

series of equal drug and as nearly as possible equal electrical stimuli was obtained. On one occasion, however, an electrical stimulation of the vagus of apparently the same strength as its predecessors evoked a markedly greater response, without any intradermal or intracorneal injections having been made. And on only one occasion did the vagus response to electrical stimulation increase markedly after intradermal injection. In all the other cases the vagus response to electrical stimulation was unaltered by an intradermal or intracorneal injection. In no case was the vagus response to arecoline or the sympathetic response to adrenalin affected by the intradermal or intracorneal injection. We are thus unable to confirm Luithlen and Molitor's findings of an increased sympathetic and parasympathetic response after intradermal or intracorneal injections of 0.1 cc. of 0.9 per cent NaCl solution.

¹ Luithlen, F., and Molitor, H., *Arch. f. Exp. Path. u. Pharm.*, 1925, cviii, 248; 1926, exi, 246; 1926, cxiv, 47.

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The Action of Mineral Oil per Os on the Organism.

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Leitch¹ has shown that mineral oils applied repeatedly to the skin of animals induce cancer. It is known that these same oils are responsible for cancers in man. This is well illustrated by the studies of the so-called "mule spinners cancer" and the prevalence of cancers of the skin among the workers of the paraffin mines of Scotland. Several paraffin cancers have also been described in America and in other parts of Europe.¹

Our studies have shown that many animal and vegetable oils^{2, 3} are not absorbed when introduced under the skin of animals, but produce lesions quite identical to those produced by various mineral oils and tar.^{4, 5}

Our analyses of cancer have shown that it is directly the result of the removal of the excess of the ergusia (fat soluble vitamins) from local areas of the tissues.⁶ Such a removal of this lipoid substance or substances leads to a disappearance of the blood vessels, a crowd-

ing of the cells and stagnation sufficient for their independent growth. Mineral oils, tars, and especially the animal and vegetable oils and fats, which are largely free from fat soluble vitamins, when introduced into the tissues, induce cancer and crowd the cells in that they are able to dissolve and remove the fat soluble vitamins from adjacent areas of the tissues.⁷

Since pastries and manufactured vitamin-free fats are common articles of diet of Europeans and Americans, and since cancer of the stomach is very prevalent in these parts of the world, and not so common in many other parts,^{8, 9} it became of interest to investigate these fats and oils as a possible cause of cancers of the gastrointestinal tract. Mineral oils, when ingested, pass directly through the entire length of the gastrointestinal tract. Vegetable and animal oils pass undisturbed through the esophagus and stomach. They are then absorbed from the intestinal canal and either burned or stored in the body.

In the light of these facts, it became evident that fats and oils of all kinds, which are free from fat soluble vitamins, may affect the intestinal canal when given in the food, as they are known to affect the skin when applied to it. In the intestinal canal they should not only tend to remove the fat soluble vitamins from the intestinal wall and cause precancerous and cancerous lesions, but they must also remove these same vitamins from other articles of food with which they come in contact during chewing, swallowing and digestion.

Different oils should act differently in this regard. The animal and vegetable oils should cause such changes only in the mouth, esophagus and stomach. When absorbed from the intestines and burned they should give these vitamins back to the body. The use of such oils should have no effect, therefore, upon the general nutrition of the animal ingesting them, but should act only to cause changes in the upper digestive tract before they are absorbed. These effects should be most marked in the places where they are brought into closest contact with the wall of the digestive tube.

Mineral oils, on the other hand, must affect the entire alimentary tract and since they are not absorbed to any extent, but are eliminated with the feces, they should tend also to strip the food taken by the individual of its fat soluble vitamins, and cause nutritional disturbances in this individual.

It had become of interest, therefore, to test for the effect of various of these oils upon the gastrointestinal tract of rats and mice, and also upon the growth and general health of these animals. Since the results of our first experiments have been so striking, it seemed

important to report them at once, especially on account of the wide use of vitamin free oils and greases at the present time, and the extensive use of mineral oils as salves, in nose and throat conditions, in X-ray diagnosis, and as a purgative. Young rats were used for these experiments. The effect upon the growth of these rats of various oils in different diets, are recorded in the curves of Fig. 1. In order to make our data more quantitative, the rats were fed on a balanced dietary of known chemical and vitamin content. To compare the effect of the oils with effects resulting from an absence of fat soluble vitamins, other rats were fed on a dietary deficient in these vitamins. In these first experiments, crisco, nujol and heavy paraffin oil have been tested.

In the first experiment, M-1, four rats were fed on a diet deficient in vitamin A:

Potato starch,	80 grams.
Egg albumen crystals,	50 grams.
Salts (McCullum),	10 grams.
Crisco,	30 grams.
Vegex,	10 grams.

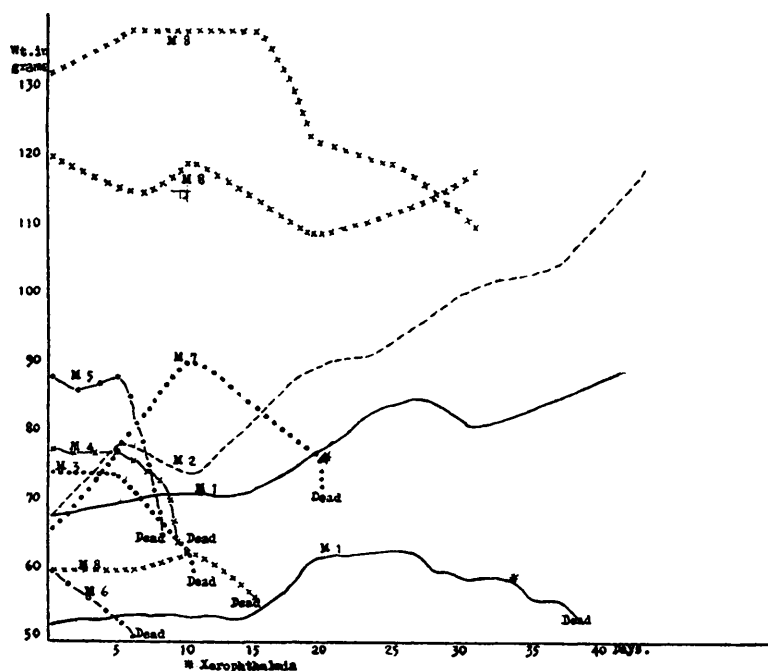


FIG. 1.

Growth curves of rats fed various dietaries with and without vegetable fats and mineral oils.

The growth curves of these rats are typical of other curves of rats fed on diets deficient in vitamin A. Two of them are included in Fig. 1, curve M-1.

The rats in Cages M-2, M-3, M-5 and M-6, were given the balanced dietary :

Potato starch,	80 grams.
Egg albumen crystals,	50 grams.
Salts (McCullum),	10 grams.
Butter,	30 grams.
Vegex,	10 grams.

Four rats eat twice this quantity each week. In Cage M-3, thirty grams of crisco (or about 14 per cent of the total diet) was added to the quantity of diet given above. Shortly after this diet was given, these rats showed fat in the stools and lost weight. Later this fat disappeared and they have gained normally since that time. The growth curve of one of these rats is Curve M-2, Fig. 1.

Thirty grams of nujol (or about 14 per cent of the total diet) was added to the balanced diet as given above, and fed to rats in Cage M-3. These rats suffered early from diarrhea and died after 10 days (Curve M-3, Fig. 1). A similar result was obtained from the study of rats in Cage M-5, where 15 grams of nujol (about 7 per cent of the total diet) was added to the balanced dietary. These rats died in 7 days (Curve M-5, Fig. 1). In Cage M-4, thirty grams of nujol was added to the minus vitamin A dietary, rather than to the balanced ration. This change had no effect. These rats lived as long as the others. They died in about 9 days. (Curve M-4, Fig. 1). In Cage M-6, forty-five grams of nujol (20 per cent of the whole dietary) was added. The destruction of these rats was immediate. The rats died in 6 days (Curve M-6, Fig. 1).

During these months of late winter and early spring, the butter is not so rich in fat soluble vitamins as at other times. In Cages M-7 and M-8, the rats were fed on the balanced diet, plus 2 per cent cod liver oil. In Cage M-8, five grams of heavy petrolatum (about 2.6 per cent of the total dietary) was added to the new balanced dietary in the proportions given above. The growth curves of two older and one younger rat of this series are included in Fig. 1, M-8. It is interesting to note that while the older rats withstood the action of the oil better than the younger ones, they also either do not gain or lose weight after a short time.

In Cage M-7, an attempt was made to administer what has been found to be a therapeutic dose per kilogram body weight for children. Two and a half grams of heavy petrolatum (about 1.3 per

cent of the total dietary) was added to the new balanced dietary given above. These rats have died in less than one-half the time of the rats on a minus vitamin A dietary (Curve M-7, Fig. 1).

The rats in all the cages, excepting where the very small doses of mineral oil were given, died without showing any xerophthalmia. In Cage 7, two rats showed for a short time before death the narrowing of the pupils and clouding of cornea, which is typical of this affliction.

As is evident, therefore, the mineral oils, quite different from the vegetable oils, not only remove the fat soluble vitamins from the food, but produce other toxic effects as well. From our studies of the effects of these oils on the tissues and in the production of cancer, it may be assumed that their toxic effect is due to the fact that they act on the mucous membrane of the intestines to further strip these tissues of the body of their fat soluble vitamin reserve.

This is a preliminary report.

¹ Leitch, A., *Brit. Med. J.*, 1924, ii, 941.

² Burrows, M. T., and Johnston, C. G., *Arch. Int. Med.*, 1925, xxxvi, 293.

³ Jorstad, L. H., *J. Can. Res.*, 1926, x, 229.

⁴ Jorstad, L. H., and Johnston, C. G., *PROC. SOC. EXP. BIOL. AND MED.*, 1926, xxiv, 86.

⁵ Burrows, M. T., and Jorstad, L. H., The Cause of Growths of Sarcoids or Oil Tumors, to appear in *J. Am. Med. Assn.*

⁶ Burrows, M. T., *J. of Can. Res.*, 1925, x, 239.

⁷ Jorstad, L. H., *J. Exp. Med.*, 1925, xlii, 221.

⁸ Williams, W. Rogers, *Natural History of Cancer*, London, 31, 1908.

⁹ Bablet, J., *Ann. de l'Inst. Pasteur*, 1926, xl, 922.

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Studies on Fatty Infiltration of the Liver Induced by Lipoid Solvents.

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In a previous paper, Johnston and the author¹ reported that fatty infiltration of the liver occurs a certain period of time after the injection of a mixture of mineral oil and coal tar into the subcutaneous tissue of rats fed a diet rich in vitamin A. We thought at that time that this mixture of lipoid solvents alone produced the fatty infiltration in these animals. More recent studies have shown that