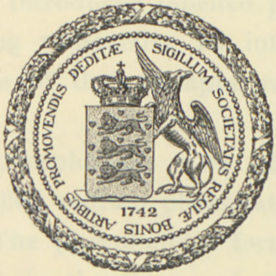
Det Kgl. Danske Videnskabernes Selskab.
Biologiske Meddelelser. **XV**, 6.

RATE OF PENETRATION OF PHOSPHATIDES THROUGH THE CAPILLARY WALL

BY

G. HEVESY AND L. HAHN



KØBENHAVN
EJNAR MUNKSGAARD
1940

Printed in Denmark.
Bianco Lunos Bogtrykkeri A/S.

Ions or molecules of crystalline substances present in the plasma can easily penetrate through the capillary wall. As soon as a few minutes after injecting labelled sodium ions ($^{24}Na^{+}$) into the jugularis, we find these ions proportionally distributed between the sodium ($^{23}Na^{+}$) ions of the plasma and those of the interspaces. On the other hand, colloidal particles like those formed by the proteins of the plasma do not under physiological conditions pass through the walls of the capillaries at any appreciable rate. The phosphatides present in the plasma can be expected to have an intermediary position as to their penetrability through the capillary wall between the crystalline constituents and the proteins present in the plasma. To determine the rate of penetration of the plasma phosphatides through the capillary wall, we introduced labelled phosphatides (phosphatides containing radioactive P) into the plasma and measured the rate of their disappearance from the circulation.

The labelled phosphatides were obtained in the following way. Labelled sodium phosphate was administered to a rabbit (A). The phosphatides formed, after the start of the experiment, in the liver and other organs of this rabbit become labelled; a part of these labelled phosphatides is liberated into the plasma. By injecting plasma of this rabbit (A) into the circulation of another rabbit (B),

we introduced labelled plasma phosphatides under strictly physiological conditions into the circulation. To avoid the increase of the plasma volume of rabbit B, we removed, previous to the injection of the labelled plasma, for example, 20 cc. blood of rabbit B. This blood was, after addition of heparin, gently centrifuged to separate the bulk of its plasma content which was then replaced by the labelled plasma of rabbit A. The blood thus obtained was injected into the jugularis of rabbit B. This rabbit, thus, gets its own corpuscles reincorporated, combined with the corresponding amount of labelled plasma of the other rabbit. An aliquot part of the plasma of rabbit A is kept to be analysed.

The labelled phosphatide molecules introduced into the circulation of rabbit B become distributed in the total plasma of the rabbit almost at once, the next step being the continuous escape of the labelled phosphatide molecules through the capillary wall and their replacement by other phosphatide molecules, originally located in the organs, which diffuse in the opposite direction, namely through the capillary wall, into the plasma. Since the phosphatide content of the plasma remains practically constant during the experiment, the exodus of a certain quantity of phosphatides must be followed by the influx of about the same amount. In view of the very minute turnover of phosphatides in the blood, the number of labelled phosphatide molecules which are decomposed in the plasma during the experiment can be neglected. The processes described above are going on under strictly physiological conditions. The replacement of ordinary phosphorus (^{31}P) by radioactive phosphorus (^{32}P) in some of the phosphatide molecules can certainly not be considered to entail the introduction

of a non physiological component into the circulation, as such a replacement cannot influence the chemical behaviour of the phosphatide molecules to any significant extent.

The rate at which the labelled phosphatides escape from the plasma of rabbits is seen in Tables 1 and 2, and also

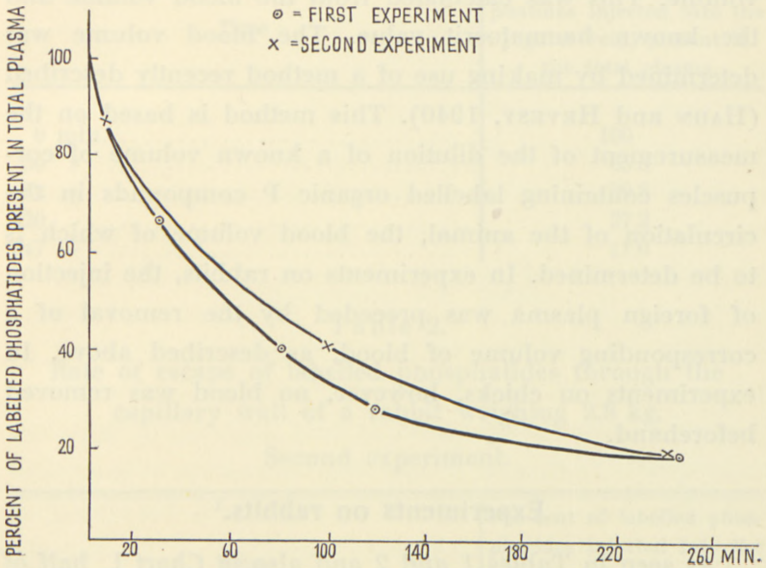


Chart I. Rate of disappearance of labelled phosphatide molecules from the plasma.

in Chart I. The figures of the tables were obtained by comparing the radioactivity of the phosphatides present in 1 cc. plasma samples of rabbit B, taken at different intervals, with that of the phosphatides of an equal plasma volume of rabbit A. The phosphatides were extracted by making use of BLOOR's method. After being converted into phosphate by wet ashing, an aliquot part of the solution obtained was used in the colorimetric measurement of the P content, another to secure an ammonium magnesium

phosphate precipitate, the activity of which was determined by a Geiger counter.

The calculation of the amount of labelled phosphatides present in the total plasma of the rabbit from that found in 1 cc. necessitates the knowledge of the total plasma volume. This was calculated from the blood volume and the known haematocrit value. The blood volume was determined by making use of a method recently described (Hahn and Hevesy, 1940). This method is based on the measurement of the dilution of a known volume of corpuscles containing labelled organic P compounds in the circulation of the animal, the blood volume of which is to be determined. In experiments on rabbits, the injection of foreign plasma was preceded by the removal of a corresponding volume of blood, as described above. In experiments on chicks, however, no blood was removed beforehand.

Experiments on rabbits.[1]

As seen in Tables 1 and 2 and also in Chart I, half of the labelled phosphatides introduced into the plasma leave the circulation by penetrating through the capillary wall in the course of about an hour. As the non-labelled phosphatides can be expected to show the same behaviour as the labelled ones, we can conclude that, from all phosphatide molecules present at the start of the experiment in the plasma, half will no longer be present after the lapse

[1] Some of the results obtained were previously published by us in a note to Nature (**144**, 204, 1939). — F. E. Haven and W. F. Bale (J. Biol. Chem. **129**, 23, 1939) injected emulsions containing labelled phosphatides prepared from the liver of the rat into the circulation of another rat and found the labelled phosphatides to accumulate mainly in the liver and the spleen.

Table 1.

Rate of escape of labelled phosphatides through the capillary wall of a rabbit weighing 2.4 kg.

First experiment.

Time	Per cent of labelled phosphatides injected into the jugular vein, present in the total plasma
0 min.	100
30 -	65.8
82 -	39.8
120 -	27.2
247 -	17.6

Table 2.

Rate of escape of labelled phosphatides through the capillary wall of a rabbit weighing 2.8 kg.

Second experiment.

Time	Per cent of labelled phosphatides injected into the jugular vein, present in the total plasma
0 min.	100
7 -	85.6
100 -	40.1
242 -	18.4

of about an hour, and will be replaced by others which were previously located in the organs.

Three objections may be raised against the conclusions drawn above: a) Labelled phosphatides can be decomposed in the plasma leading, for example, to the formation of labelled inorganic P; b) they can be incorporated into the

corpuscles; c) they can be synthesised in the body of rabbit B, into which labelled plasma was injected. In that case, besides a loss of the labelled phosphatides introduced into the circulation of rabbit B, a gain of such phosphatides due to a synthesis of labelled phosphatides in rabbit B would take place.

The objections mentioned above are, however, not justified, as

a) We recovered (see Table 6) more than 1/2 of the labelled phosphatides injected into the plasma of rabbit B 4 hours later in the organs investigated, in spite of the fact that the latter did not include the skin, the skeleton, and large parts of the digestive tract, which presumably took up an appreciable part of the labelled phosphatides. Furthermore, in the course of 4 hours, a non-negligible part of the phosphatides present in some of the organs and, thus, also that of the labelled phosphatides taken up by these organs, gets decomposed. In the liver, about 1/6 of the phosphatides present was found to be renewed in the course of 4 hours[1]. In view of the above considerations, the amount of phosphatides decomposed in the plasma in the course of a few minutes can certainly be disregarded.

b) That in the course of a few hours the replacement of corpuscle phosphatides by plasma phosphatides is a restricted one, is seen from the following figures. In two experiments, after the lapse of 4 hours, 2 resp. 1.3 per cent of the labelled phosphatides originally present in the plasma of rabbits were found to be located in the corpuscles.

As to objection c), the formation of labelled phosphatides does not take place in rabbit B to any significant extent

[1] G. Hevesy and L. Hahn, Det Kgl. Danske Vidensk. Selskab, Biol. Medd. XV, 5 (1940).

in view of the absence of a sufficient amount of labelled phosphate. This fact is seen from the following consideration: We administered to rabbit A 5×10^6 counts as phosphate and found the next day in the plasma of this rabbit 40.000 counts. We injected into rabbit B 20 cc. plasma containing 8.000 counts, of which 4.000 were due to phosphatide P and 4.000 to inorganic P. As from 5×10^6 inorganic P counts introduced 20.000 phosphatide counts were found after the lapse of a day in rabbit A, we can conclude that, within that time, less than 20 phosphatide counts were formed in rabbit B, thus an insignificant amount.

Experiments on chicks.

Labelled phosphate[1] was administered by subcutaneous injection to chicks (A_1, A_2, and A_3, respectively). After the lapse of a day, plasma samples of these chicks were taken. One part (1 cc.) of the sample was injected into the jugularis of the chicks B_1, C_1, D_1, E_1, B_2, C_2, D_2, and B_3, C_3, D_3, E_3, F_3, respectively; another part was analysed. After the lapse of 7 to 67 minutes, plasma samples of chicks B, C, D, E, and F, respectively, were taken and the activity of their phosphatide content determined; heparin was added to the blood before it was centrifuged. In Tables 3, 4, and 5, the results of these experiments are recorded. The time recorded in Tables 3 and 5 was reckoned from the middle of the time of injection, which took about one minute.

As seen in Table 3, after the lapse of 17.0 to 17.9 min., 1 cc. of the plasma of chicks B_2, C_2, and D_2, respectively, contains only about 7 per cent of the labelled phosphatide

[1] We are much indebted to Mrs. SVENDSEN for administering the labelled phosphate to the chicks.

Table 3.

Percentage of labelled phosphatides present in the plasma of chicks B_2, C_2, D_2, after injection of 1 cc. plasma of chick A_2 containing labelled phosphatides.

Chick	Weight of the chick	Total plasma volume	Time	Per cent of the labelled phosphatide injected	
				present in 1 cc. plasma	present in the total plasma
B_2	114 gm.	3.6 + 1 cc.	17.4 min.	8.02	36.9
C_2	127 -	4.1 + 1 -	17.9 -	7.34	37.4
D_2	134 -	4.3 + 1 -	17.0 -	7.12	37.7

present in 1 cc. of the plasma of chick A injected into chicks B_2, C_2, and D_2, respectively. This decrease is partly due to a dilution of the labelled phosphatides present in 1 cc. by the non-labelled phosphatides present in about 4 cc. plasma of chicks B_2, C_2, and D_2, and partly to an escape of the labelled phosphatides through the capillary wall into the organs and its replacement by non-labelled ones previously present in the organs. As seen in the last column of Table 3, from 100 labelled phosphatide molecules introduced into the circulation of the chicks, only about 37 were present in the plasma after the lapse of about 17 min.

Since the labelled phosphatides cannot be expected to show a different behaviour from the non-labelled ones, we can conclude that 63 per cent of all individual phosphatide molecules originally present are no longer in the plasma of the chick after the lapse of 17 min., being replaced by phosphatide molecules originally located outside the capillary wall.

In the first experiment which we carried out on chicks (see Table 4), we have chosen another procedure. We

Table 4.

Change in the specific activity of the plasma phosphatide of chicks B_1, C_1, D_1, E_1, after the injection of plasma of chick A_1 containing labelled phosphatides.

Chick	Weight of chick	Ratio of specific activity of the phosphatide P obtained after 7 and 67 min.
B_1	138 gm.	2.2
C_1	156 -	2.1
D_1	138[1] -	1.9
E_1	107[1] -	2.8

[1] These chicks have shown pronounced exsudates due to E-avitaminosis and were kindly put at our disposal by Dr. H. DAM. The injection was kindly carried out by Mrs. SVENDSEN. The above figures do not permit us to draw any conclusion as to a difference in the permeability of, for example, the muscle capillaries of normal chicks and chicks suffering from E-avitaminosis. To arrive at such a conclusion it would be necessary to compare the labelled phosphatide content of the muscle tissue of normal chicks and of chicks suffering from E-avitaminosis at the end of the experiment.

compared the activity of 1 mg. phosphatide P extracted from 1 cc. plasma of chick A with the activity of 1 mg. phosphatide P extracted from 1 cc. plasma of chick B, C, D, and E, respectively. Should the phosphatide concentration in the plasma of the different chicks used in this experiment be about the same, we could calculate from the data obtained the loss of labelled phosphatides through the capillary wall in the course of the first 7, and the consecutive 60 min. as well. When determining the phosphatide content of the plasma in our second experiment, we found, however, very pronounced differences between the plasma phosphatide contents of the chicks used. (Chick A_2 = 6.5 mg. %; B_2 = 7.5 mg. %; C_2 = 4.0 mg. %;

$D_2 = 4.8$ mg. %)[1]. From these variations in the phosphatide contents of the plasma we followed that, from the data obtained in the first experiment, we cannot calculate the loss of labelled phosphatides by the plasma in the course of the first 7 min., while we can state the loss sustained in the interval between 7 and 67 min. after the start of the experiment. It is this value which is recorded in Table 4.

Effect of histamin.

We also carried out experiments in which histamin was injected simultaneously with the plasma containing labelled phosphatides. The results of these experiments are seen in Table 5.

The administration of histamin did not much affect the appearance of chicks C_3 and D_3, while chicks E_3 and F_3 could not stand on their feet for the first 5—10 min. which elapsed after the injection of histamin. From the last mentioned two chicks, only small blood samples, about 0.4 cc., could be secured, while we collected several cc. from chicks which got no or only minor doses of histamin administered. The total plasma volume of the chick was calculated as described on p. 6. The average figure obtained for the labelled phosphatide content of the plasma of chicks C_3, D_3, E_3, and F_3, to which histamin was administered, 20 min. after the start of the experiment is about 7. The corresponding average figure for the labelled phosphatide content of the plasma of chicks B_3 and B_2, C_2, D_2 (see Table 3) is as well. No striking effect of the administration of

[1] Comp. also the great variations in the phosphatide content of the blood of chicks found by F. W. Lorenz, J. L. Chaikoff and C. Entenman, J. Biol. Chem. **123**, 577, 1938.

Table 5.

Percentage of labelled phosphatides present in the plasma of chicks B_3, C_3, D_3, E_3, and F_3 after the injection of 1 cc. plasma of chick A_3 containing labelled phosphatides.

Chick	Weight of the chick	Time	mg. histamin-dihydrochloride per gm. chick weight	Per cent of labelled phosphatides injected, present in	
				1 cc. plasma	total plasma per gm. body weight
B_3[1]	113 gm.	21 min.	0	8.1	37.8
C_3	104 gm.	23 min.	3×10^{-3}	5.5	23.8
D_3	95 -	23 -	5×10^{-3}	10.0	40.5
E_3	113 -	22 -	5×10^{-3}	4.0	18.5
F_3	124 -	19 -	1×10^{-2}	7	34.8

[1] Comp. also Table 3.

histamin on the permeability of the capillaries by phosphatides is, thus, found. In view of the large fluctuations shown by the values obtained in the experiments in which histamin was administered, the above result is, however, to be interpreted cautiously.

The permeability of different artificial membranes to phosphatides was investigated by Süllmann and Verzár (1934). They found that through such membranes which are permeable to water blue and Congo red the plasma phosphatides can penetrate as well.

Uptake of labelled phosphatides by the organs.

In the preceding chapters, we discussed the rate at which labelled phosphatide molecules located in the plasma penetrate through the capillary wall. We will now describe

experiments which were carried out in order to determine to what extent the various organs took up the labelled phosphatides which left the circulation. We arrive at these figures by extracting the phosphatides of the organs and by determining their activity.

In Table 6, the percentage of labelled phosphatides introduced into the circulation, present at the end of the experiment in several organs, is recorded in the third column. The fourth column of the table contains data on the labelled phosphatide content of the interspaces computed on the assumption that all the labelled phosphatides present are to be found in the extracellular volume. For the extracellular volume of the organs of the rabbit we utilised the figures arrived at by Manery and Hastings (1939). In the fifth column, the distribution of the labelled phosphatides between equal volumes of the plasma and the extracellular fluid of the organs in question is shown on the assumption that the labelled phosphatides are solely to be found in the interspaces of the organ in question. The conclusion to be drawn from the figures of this column are discussed on page 16. Correctly, we should not compare the distribution of labelled phosphatides between equal volumes of plasma and of extracellular tissue spaces, but the specific activities of phosphatides of the plasma and those of the extracellular phosphatides. In view, however, of the fact demonstrated that the phosphatide molecules penetrate easily through the capillary wall, the phosphatide content of the interspace presumably not much differs from that of the plasma[1].

[1] As to the phosphatide content of the lymph from the leg of the rabbit, Aakuma (1937) states an average value of 1.7 mg. per cent, while 2.1 mg. per cent were found by him in the plasma.

Table 6.

Labelled phosphatides found in the organs of rabbit B after the lapse of 4 hours.

Organ	Weight	Percentage of the labelled phosphatides injected into the vein, present in		Distribution coefficient[1] of labelled phosphatides between equal volumes of extracellular water and plasma water
		the blood-free organ	1 cc. extracellular fluid[1]	
Liver	62 gm.	28.9	2.17	9.8
Kidneys	9 -	0.88	0.19	0.85
Muscles	910 -	2.5	0.018	0.082
Heart	5 -	0.21	0.12	0.54
Spleen	1.2 -	0.06	0.16	0.72
Small intestine mucosa	46 -	1.1	0.065	0.29
Lungs	10 -	1.0	0.22	1.0
Brain	6 -	0.05	0.022	0.10
Plasma	79 gm.	17.6	0.22	..

[1] Calculated on the assumption that no penetration of labelled phosphatides into the cells took place.

In another experiment, only the labelled phosphatide content of liver and muscles were determined. The liver, weighing 85 gm., contained 38 per cent of the labelled phosphatides injected after the lapse of 4 hours, while in the blood-free muscles, weighing 1060 gm., 2.7 per cent of the labelled phosphatides administered were present.

The figures given above relate to the labelled phosphatide content of organs of rabbits killed by bleeding. While such organs have only a comparatively small blood content, this cannot be entirely disregarded. Some of the labelled phosphatides present in the organs will be due to their

blood content. In the muscles of the rabbit we found, by making use of the method of Eichelberger and Hastings (1937), that the blood content amounted to 0.5 per cent of the organs' weight. In the experiment described above, in which the weight of the muscles was 1060 gm. and the total plasma of the rabbit amounted to 97 cc., the blood present in the muscles contained 1.0 per cent of the labelled phosphatides injected. In the case of the liver, the corresponding figure works out to be less than 1 per cent; in the case of the other organs the correction is insignificant.

As seen in Table 6, the labelled phosphatide content of all the organs but that of the liver can be interpreted as being present in the interspaces, though this must not actually be the case. The liver contained, after the lapse of 4 hours, about ten times more phosphatides as can be explained by an uptake of the liver interspaces. This result suggests the explanation that not only the capillary wall but also the membrane of the liver cells is very easily permeable to phosphatides. The capillary wall of the lungs, kidneys, spleen, heart, small intestine, brain, and muscles is but fairly permeable, its permeability decreasing in the above sequence. The uptake of labelled phosphatides by 1 gm. muscle makes out only about 1/170 part of the labelled phosphatides taken up by 1 gm. liver. The corresponding figure for the small intestine mucosa is about 1/20.

Formation and exchange of phosphatides in the liver.

It is of interest to compare the amount of phosphatides synthesized in the liver with the amount which reaches the liver through an exchange process from the plasma. In the first case, we investigate the formation of labelled phos-

phatide molecules, in the second case no new labelled molecules were formed but all the labelled phosphatide molecules present were taken up by the liver from the plasma. This uptake is presumably followed by the release of a similar amount of phosphatide molecules previously present in the liver. An alternative explanation would be that the uptake of phosphatide molecules from the plasma by the liver is followed by a destruction of these molecules in the liver, the phosphatides lost by the plasma being replaced by phosphatides synthesised in other organs and liberated into the circulation.

As found by us, in the course of 4 hours 150 mg. liver phosphatides were newly formed, while during the same time 52 mg. phosphatides are carried from the plasma into the liver; if this amount is not replaced, at least to a large extent, by an equal amount of phosphatides migrating in the opposite direction, then it must be supplied by another source to the plasma. The organ responsible for such a supply must be one in which phosphatide molecules are formed at an appreciable rate. This is primarily the case — besides the liver — in the small intestine. We have, therefore, to ask if the amount of phosphatides supplied during 4 hours by the intestine into the circulation suffices to compensate the uptake of phosphatide molecules by the liver from the plasma. SÜLLMANN and WILBRANDT (1934) determined the amount of phosphatides carried into the circulation by the intestinal lymph of the rabbit. They found that up to 1/2 mg. phosphatide P can be carried by the lymph stream in the course of 4 hours, thus appreciably less than given off by the plasma to the liver during the same time. As the amount of phosphatides brought into the circulation from the intestine does not suffice to com-

pensate the loss of phosphatides by the plasma due to the uptake of phosphatide molecules by the liver, we can hardly expect the amount released by other organs to compensate the loss of the phosphatides. We have, thus, to conclude that in the liver not only a very marked turnover of phosphatides takes place, but that phosphatide molecules exchange also with great ease between the liver cells and the plasma.

Calculation of the amount of phosphatides given off by the plasma to the liver.

We saw that, after the lapse of 4 hours, 29 to 38 per cent of the labelled phosphatide molecules originally present in the plasma were found in the liver of rabbits. We wish to calculate from the average of these figures the total amount of phosphatides which, originating from the plasma, reached the liver in the course of 4 hours. When calculating this amount, we must envisage that large amounts of labelled phosphatides were taken up by the liver and, to some extent, by other organs as well and were replaced by non-labelled ones. These processes clearly lead to an increase of the sensitivity of the radioactive indicator in the course of the experiment. While, at the start of the experiment, 1 count indicates, for example, 1 μ mg. phosphatide P, at the end of the experiment it will indicate the presence of 5 μ mg.

Let us denote by L_0 the concentration of the labelled phosphatide molecules of the plasma at the start of the experiment, and by L_t that found after the lapse of t hours. The amount of phosphorus corresponding to L_0 (average of the values obtained in two experiments) was found to

be 2.4 mg. The decrease of the labelled phosphatide content of the plasma is assumed to take place according to the equation

$$L_t = L_0 e^{-\lambda t},$$

where λ is the constant of disappearance (analogous to the decay constant of radioactive bodies). If the liver alone would take up phosphatide molecules from the plasma, the amount of labelled phosphatides which, coming from the plasma, were located in the liver, would be equal to $L_0 - L_t$. As this is not the case, we must determine experimentally the percentage of the labelled plasma phosphatides present in the liver at the end of the experiment, which we denote by E. To arrive at the figure giving the percentage of the total amount of plasma phosphatide molecules (X) which were found in the liver after the lapse of t hours, we must multiply E by

$$\frac{\lambda t}{1 - e^{-\lambda t}} = Y.$$

From $\lambda = 0.69$ hour^{-1}, and $t = 4$ hours, it follows[1] that

$$Y = 3.$$

The value obtained for Y is too high, as the decrease of the labelled phosphatide content of the plasma takes place in the later stages of the experiment at a slower rate than according to the equation mentioned above. By taking into account this deviation we arrive at the values

$$Y = 2.6 \text{ and } X = 87.$$

[1] We are much indebted to Mr. ARLEY for kindly carrying out this calculation.

From the fact that the phosphatide content of the plasma of the rabbit amounted to 60 mg. it follows that, from the phosphatide molecules present in the liver after the lapse of 4 hours, 52 mg. were such as migrated from the plasma into the liver during the experiment.

Rate of penetration of phosphatides from the organs into the plasma.

We can draw conclusions as to the rate of penetration of labelled phosphatides from the organs into the plasma from an entirely different type of experiments as from those discussed in this paper. We administer labelled inorganic phosphate to rabbits and follow the rate at which labelled phosphatides accumulate in the plasma of such rabbits. Since the amount of labelled phosphatides formed in the plasma can practically be disregarded, we can follow that the labelled phosphatides present in the plasma were brought there from the organs, primarily from the liver. If, in first approximation, we disregard the labelled phosphatides liberated from other organs into the plasma, we find that, in the course of 4 hours, 1.1 per cent of the labelled phosphatides formed during that time in the liver were brought into the circulation, which amount corresponds to about 1/6 of the plasma's phospatide content. We arrive then at the result that about 16 per cent of the plasma phosphatides were replaced, in the course of 4 hours, by labelled phosphatides formed in the liver in the course of the experiment. As, in the early stages of the experiment, the labelled phosphatide content of the liver was much lower than in the later stages, we can expect the amount of total phosphatides liberated from the liver

into the plasma in the course of 4 hours to be larger than 16 per cent of the phosphatide content of the latter.

In the course of 12 hours, we found the labelled plasma phosphatide content to amount to 1/18 of that of the liver. In this experiment, an almost proportional partition of the labelled phosphatide molecules between plasma phosphatides and liver phosphatides was obtained, as the distribution coefficient of the labelled phosphatides between liver phosphatides and plasma phosphatides works out to be 0.76.

Summary.

Plasma of rabbits containing labelled phosphatides was injected to other rabbits. Plasma samples of the last mentioned rabbits were taken at intervals and their labelled phosphatide content determined. The labelled phosphatide content of the organs was determined as well. The labelled phosphatides were found to disappear at a fairly rapid rate from the circulation. Half of those originally present left the circulation in the course of about 1 hour.

The labelled phosphatide molecules penetrate at a fast rate into the interspaces of the liver, at a much slower rate into that of other organs; the sequence of the decreasing rate of penetration being lungs, kidneys, spleen, heart, small intestine, brain, and muscles.

The accumulation of labelled phosphatides in the liver in the course of 4 hours was ten times larger than expected in the case that the interspaces alone contained these phosphatides. From this fact follows a very great permeability of the cell walls of the liver to phosphatides. This is not the case for the other organs investigated. In view of the small amounts of phosphatides which penetrate, in the

course of 4 hours, from the plasma into the muscles and the brain, we can conclude that the exchange of phosphatides between the cells of these organs and the circulation is almost negligible.

The total amount of phosphatides taken up from the plasma by the liver in the course of 4 hours was found to be 52 mg. This uptake is accompanied by a migration of a similar amount in the opposite direction. Not only is the rate of turnover of phosphatides in the liver very high, the exchange of phosphatide molecules between the liver cells and the plasma takes place at a much higher rate than the corresponding process between other organs and the circulation.

In the course of 17 min., about 65 per cent of the labelled phosphatides originally present in the plasma of the chicks left the circulation.

Administration of large doses of histamin had no very striking effect on the rate of penetration of phosphatides through the capillaries of the chick.

We wish to express our hearty thanks to Professor Niels Bohr for numerous facilities kindly put at our disposal, to Professor A. Krogh for many valuable suggestions, and to Dr. H. Dam for his effective help in carrying out the experiments on chicks.

Institut for teoretisk Fysik, København.

Indleveret til Selskabet den 29. April 1940.
Færdig fra Trykkeriet den 6. Juli 1940.