the plasma. This seems not to be the case in the blood after it is taken from the body.

TABLE II.

TO ILLUSTRATE EFFECT OF TIME AFTER DRAWING BLOOD ON THE INORGANIC PHOSPHATE.

	Within ½ Hr.	Within 1 Hr.	After 5 Hrs.	After 20 Hrs.
I. Plasma.....		2.4	2.5	
Blood.....	2.5	2.8	3.3	
II. Plasma.....		2.55		2.53
Blood.....	2.6	3.08		4.02

These results lead to the following conception of the rôle of inorganic and organic acid soluble phosphorus in the blood: The red cell is totally permeable to the phosphate ion, *i.e.*, no "osmotic influences" control the distribution of the phosphate ion inside and outside of the cell. Phosphate ions can be taken up by the cell and stored as organic acid soluble phosphate (Iverson). This organic phosphate is hydrolyzed very easily when there is need for phosphate ion in the plasma, similar to the liver glycogen yielding blood sugar. The diffusion of the phosphate out of the cell, however (at least in vitro), is slower than its rate of formation by hydrolysis. To substantiate this view we will still have to show under what conditions inorganic phosphate can diffuse out of the cell. We have no indication so far that phosphate distribution is influenced by the CO_2 tension. We are now collecting data on this point, as well as on the whole subject from the point of view of the acid soluble phosphate.

79 (1826)

Observations on the inorganic phosphate of blood in experimental rickets of rats.

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The work of Howland and Kramer[1] on the level of the inorganic phosphate in the blood in human rickets, and some con-

[1] Howland, J., and Kramer, B., *Amer. Jour. Dis. of Child.*, 1921, xxii, 105.

firmatory experiments undertaken by Hess[1] led to the conclusion that during the period of active rickets in children, the inorganic phosphate of the blood is reduced, and that during the process of cure by either sunlight or cod-liver oil, the phosphate rises again to its normal level.

Since the experimental rickets produced in rats is comparable in most important respects to human rickets, it was thought of interest to determine whether the same changes in blood phosphate could be demonstrated in rats. In applying the work of Howland and Kramer to experimental rat rickets, we have obtained results which on the whole agree very well with those of theirs reported at a recent meeting of the Society of Biological Chemists.

Because of the small quantities of blood which can be obtained from the animals, it seemed advisable to make the determinations on whole blood rather than plasma if possible. Experiments undertaken to show the relative distribution of the inorganic phosphate in plasma and whole blood indicate that the level of the phosphate is practically the same inside and outside the cells and is maintained at a constant level from day to day. Therefore, as far as the inorganic phosphate is concerned, it is immaterial whether the determinations are made on whole blood or plasma. (By the colorimetric method of Bell and Doisy.[2])

Table I shows average figures for the inorganic phosphate in theb lood of rats on rickets-producing, normal and high phosphorus diets.

TABLE I.

INORGANIC PHOSPHATE OF RAT'S BLOOD.

Inorganic Phosphate as Mgs. P per 100 c.c. Whole Blood.

Diet.			No. of Rats.	Determinations.	Rickets.	Blood Phosphate.		
No.	% P.	% Ca.				Max.	Min.	Av.
Norm..	?	?	55	43	None in 95%	8.2	5.1	6.2
84.....	86	550	40	18	Marked in 100%	4.9	2.0	3.2
D.....	72	380	10	7	Marked in 100%	5.0	2.3	3.5
85.....	160	550	7	2	Sl. osteoporosis	5.5	5.3	5.4
E.....	120	380	16	14	Sl. rickets in 25%	7.4	3.1	6.1
85 c...	596	020	16	6	Mod. atypical ric.	7.6	6.0	6.6
F.....	596	015	12	9	Mod. atypical ric.	9.8	6.5	8.4
G.....	310	550	3	3	None	9.8	9.4	9.6

[1] Hess, A. F., and Gutman, P., PROC. SOC. EXPER. BIOL. AND MED., 1921, xix, 31.

[2] Bell and Doisy, *J. Biol. Chem.* 1920, xliv, 55.

We find that in general a reduction in the inorganic phosphate of the blood runs parallel to the degree of severity of the rachitic lesions. It will also be seen that the blood phosphate of rats (on these rather specialized diets) may be greatly influenced by the level of phosphate intake. On normal diets the range is from 5.0 to 8.2, averaging 6.2, and on high phosphorus intake a very wide range from 6.0 to 9.8, averaging about 8.5 (mg. P per 100 c.c.).

The dividing line between rickets-producing diets is however sharp. Rats on diets containing 86 mg. per cent. phosphorus all develop rickets and the range of blood phosphate from 2.0 to 5.0 averages usually around 3.2. When as little as 75 mg. per cent. phosphorus is added to the diet, the rachitic lesions fail to appear and the blood phosphorus averages between 5.5 and 6.0.

The study of the blood phosphate on rats under light or cod-liver oil therapy brings up several interesting points.

TABLE II.

PREVENTION AND CURE OF RICKETS.

Inorganic Phosphate as Mgs. P per 100 c.c. Whole Blood.

Diet.	No. of Determinations.	Treatment.	Rickets.	Blood Phosphate.		
				Max.	Min.	Av.
84	18	Untreated	Beading + to +++	4.9	2.0	3.2
84	10	Mercury vapor lamp	Beading + to +	5.4	2.9	4.1
84	8	Cod-liver oil preparations	Calcification + to +++	5.9	2.4	3.95

As shown in Table II one group of rats on diet 84 (containing 86 mg. per cent. P) were treated with the light from the mercury vapor lamp as a preventive measure. In almost every case complete prevention was secured but the blood phosphorus, while distinctly above that of the controls, was nevertheless in the upper range of rachitic blood. This would seem to indicate that the rats can produce non-rachitic bone at a lower level of phosphorus intake, under the influence of light, than is possible without its presence.

Curative experiments with cod-liver oil preparations on another group of rats on the same diet show active calcification of cartilage

going on while the blood phosphate is still in the rachitic range. We therefore conclude that a definite deposition of calcium salts may occur before the blood phosphorus regains its normal level. We have as yet no experiments in which the rats were carried through till the healing process was complete, but if we may draw analogies from the work of Howland and Kramer on human rickets, we ought to find that when healing is complete the blood phosphate will regain and maintain its normal level. It seems therefore that calcification is not directly controlled by the level of the blood phosphate. Experiments are, however, in progress to determine the nature of the relation between these two factors.

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Experiments with quinidine on conduction and on the refractory period in the dog's heart.

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These experiments are based on the theory of fibrillation developed by Garrey and Mines on the suggestion of A. G. Mayer and recently elaborated by T. Lewis. The theory, although it illustrates best the condition known as flutter, is directly applicable also to the state of fibrillation. In the normal heart the stimulus for contraction arises at the sinus node and passes in a radial fashion to the rest of the muscle of the auricle. In flutter, and in fibrillation, there is apparently no fixed point at which the stimulus originates. It appears to be dislocated from the node but it is not yet known what activity goes on in this structure when the abnormal rhythm prevails. Instead of the usual arrangement, an excitation wave courses continuously through the muscle of the auricle, usually over a circular path about the openings of the great veins, as Lewis's experiments show. In order that a continuous circuit may be maintained it appears to be necessary (1) that the path shall have a sufficient length; (2) that the rate of passage shall be sufficiently slow, and (3) that when the stimulus returns to its starting point, the muscle is ready to receive it. It is clear, on this plan, that: (1) if the muscle