

Chemical and pharmacological studies of metabolites of lysergic acid derivatives produced in the animal body have been carried out by two main groups[2,3]. AXELROD, BRADY, WITKOP, and EVARTS[2], in particular, have shown that with guinea pig liver homogenates only one metabolite was produced from lysergic acid diethylamide (LSD). This metabolite had no LSD-like action in the central nervous system, gave negative Ehrlich tests and was shown[4] to be 2-oxy LSD by methods including spectrophotometry, paper chromatography, and synthesis. However, STOLL, ROTHLIN, RUTSCHMANN, and SCHALCH[3] with C-14 side chain labelled LSD isolated three radio-active metabolites from rats, two of which fluoresced in ultraviolet light and gave a positive Ehrlich colour reaction. Repetition of the work of STOLL *et al.*[3] in this laboratory substantiated their results. Two metabolites were shown to be present in extracts of bile collected from male rats after an intravenous dose of 3 mg/kg of LSD when run on downward paper chromatograms using butanol:acetic acid:water (4:1:5)[5]. The more polar metabolite (metabolite A, *Rf* 0·10) was produced in much larger quantities than the less polar substance (metabolite B, R_f 0·14) whereas LSD had an R_f value of 0·77.

Similarly, two metabolites were produced from ergometrine, a predominant one with an R_f of 0·07 and a second with an R_f of 0·10 on the same paper chromatographic system. Both metabolites gave a positive Ehrlich reaction and a blue fluorescence in ultra-violet light characteristic of lysergic acid derivatives. On this chromatography system ergometrine has an R_f of 0·6. The mixture of these two metabolites contracted isolated guinea pig uterus in the same manner as ergometrine.

Metabolites A and B produced from LSD have been shown to inhibit 5-hydroxy-tryptamine (5-HT) using the isolated rat uterus preparation. The inhibitory effect of each metabolite was expressed in terms of a dose ratio[6], which ranged from 5 to 7 at a concentration of $2:10^{-8}$ for each metabolite after a period of 10 min contact with the muscle. The small amount of metabolite B available precluded determination of the effect of further increasing the exposure time on the dose ratio. However, this was possible with metabolite A, and after 20 min exposure the dose ratio exceeded 50. The inhibitory action of this metabolite developed slowly after its addition and disappeared slowly after its removal. From preliminary experiments metabolite A has approximately 5% of the inhibitory potency of LSD, though the accuracy of this figure is limited by the purity of the metabolite at present available and by its stability in aqueous solution.

The blue fluorescence exhibited by all these metabolites is characteristic of the lysergic acid nucleus. STOLL *et al.*[3] showed that the side chain of LSD is retained in the metabolite and the positive Ehrlich reaction indicates the presence of an indole nucleus with unsubstituted α-position. Hydrolysis of metabolite A by boiling with N-hydrochloric acid for 1 h gives a compound exhibiting the blue fluorescence and Ehrlich reaction and having an R_f of 0·50 on the butanol:acetic acid:water system. This could indicate the presence of a conjugated hydroxyl group in the metabolite. That the LSD metabolites act as 5HT antagonists precludes the possibility that hydroxylation of the 9:10 double bond has occurred to give a lumialkaloid derivative which would be inactive[7]. From known biological examples position 5 and possibly position 7 of the indole ring are most likely to be hydroxylated. Further evidence of the extreme polarity of metabolite A was indicated by its low R_f value (0·34) on the basic system used by FRETER *et al.*[4] (2:4-lutidine:tert-amyl alcohol:water). On this system 2-oxy LSD had an R_f of 0·85.

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Zusammenfassung

Vorläufige Untersuchungen über die Verwandlung von LSD und Ergometrin bei der Ratte zeigen, dass von beiden Substanzen zwei Hauptprodukte gewonnen werden. Beide Metaboliten von LSD antagonisieren 5-HT am isolierten Rattenuruspräparat; es scheint sich um hydroxilierte und konjugierte Derivate des LSD zu handeln.

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