sections of the cortex. No unmistakable sign of inflammation was present in the cortical substance. The arteries and arterioles were normal.

Sections stained with Sudan III revealed heavy fatty infiltration or degeneration of the tubular epithelium (Fig. 2). Lipoids were also seen in the desquamated cells and tubular casts. To a much less degree than in the tubules there was fat staining material in the glomerular tufts. In the case of the animal that died 3 days after the last injection of sodium hydnocarpate numerous minute fat globules were found lying free in the blood vessels. Lipoid degeneration as indicated by the presence of doubly refracting lipoids could not be demonstrated by the polarization method.

In summary it can be said that non-inflammatory, degenerative tubular lesions of the kidney closely similar morphologically to those of nephrosis in man have been produced experimentally through the action of dilute solutions of a soap consisting of the more water soluble sodium salts of the unsaturated fatty acids of hydnocarpus oil. The method is presented as a technique which may be applicable to the study of nephrosis experimentally.

5717

The Effect of Cortin in Asthenia.*

FRANK A. HARTMAN AND GEORGE W. THORN.

From the Department of Physiology, University of Buffalo.

We have studied the effect of cortin in the asthenia of many clinical conditions including Addison's disease. These findings have been compared with observations on normal individuals.

In asthenia there is increased susceptibility to fatigue although the dynamic power of the muscle may not decrease materially. Therefore the measurement of asthenia should test the threshold for fatigue rather than the strength of a single contraction. An ergometer can be successfully used to measure the fatigue threshold provided certain precautions are observed. We employed the ordinary type which uses the middle finger to lift a weight. A load is chosen which will cause definite fatigue in 3 to 5 minutes when lifted every 2 seconds. If too heavy the error due to variation from

* Aided by a grant from the National Research Council.

one test to another may be large. The intervals between tests are great enough to eliminate the practise factor. The base level for fatigue shows less variation in many asthenic individuals than in normals. In all subjects it is necessary to avoid unusual exercise as this may increase the threshold for fatigue by practise on the one hand or decrease it if the exercise is too strenuous on the other.

Four normal individuals have been tested at frequent intervals before and after the injection of cortin. Many others have been tested without the injections. Occasionally in normals, the day to day variation is so great that it is almost impossible to obtain a consistent base level for fatigue. All normals showed an increase of 20 to 50% in the power to do work before fatigue developed, within 1 to 4 days after cortin was begun. The high point came several days after cortin was started, often after the latter had been discontinued. Two showed a maximum increase of 50%; one an increase of 125% and the fourth reached 500%. In some normal individuals a more immediate subjective effect is noted. In an hour or less after the injection the subject feels sleepy and if he yields to the desire to sleep it is unusually sound and restful. Even though he does not sleep, in a couple of hours the feeling of drowsiness passes and he experiences a sense of increased well being and mental alertness which usually lasts for 2 or 3 hours. These effects appear to be more pronounced if one is tired or recovering from a minor infection.

The effect of cortin on the fatigue point has been studied in 6 cases of Addison's disease, 2 in which the cortical insufficiency was almost absolute and the other 4 in which it was less marked. The power to do work without fatigue was increased 700% in one of the severe cases and none in the other thus far. One of the less severe cases has shown no increase, 2 have shown 400% and the third 4900% increases. The maximum often came a few weeks after treatment was started, sometimes many days after it had been stopped. Increase in power to work without fatigue is associated with general improvement, although in some instances raising of the fatigue threshold precedes definite subjective sensation of improvement. When remission follows cessation of treatment the threshold for fatigue falls. The doses employed in these cases ranged from 150 gm. to 3000 gm. cortex daily.

The vomiting, muscular weakness and increase in pigmentation, in some cases of pregnancy indicate adrenal insufficiency. One of the worst cases which Dr. Irving W. Potter has seen was treated with cortin. She was 8 months pregnant, appetite poor, weight

had fallen from 160 to 105 lb. She was so weak that during the day she often had to lie down and had frequent fainting spells. After a few days' treatment, she gained over 10 lbs., appetite was much better, she could be up all day and there were no fainting spells. Blood pressure rose from 78 to 95 mm. systolic.

A case of Graves' disease showed an increase of 200% during the treatment (300-400 gm. of cortex per day) and a marked increase in the sense of well being. These improvements have persisted (3 months since the extract was discontinued).

A case of muscular dystrophy reached a maximum increase of 2700% 3 weeks after the extract was discontinued (the product of 300 to 400 gm. of cortex was injected daily for 14 days). No subjective change was noted for several days except that the patient could sleep better and felt more rested afterward. After 4 months without treatment the fatigue threshold returned toward the old level. With this patient and with others, including normals that show an increase in the power to work, there is no consciousness of a greater ability to work until the test is under way.

Two cases of osteomyelitis in children have been treated. One showed a 300% increase in working power and the other 700%. One month before treatment the latter patient had had scarlet fever.

Marked improvement has been produced by cortin (300 gm. cortex daily for 8 days) in persistent asthenia following diphtheria ("bull neck"). For weeks the patient lay in his bed. In 2 days after cortin was instituted he was sitting up and much brighter. Nine days after the extract was discontinued his power to do work before fatigue had been increased 130%. He steadily improved and finally went home.

A case of rather marked asthenia of possibly neurasthenic origin showed no definite improvement from cortin (as much as 100 gm. of cortex per day).

We have treated a case of *Myasthenia gravis* with large amounts of cortin (600 to 900 gm. of cortex) without effect. Drs. Bassett and Garvey of the University of Rochester have used smaller doses in a similar case without result.

The positive effects obtained in such widely varying clinical cases as well as to a minor degree in some supposedly normal individuals indicate a pharmacological action of cortin.