Δ^1-9α-fluorocortisol and/or the experimental routine thus concerns the phase relations of (microfilarial) rhythm in the three individuals composing the group studied (the studies on the three subjects were carried out at the same time). Another effect of treatment relates to the time relations of the rhythms in microfilariæ and eosinophils, in a given subject. Before treatment, correlation coefficients for microfilarial and eosinophil counts in the three patients were not significant, whereas all three r values were higher after treatment and two of these were statistically significant.

Those factors which determine the various phase relations of certain mammalian 24-hr. rhythms are not necessarily analogous with those physiological mechanisms which maintain a given rhythm[1]. The question whether or not the adrenal cortex is critical for the maintenance of microfilarial periodicity awaits further study, in subjects with verified cortical adrenal insufficiency. Microfilarial periodicity may persist in such cases, as does the 24-hr. rhythm in serum iron from patients suffering from Addison's disease[5,6]. The data shown herein suggest, however, that certain phase relations of microfilarial periodicity may be influenced by exogenous corticoids and may, perhaps, be regulated by endogenous periodic cortical adrenal secretions.

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Sodium Content of Erythrocytes in Hyperthyroidism

Until recently little was known about variations in sodium content of human erythrocytes. Harrison[1] found a significant increase of red-cell sodium in a number of patients with tuberculous meningitis, Love and Burch[2] noticed higher cell sodium values in Negroes than in White donors, Overman[3] found increased sodium concentrations in normal infants up to two years of age, Nichols[4] saw low values during diabetic acidosis, Roegholt[5] sometimes found increased values in patients with congestive heart failure.

Using the direct analysis of diluted erythrocytes of 41 healthy subjects by flame photometry we found normal values between 8·6 and 12·9 m.equiv. sodium per litre cells (11·8 and 17·7 m.equiv. sodium per litre cell water). By means of human albumin labelled with iodine-131 we found the proportion of plasma trapped between the red cells to be 1·7 per cent when the blood was centrifuged for 60 min. at 2,700g.

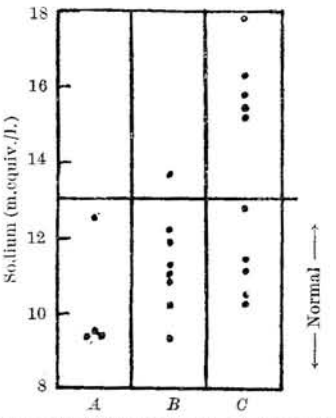

Fig. 1. Sodium content of erythrocytes of subjects with low (*A*), normal (*B*), and high (*C*) thyroid function

In agreement with Keitel *et al.*[6] we found a variation in the composition of erythrocytes from different portions of the centrifuged cells, the middle layer showing a sodium content 1 m.equiv. lower than the top and bottom layers.

We examined the cell sodium of 22 patients whose thyroid function was determined by giving tracer doses of iodine-131 (Fig. 1). In the subjects with low or normal thyroid function the cell sodium with one exception was normal. In 50 per cent of the subjects with high thyroid function a significant increase of cell sodium with a normal amount of cell water was observed. Two cases with high cell sodium were followed up after thyroidectomy; during the next 5 months the cell sodium decreased gradually to normal values.

These results suggest a relationship between the red cell sodium and hyperthyroidism.

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Comparison of Effect of Lysergic Acid Diethylamide with Potassium Cyanide and other Respiratory Inhibitors on the Siamese Fighting Fish

Although it is known that lysergic acid diethylamide enters the brain, the mechanism by which it acts to produce the psychotic patterns in man is unknown. Experiments which are designed to investigate the brain process in the intact animal might lead to a concept that could be developed to study the chemical process originating or connected with clinically occurring schizophrenia.

We have recently been studying the effect of potassium cyanide, sodium azide, hydrazine and lack of oxygen among other respiration inhibitors on an intact animal, the Siamese fighting fish. In addition, the action of oxidation-reduction indicators like methylene blue, Bindschedler's green and other dye systems have been explored. It has previously been

shown that the behaviour of the Siamese fighting fish changes markedly in the presence of small doses of lysergic acid diethylamide in the surrounding water[1,2]. It may now be reported that potassium cyanide and sodium azide act on the Siamese fighting fish in a way which is very similar to that of lysergic acid diethylamide. Hydrazine sulphate in much higher concentration was essentially without effect. However, anoxia and asphyxia can also produce reactions somewhat similar to lysergic acid diethylamide.

The methods used were those previously described by Abramson and Evans[1] for the reaction of the Siamese fighting fish to lysergic acid diethylamide. For the purpose of this study, four of these, or related criteria, were usually chosen for analysis, as described by Abramson, Sklarofsky, Baron and Gettner[2].

With concentrations of potassium cyanide analogous to those used to obtain readily observable effects of lysergic acid diethylamide, that is, 1 μgm. per ml. in the outside liquid, the fish, in general, act as if they were under a slightly lower concentration of lysergic acid diethylamide, rising to the surface and assuming a nose up–tail down position. The Cartesian diver position is often assumed, although some of the motor characteristics of the effect of lysergic acid diethylamide are different. Casual inspection of fish under lysergic acid diethylamide and potassium cyanide might not reveal an important difference in the response. However, certain differences in the response are present, and a trained observer can usually distinguish between the effect of cyanide and the effect of lysergic acid diethylamide, especially by the absence of the kinking of the tail. Apparently, the potassium cyanide is utilized more rapidly than lysergic acid diethylamide by the fish, because if the fish are transferred to fresh water, they recover faster from the former than they do from the latter.

Hydrogen sulphide at high concentrations (100 μgm. per ml.) was lethal, but the surviving fish assumed a nose up–tail down position at the surface. The effect of hydroxylamine hydrochloride up to concentrations of 100 μgm. per ml., as well as hydrazine sulphate to 10 μgm. per ml. has thus far been negative. Most interesting was the effect of azide. Although sodium azide is more toxic than potassium cyanide, an effect analogous to lysergic acid diethylamide is readily observed at concentrations of sodium azide similar to those observed for lysergic acid diethylamide.

Preliminary results indicate that a decreased oxygen supply with simultaneous prevention of accumulation of carbon dioxide resulted in the nose up–tail down position similar to lysergic acid diethylamide in several hours—the fish remaining alive. When carbon dioxide was permitted to accumulate in the absence of renewed oxygen all the fish assumed the nose up–tail down position in several hours. They rose rapidly to the surface when disturbed. Recovery was rapid from both anoxia and asphyxia. Experiments are in progress with improved techniques of observation.

A concentration of methylene blue of 100 μgm. per ml. produced a suggestive lysergic acid diethylamide reaction. Bindschedler's green affected the fish, producing a noticeable excitatory period; 20 μgm. per ml. produced the nose up–tail down position with no kink in the tail. In a comparative experiment 20 μgm. per ml. of Bindschedler's green was more effective than 1 μgm. of potassium cyanide. It is of interest that the effect of methylene blue increased with time. 50 μgm. per ml. of toluene blue and indigo disulphonate were without an important effect. 50 μgm. per ml. of indigo tetrasulphonate was also ineffective. Sodium 2,6-dichlorobenzene indophenol was effective, the effect increasing with the concentration up to 50 μgm. per ml., where an effect equivalent to 1 μgm. per ml. of lysergic acid diethylamide was observed. Although 50 μgm. per ml. of gentian violet and methyl violet killed the fish, lower concentrations, 20 μgm. per ml. of each, produced a nose up–tail down position in more than half the fish at the end of 4 hr.

It has often been observed that human subjects under the influence of comparatively small doses of lysergic acid diethylamide have the confusion and other symptoms that are associated with anoxia. Its effects in man, therefore, are not incompatible with the assumption that lysergic acid diethylamide in the fish and in man acts by poisoning some parts of the enzymatic processes connected with oxidation. Although at the time that this report was written we have not had access to the data dealing with the effects of non-lethal doses of potassium cyanide on the mental state of man, the available data in the literature indicate that an exogenous psychosis with loss of sense of reality is produced with non-lethal doses. Indeed, potassium cyanide has been used in the therapy of schizophrenia, apparently to stimulate the respiratory enzymes. It is worthwhile on the basis of these results to explore the possibility that not only the lysergic acid diethylamide psychosis in man may be connected with poisoning of special oxidative enzymes, but also that the schizophrenic process may be connected with a similar process where special respiratory enzymes of the brain are not functioning adequately.

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Lead-Reactive Substances in Myoneural Synapses

Biochemical investigations[1] have revealed that —SH compounds take an essential role in the transmission of impulses. By precipitating these compounds with lead nitrate we have succeeded in demonstrating the subneural apparatus of motor end-plates in cross-striated muscles.

Entire diaphragms of rats were fixed for 15 min. in 8 per cent formalin containing 5 per cent lead nitrate. Frozen sections of 30–40μ were cut, washed rapidly in distilled water and immersed in a 2 per cent aqueous solution of sodium sulphide. After this treatment the characteristic patterns of the subneural apparatus were visible.

Investigations as to whether other histological structures also contain a lead-reactive substance, and to determine what kind of chemical substances are responsible for this reaction are in progress. Localization of the lead-reaction in myoneural synapsis is