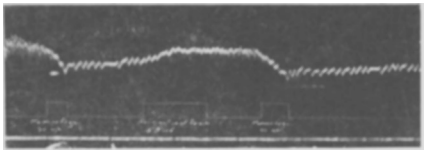

FIG. 3.

Note that the irregular chloral heart returns to normal after bleeding (20 cc.), that the irregularity returns when the blood is reinjected, and becomes regular again when 20 cc. of blood is once more withdrawn.

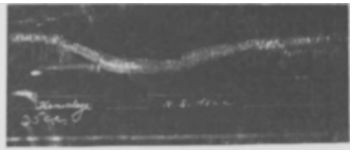

FIG. 4.

The irregular chloral heart becomes regular when 35 cc. of blood is withdrawn and becomes irregular again when 45 cc. of saline is injected.

remove the arrhythmias in a weakened heart, and that the reinjection of rather small amounts of normal saline precipitates the irregularity, indicate the importance of relieving the excessive load in cardiac disease.

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Addiction Edema and Withdrawal Edema in Morphinized Rats.

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Healthy adult male rats on a diet of whole wheat (plus 2% NaCl) were subjected to morphine addiction starting with daily doses of 10 mgm. morphine sulphate (5% solution) per 100 gm. rat, increased every 3 or 4 days up to 100 or more mgm. per kilo. The rats ate well throughout the work except in the early stages of morphine addiction. Weight was usually well maintained. The rats were killed in pairs at various stages, and samples of brain, muscle, skin and liver were dried to a constant weight, with the results shown in the table.

Water Content of Tissues. In the first series the rats were first killed on the 28th day of addiction when all of the tissues were found abnormally wet. The relation of the solids to normal was: brain –22%, muscle –9%, skin –22%, liver –13%. On withdrawal the only analyses in this series were made on the fourth day when the brain was found normal and the other 3 tissues about half recovered. In the second series the changes were followed every 3 or 4 days, and withdrawal begun on the twenty-fourth day.

Addiction edema was found at its maximum at the following

times; in the brain, tenth day; muscle, twenty-third day; skin, third and fourteenth days; liver, tenth day. On the last (twenty-third) day of addiction only the muscle showed maximal edema, liver and skin were half recovered and brain nearly normal. Although never much above the normal level, the brain solids usually varied inversely with those of the skin.

The first day of withdrawal was marked by the *sudden onset of a new edema* in the brain and liver, compensated by drying of the skin. The brain solids change in the one day amounted to −14%, the skin solids *gaining* 10%. The third day of withdrawal shows results all agreeing closely with the fourth day (only day studied) of the first series. The water changes in the tissues may be summarized as follows:

	ADDICTION	WITHDRAWAL
Brain	wet gradually; late recovery	wet suddenly; recovery; relapse
Muscle	wet gradually	recovery; relapse
Skin	wet suddenly; late partial recov.	dry suddenly; shift to wet
Liver	wet gradually; partial recovery	wet suddenly; partial recovery

Thus we have an *addiction edema* perhaps due largely to malnutrition (from digestive impairment?) and a *withdrawal edema* in brain and liver corresponding to the withdrawal edema demonstrated in dogs,[1] and compensated by drying of the skin. The withdrawal edema occurs suddenly and is more temporary in rats than in dogs. It appears to be parallel to the following changes: on the first day of withdrawal were found soft stools, a sudden marked fall in body weight and body temperature (in both series) all of which conditions were recovered from gradually in the succeeding few days.

The food and water intake and urine volume were followed in 7 rats of the second series during the last 6 days of addiction and for a like period during withdrawal.

Addicted rats consumed normal amounts of food. Withdrawal produced an immediate increase to a level about 25% above normal.

Morphine addiction increased the water intake to 25 to 50% above normal and the urine by at least 200%. On the first day of withdrawal the water intake fell to *below normal* but by the fourth day had increased to *double the addiction level.* The urine volume varied similarly but not so greatly.

Supernormal water drinking during addiction followed by subnormal intake immediately on withdrawal is in striking contradic-

[1] Barbour, H. G., Hunter, L. G., and Richey, C. H., *J. Pharm. and Exp. Therap.*, 1929, in press.

tion to a uniform experience with dogs in which morphinism suppresses the water exchange.

Conclusions: Morphinism in rats causes edema which tends to advance and decline at different rates in different tissues. Early and extensively affected is the skin. The water exchange becomes decidedly increased. Sudden withdrawal induces a fresh edema, especially of the brain, the skin passing first through a dry stage. The water exchange is first depressed, then greatly increased. Ingestion of food has not varied sufficiently in amount to account for any of the findings.

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Further Notes on the Relation of Nutrition to the Development of Cancer.

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In previous papers[1] we had shown that malignant tissue differs from the normal tissues of the body in that it contains no demonstrable or very little of the growth promoting fat soluble vitamins. We had also shown that many of the so-called cancer producing substances and forces, such as coal tar, other lipoid solvents, x-rays, radium, other lights and heat act directly to dissolve or otherwise remove these fat soluble vitamins from the tissues. While these studies were interesting in that they indicated that cancer may be nothing more than the result of the removal of the fat soluble vitamins from a tissue, it seemed quite unlikely that a lipoid solvent, no matter how often applied to a tissue, could remove sufficient of the vitamin to induce cancer. When a solvent is brought into contact with a medium it removes only a certain fraction of the dissolved substances from the medium.

That the local action of coal tar is not alone responsible for coal tar cancer has been indicated further by the fact that all animals painted with coal tar do not develop the disease while cancers have been known to develop in man years after a single injection of paraffin or a single dose of x-rays. There seems also to be little evidence to show that the appearance of cancer in man is related directly to the extent or severity of a previously existing local lesion. In fact, many patients carry definite precancerous lesions for years without

[1] Burrows, M. T., and Jorstad, L. H., *Am. J. Physiol.*, 1926, lxxvii, 24.