THE RÔLE OF THE LIPOIDS AND PARTICULARLY LECITHIN IN NARCOSIS.*

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The discovery of the anesthetic properties of ether by Jackson and Morton in 1846 led to extensive investigations with the view of finding a common property upon which the narcotic power of the entire group of anesthetics depends. Thirty years later Meyer (1) and Overton (2) formulated their well known theory of narcosis; but it was not long before additional facts presented by various investigators clearly demonstrated the inadequacy of this simple theory and necessitated the advancement of new theories to explain this phenomenon.

It had been known that narcotics are more soluble in fats and oils than in water. With this in mind, von Bibra and Harless, in 1847, carried on a series of experiments on rabbits. Half the animals were anesthetized, and the other half were used as controls. All the animals were killed and the fat content of the brains and livers was determined quantitatively by extraction with alcohol and ether. They found the fat content of the brains of the narcotized animals to be less, and that of their livers greater, than the fat content of these organs in the controls. They, therefore, suggested that narcosis is due to a solution of brain lipoids or fats by the narcotic.

Reicher (3), working in Salkowski's laboratory, repeatedly demonstrated a considerable increase in the total quantity of fat in the blood during and after narcosis, especially with ether or chloroform. He determined the fat content of the blood by extraction with alcohol and ether. Pflüger's school(4) has shown that after digesting the residue obtained by this method with pepsin and again extracting with ether an additional quantity of fat may be obtained. Mansfeld (4) has shown that the total fat obtained from the blood by extracting with ether is only half the actual amount of fat present, and he has further called attention to the fact that the lipemia found in phosphorus poisoning is really due, not to an increase in total blood fat, but to a relative increase in free fat.

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Hermann (5) first demonstrated the presence of lecithin in red blood cells and then showed that all narcotics of the aliphatic group were able to dissolve red blood corpuscles and suggested an analogy between the solution of red blood cells, which he attributed mainly to a solution of the lecithins, and the solution of lecithins, cholesterins, and lipoids in the central nervous system during narcosis. Additional strength was given to this hypothesis by the findings of Pohl* that, during chloroform narcosis, the greater part of the narcotic in the blood is bound to the red blood cells and particularly to the lecithin and cholesterin constituents thereof; and furthermore, as was to be expected, that the cells of the central nervous system bind still more of the narcotic than the blood, since they are much richer in lecithin and cholesterin. Meyer (1) had previously shown that during alcoholic narcosis the organs that are richer in lipoids contain a much larger quantity of alcohol. Overton (2) maintained that the process consisted in a "solution of the anesthetic in the lipoids, thus changing the normal relationship of these to other cell constituents, but that there was no actual excretion of lipoids into the circulation." Voit (6) has shown that even where the reserve fats and lipoids enter the circulation and are carried to distant organs to be burned, as in extreme degrees of inanition, the fats and lipoids of the brain are spared, and the same has been proved to be the case in phosphorus poisoning (Mansfeld (4)).

Richet (7) called attention to the fact that the less soluble a substance is in water the more marked are its narcotic powers, and he sought to lay this down as a general law, but it is easily demonstrable that such is not the case. For example, alcohol and chloral are equally soluble in water, yet chloral is a much more powerful narcotic. Meyer (8) and Overton, working independently, attempted to show what relation, if any, existed between the solubility of a narcotic in fats and oils and its narcotic power, and later Baum (9) showed that the anesthetic properties of a drug depend not so much on its lack of solubility in water or its solubility in fats as on its distribution coefficient or relative solubility in a mixture of water and some oily or fatty substance, and that anything that changes this coefficient correspondingly alters the narcotic power of the drug.

In the animal body we have a multitude of cells composed of semifluid protoplasm and fatty bodies or lipoids. These cells are surrounded by a tissue fluid or watery lymph. If these facts are applicable to the animal body, the following postulates stated by Meyer must be true.

1. All chemically indifferent substances that are soluble in fat and fat-like substances must have a narcotic action upon protoplasm in proportion to their ability to diffuse therein.

2. The narcotic effect will appear first and most powerfully in cells in whose chemical constitution the fat-like bodies predominate and particularly in nerve cells.

3. The degree of narcosis produced by any one of these drugs depends, on the one hand upon its affinity for fat-like substances, on the other hand upon its affinity for the other cell body constituents, foremost among these water; in other words, upon its distribution coefficient as determined by its distribution in a mixture of water and fat-like substances.

Baum (9) determined the distribution coefficient for a number of narcotics, using a mixture of water and olive oil, and was able to show that the degree of narcotic power of any drug depends upon its distribution coefficient in this mixture. He showed further that anything that alters this coefficient, even though the chemical composition of the drug remains the same, correspondingly alters the degree of its narcotic power, and that substances having the same distribution coefficient have the same narcotic power, although their chemical composition and properties are different. With these facts in mind, Meyer and Overton independently advanced the following theory.

The narcotizing substance enters into a loose physicochemical combination with the lipoids of the cells, perhaps with the lecithin, and in so doing changes their normal relationship to the other cell constituents through which an inhibition of the entire cell chemism results.

This simple theory explains why and how the narcotic, which is a protoplasmic poison, is able to pass the semipermeable lipoid membrane, and enter the cell, but it casts no light upon the nature of the alterations in cell chemism that follow. In fact, the implication is that, since the narcotics are chemically indifferent bodies, they do not take part in the chemical processes of the cell. That the chemistry of the cell undergoes decided changes was soon demonstrated when Becker (10) first discovered acetone in the urine of patients who had been anesthetized, and that the narcotic state is dependent upon these alterations in cell chemism has been shown by Verworn (11), Mansfeld (4), Bürker (12), Heaton (13), and others.

Reicher (2) showed that the following metabolic changes are constantly present after prolonged narcosis:

1. An increase in the total, and particularly in the ammonia nitrogen in the urine. 2. An increase in the acetone bodies in the urine and expired air. 3. An increase in the total fat of the blood as determined by extraction with ether and alcohol. This increase amounted in some cases to three and four times the normal amount. 4. An increase in the lecithin and cholesterin, the sum of which was often equal to that of the fat; in other words, there was not only a lipemia but also a lipoidemia. 5. An increase in the quantity of fatty acids in the blood.

Reicher (3) suggests that the lipemia is not a meaningless phenomenon, but, on the contrary, represents a mechanism by means of which the body cells protect themselves against the poisonous narcotic. The fat molecules which are excreted by the cells into the circulation and which have a strong affinity for the narcotic he considers as amboceptors that unite with molecules of the invading narcotic just as an antigen with its antibody, and in this way the poison is neutralized and the vital body cells are protected.

Although at first sight this assumption seems plausible, it has almost no experimental basis and Nerking (14) attempted to supply the necessary experimental proof. He narcotized various animals (dogs, rabbits, and rats) with different anesthetics, such as chloroform, ether, morphin-scopolamin, and chloral-urethan, and, either before starting the anesthesia or after the narcotic state had been established, he injected a given dose of a 1 to 10 per cent. emulsion of lecithin in normal salt solution intravenously, subcutaneously, intraperitoneally, or intraspinally, in order to show what effect, if any, the lecithin
had upon the quantity of a given narcotic that was necessary to induce a given
degree of narcosis, or whether lecithin could accelerate the reaction from the
anesthetic state and eliminate some or all the unpleasant after effects. As
a result of his experiments he came to the following conclusions: the injection
of lecithin has an undoubted influence upon the duration and after effects of
anesthesia in that it shortens its duration, brings about a more rapid return
of consciousness, and eliminates unpleasant after effects. Lecithin itself is a
harmless agent and it exerts a beneficial effect upon the entire organism.

Nerking's work is open to objections as regards (1) dosage and (2) the
depth of the narcotic state. The narcotics he administered were given by inhala-
tion chiefly, by subcutaneous injection, by intravenous injection as in the
chloral-urethan experiments, and intraspinally. It is obvious that, except by
the last two methods, accurate dosage is impossible.

METHOD.

The narcotic, in the experiments to be reported, was administered
intravenously. Nerking (14), Burkhardt (15), Kümmel (16),
and others had already shown the practicability of this method
of anesthesia, and some of them, particularly Burkhardt and Kümmel,
had already used it on a number of human beings. In one
series of experiments a 5 per cent. solution of ether in normal saline
was used, in another a 10 per cent. solution, and in the last series a
mixture was used containing one part of a 4 per cent. solution of
morphin sulphate and two parts of a 20 per cent. solution of chloral
hydrate. In each case the solution was put into a long glass tube
graduated in five cubic centimeter divisions. To the end of this tube
a rubber tube was attached, which was tied to a cannula inserted
into a small tributary of the external jugular vein. The rate of flow
was regulated by means of a clamp screw. To exclude the influ-
ence of the height of the liquid column upon the rate of flow, the
height of this column was the same both in the control and in the
lecithin experiments and the injection in each case was commenced
at the same rate.

The same animal was used both for the control and the lecithin
experiments, an interval of thirty-six to seventy-two hours being
allowed to elapse between the experiments in order to allow the
animal to recover from the previous anesthesia. In each case sterile
water was used as a local anesthetic. The criteria used were: (1)
the disappearance and reappearance of the corneal reflex, which was
tested by drawing a fine wire across the cornea, as this will often
elicit a reflex when simply touching it will not; (2) the time when
the animal raised its head; (3) the time when it first got upon its
feet; and (4) the time of complete disappearance of all ataxia.
Cutaneous sensation was determined by pinching the skin with dull
scissors, the same part of the skin being used each time. The
lecithin in the form of a 5 or 10 per cent. emulsion in saline was
injected directly into the vein through the same cannula as the
narcotic solution.

PROTOCOLS.

SERIES I.

Experiment 1. Control.—April 3, 1912. Rabbit, black. Weight 1,200 gm.
Local anesthetic, sterile water.
3.05 P.M. Injection of 5 per cent. ether solution begun. Rate 15 c.c. per
minute.
3.07 P.M. Corneal reflex gone. Solution used, 25 c.c. Rate of injection
reduced to 10 c.c. per minute. Respiration, 82 per minute.
3.17 P.M. Injection discontinued. Total solution used, 95 c.c.
3.21 P.M. Corneal reflex present.
3.26 P.M. Raises head and tries to get up.
3.30 P.M. Upright position readily regained when disturbed, but animal is
quiet.

Lecithin.—April 7, 1912. Same rabbit. No local anesthetic.
10.35 A.M. 17 c.c. of 5 per cent. lecithin emulsion injected into vein through
cannula in 3 minutes.
10.45 A.M. Injection of 5 per cent. ether solution begun.
10.47 A.M. Corneal reflex gone. Solution used, 20 c.c.
Pulse, 240. Respiration, 60.
10.57 A.M. Injection discontinued. Total quantity of solution used, 95 c.c.
Total time, 12 minutes.
11.09 A.M. Corneal reflex distinct.
11.20 A.M. Raises head.

Experiment 2. Control.—April 8, 1912. Rabbit, white.
9.50 A.M. Injection of 5 per cent. ether solution begun.
9.55 A.M. Corneal reflex gone; solution used, 60 c.c.
10.00 A.M. Injection stopped. Total solution used, 105 c.c.
10.05 A.M. Corneal reflex present.
10.10 A.M. Raises head after stimulation.
10.12 A.M. Very active but cannot regain vertical position.
10.17 A.M. Still drags hind legs; otherwise normal.

Lecithin.—April 10, 1912. Same rabbit.
3.05-3.09 P.M. Injection of 20 c.c. of 5 per cent. lecithin emulsion.
3.12 P.M. Injection of 5 per cent. ether solution begun.

* The lecithin was obtained from Poulence Frères, Paris, from whom Werking
obtained his product.
<table>
<thead>
<tr>
<th>Animal</th>
<th>5 per cent. lecithin emulsion injected</th>
<th>Injection begun</th>
<th>Corneal reflex gone in</th>
<th>Injection stopped</th>
<th>Rate per minute until under anaesthetic</th>
<th>Rate per minute after under anaesthetic</th>
<th>Total solution used</th>
<th>Corneal reflex present in</th>
<th>Head raised in</th>
<th>Recovered in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit 1, black, male; weight 1,200 gm.</td>
<td>Control 17 c.c. 10.45 A.M.</td>
<td>3.05 P.M. 2 min.</td>
<td>2 min. 3.17 P.M.</td>
<td>15 c.c. 10 c.c.</td>
<td>95 c.c. 4 min. 9 min. 13 min.</td>
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<td></td>
<td>Lecithin 10.35 A.M.</td>
<td>2 min. 10.57 A.M.</td>
<td>10 c.c. 7.5 c.c.</td>
<td>95 c.c. 12 min. 23 min.</td>
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<tr>
<td>Rabbit 2, white, male</td>
<td>Control 9.50 A.M.</td>
<td>5 min. 10.00 A.M.</td>
<td>12 c.c. 9 c.c.</td>
<td>105 c.c. 5 min. 10 min. 17 min.</td>
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<tr>
<td></td>
<td>Lecithin 3.12 P.M.</td>
<td>5 min. 3.73 P.M.</td>
<td>10 c.c. 9 c.c.</td>
<td>105 c.c. 7 min. 13 min. 22 min.</td>
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</tbody>
</table>
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3.17 P.M. Corneal reflex gone. Solution used, 50 c.c.
3.23 P.M. Anesthetic stopped; 105 c.c. used.
3.30 P.M. Corneal reflex present but animal is still very drowsy.
3.36 P.M. Raises head but is still very drowsy.
3.40 P.M. More lively, is able to regain vertical position.
3.45 P.M. Fully recovered.

The results in table I do not indicate that lecithin administered before anesthesia is begun has any influence upon the readiness with which the narcotic state may be induced, or that it accelerates the animal's reaction from the effects of the narcotic.

Series 2.

Experiment 1. Control.—Rabbit, gray. Weight, 1,200 gm.
Local anesthetic, sterile water.
2.54 P.M. Injection of 10 per cent. ether solution begun. Rate, 10 c.c. per minute.
2.58 P.M. Corneal reflex gone. Solution used, 23 c.c. Respiration, 74.
3.03 P.M. Injection discontinued. Total solution used, 43 c.c.
3.06 P.M. Corneal reflex present; moves jaw, raises head.
3.12 P.M. Assumes erect position but hind legs show marked weakness.
3.20 P.M. Fully recovered.

Lecithin.—Same rabbit.
11.34 A.M. Injection of 10 per cent. ether solution begun.
11.39 A.M. Corneal reflex gone. Solution used, 25 c.c.
11.44 A.M. Injection stopped. Additional solution used, 25 c.c.
11.45 A.M. Injection of 7 c.c. of 5 per cent. lecithin emulsion into vein.
11.46 A.M. Corneal reflex present.
11.51 A.M. Moves left leg.
12.02 P.M. Tries to hop.
12.07 P.M. Fully recovered.

Experiment 2. Control.—Rabbit, gray. Weight 1,120 gm.
Local anesthetic, sterile water.
2.14 P.M. Injection of 10 per cent. ether solution begun. Rate, 10 c.c. per minute.
2.17 P.M. Corneal reflex gone. Solution used, 35 c.c.
2.23 P.M. Injection discontinued. Total solution used, 55 c.c.
2.28 P.M. Corneal reflex present; raises head.
2.31 P.M. Assumes upright position but shows marked ataxia.
2.34 P.M. Still shows incoördination on attempting to move.
2.36 P.M. Hops about. Normal.

Lecithin.—Same rabbit.
10.44 A.M. Injection of 10 per cent. ether solution begun.
10.48 A.M. Corneal reflex gone. Solution used, 35 c.c.
10.53 A.M. Injection discontinued. Total solution used, 55 c.c. 8 c.c. of 5 per cent. lecithin emulsion injected into vein.
10.57 A.M. Corneal reflex present.
### Table II.
**Series 2.**

<table>
<thead>
<tr>
<th>Animal</th>
<th>Control Lecithin</th>
<th>Amount of solution used</th>
<th>Corneal reflex present in</th>
<th>Head raised in</th>
<th>Position erect in</th>
<th>Recovered in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit 1, gray; weight 1,120 gm.</td>
<td>8 c.c.</td>
<td>55 c.c.</td>
<td>5 min.</td>
<td>5 min.</td>
<td>8 min.</td>
<td>13 min.</td>
</tr>
<tr>
<td></td>
<td>10.57 A.M.</td>
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<td></td>
</tr>
<tr>
<td>Rabbit 2, gray; weight 1,200 gm.</td>
<td>7 c.c.</td>
<td>43 c.c.</td>
<td>3 min.</td>
<td>3 min.</td>
<td>11 min.</td>
<td>17 min.</td>
</tr>
<tr>
<td></td>
<td>12.08 P.M.</td>
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<td></td>
</tr>
<tr>
<td>Rabbit 3, gray; weight 1,200 gm.</td>
<td>10 c.c.</td>
<td>55 c.c.</td>
<td>3 min.</td>
<td>14 min.</td>
<td>19 min.</td>
<td>24 min.</td>
</tr>
<tr>
<td></td>
<td>12.39 P.M.</td>
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</tr>
</tbody>
</table>
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11.01 A.M. Lies on side, cannot raise head.
11.08 A.M. Holds up head.
11.10 A.M. Hops about but still shows ataxia.
11.12 A.M. Fully recovered.

Experiment 2. Lecithin.—Same rabbit.
12.37 P.M. Injection begun. Rate, 7 c.c. per minute. Solution used, 25 c.c.
12.39 P.M. Corneal reflex gone. Respiration, 80 per minute. Rate, 4 c.c. per minute.
12.37 P.M. Injection discontinued. Total solution used, 50 c.c.
12.41 P.M. Corneal reflex present.
12.46 P.M. Lies on side. Expression dull.
12.48 P.M. Cannot raise head.
12.51 P.M. Raises head after stimulation.
12.52 P.M. Standing, but shows signs of weakness.
12.55 P.M. Hops about. No ataxia.

In only one of the experiments (rabbit 3) given in table II does the administration of lecithin seem to have had any accelerating effect on the recovery, and this was seen during the latter stages. The other experiments show a distinct retardation.

SERIES 3.

Experiment 1. Control.—Rabbit, gray.
3.20 P.M. Injection of a 5 per cent. ether solution begun.
3.34 P.M. Corneal reflex gone. Solution used, 65 c.c.
3.39 P.M. Injection discontinued. Total solution used, 95 c.c.
3.45 P.M. Corneal reflex present; animal raised head.
3.50 P.M. Erect position.
3.55 P.M. Fully recovered.

Lecithin.—Same rabbit.
11.27 A.M. Injection commenced.
11.39 A.M. Corneal reflex gone. Solution used, 65 c.c.
11.44 A.M. Injection discontinued. Total solution used, 95 c.c.
11.46 A.M. 10 c.c. of 5 per cent. emulsion injected.
11.48 A.M. Corneal reflex present.
11.53 A.M. Fully recovered.

Experiment 2. Control.—Dog, male. 10 per cent. solution of ether used.
3.27 P.M. Injection begun. Rate, 40 c.c. per minute.
3.34 P.M. Corneal reflex gone. Total solution used, 140 c.c.
3.27 P.M. Injection discontinued. Total solution used, 170 c.c.
3.26 P.M. Corneal reflex present.
3.40 P.M. Moves about, but is ataxic.
3.45 P.M. Fully recovered.

Lecithin.—Same animal.
10.40 A.M. Injection begun. Rate, 35 c.c. per minute.
10.48 A.M. Corneal reflex gone. Solution used, 190 c.c.
10.49 A.M. Respiration ceases; artificial respiration.
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10.51 A.M. Injection discontinued.
10.52 A.M. 30 c.c. of 5 per cent. lecithin emulsion injected.
10.56 A.M. Animal raises head.
10.59 A.M. Upright position; very ataxic.
11.03 A.M. Fully recovered.

TABLE III.

Series 3.

<table>
<thead>
<tr>
<th>Animal</th>
<th>5 per cent. lecithin emulsion injected</th>
<th>Amount of solution used</th>
<th>Corneal reflex present in</th>
<th>Head raised in</th>
<th>Position erect in</th>
<th>Recovered in</th>
</tr>
</thead>
</table>
| Rabbit, gray    | Control Lecithin
0 c.c. 10 c.c. | 95 c.c. 95 c.c. | 6 min. 4 min. | 6 min. | 14 min. | 18 min. 11 min. |
| Dog, black      | Control Lecithin
10.52 A.M. 30 c.c. | 170 c.c. | 1 min. | 4 min. | 10 min. | 11 min. |

Series 3 shows a somewhat more rapid recovery from the effects of the anesthesia when lecithin was injected.

Morphin-Chloral Experiments.

In this series a mixture consisting of two parts of a 20 per cent. solution of chloral-hydrate and one part of a 4 per cent. solution of morphin-sulphate was used. The solution was injected slowly into a tributary of the external jugular vein, the injection of three to four cubic centimeters taking about five minutes. In each case the respirations became very slow and shallow, and in some cases ceased entirely and artificial respiration was used.

Series 4.

Experiment 1. Control.—August 30, 1912. Rabbit, male. Weight 3,300 gm.
3.30-3.35 P.M. Injected 4 c.c. of above solution. Immediate loss of sensation with marked reduction in sensitiveness of cornea, but no loss of corneal reflex.
3.35 P.M. Raises head after severe cutaneous stimulation.
4.10 P.M. Moves legs involuntarily.
4.15 P.M. Can regain vertical position but is very ataxic.
4.50 P.M. Still shows ataxia and cannot move even after stimulation.
Lecithin.—August 31, 1912. Same rabbit.
12.09-12.15 P.M. Injected 3 c.c. of same solution. Respiration stopped. Corneal reflex present. Sensitiveness of cornea very much reduced. Respiration, 2 per minute.
<table>
<thead>
<tr>
<th>Animal</th>
<th>Solution Used</th>
<th>Amount of Solution Used</th>
<th>Inensitive to Pain in</th>
<th>First Response to Pain in</th>
<th>Head Raised in</th>
<th>First Voluntary Movement in</th>
<th>Recovered in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit A, white, male; weight 3.300 gm.</td>
<td>Control</td>
<td>6 c.c.</td>
<td>3 min.</td>
<td>20 min.</td>
<td>20 min.</td>
<td>35 min.</td>
<td>No response to pain after 1½ hrs.</td>
</tr>
<tr>
<td></td>
<td>Lecithin</td>
<td>3 c.c.</td>
<td>3 min.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbit B, white, female; weight 2.200 gm.</td>
<td>Control</td>
<td>3 c.c.</td>
<td>5 min.</td>
<td>20 min.</td>
<td>20 min.</td>
<td>20 min.</td>
<td>32 min.</td>
</tr>
<tr>
<td></td>
<td>Lecithin</td>
<td>9.5 c.c.</td>
<td>2 min.</td>
<td>32 min.</td>
<td>32 min.</td>
<td>32 min.</td>
<td>44 min.</td>
</tr>
</tbody>
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12.20-12.25 P.M. 6 c.c. of 10 per cent. lecithin emulsion injected into vein.
12.25 P.M. Corneal reflex present.
12.50 P.M. Winks eyes. No response to pain stimuli.
1.50 P.M. Sewing up wound caused no response.
2.00 P.M. Still no response to intense pain stimuli.

Experiment 2. Control.—August 29, 1912. Rabbit, female, white. Weight, 2,200 gm.
4.05-4.10 P.M. Injected 3 c.c. of same solution into tributary of external jugular vein. Respiration very slow and shallow. Corneal reflex slightly sensitive. No pain sensation.
4.30 P.M. Responds to stimulation, winks eye, raises head.
4.45 P.M. Fully recovered.

Lecithin.—August 31, 1912. Same rabbit.
1.09 P.M. Injected 0.5 c.c. of same solution. Leak found in tube, clot in cannula. Injections stopped.
1.12 P.M. Injected 3 c.c. of solution. Respiration stopped. Corneal reflex gone.
1.15 P.M. Breathing again, slowly but deeply.
1.15 P.M. 9.5 c.c. of 10 per cent. lecithin emulsion injected into vein.
1.30 P.M. Winks; corneal reflex present; no sensitiveness to pain present.
1.45 P.M. Responds to stimulation, raises head, hops about when stimulated but is very ataxic.
1.57 P.M. Fully recovered.

Series 4 demonstrates the ineffectiveness of lecithin in shortening the duration of anesthesia. In each case in which lecithin was used there was a distinct retardation in the reaction time.

From the above experiments the following conclusions may be drawn.
1. The intravenous injection of five to thirty cubic centimeters of a 5 or 10 per cent. emulsion of lecithin, depending upon the size of the animal used, does not interfere with the induction of anesthesia, and this can be accomplished as readily in animals thus injected as in controls.

2. In six out of nine experiments lecithin had no effect upon the rapidity with which the various phenomena which indicate the animal's recovery from the effects of the anesthetic appeared.

The above experiments do not bear out Reicher's assumption as to the cause of the lipoidemia, and the explanation of this phenomenon still remains an open question.

In conclusion, I desire to express my thanks to Dr. John R. Murlin for suggesting the subject and for his assistance, and to
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Professor Graham Lusk for permission to carry on the work in his laboratory.

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