OSMOTIC HOMEOSTASIS MAINTAINED BY MAMMALIAN LIVER, KIDNEY, AND OTHER TISSUES*

By EUGENE L. OPIE, M.D., and MARY B. ROTHBARD, M.D.

(*From the Laboratories of The Rockefeller Institute for Medical Research*)

(Received for publication, November 24, 1952)

The osmotic changes that red blood corpuscles undergo under varied conditions have been carefully studied during the last half century but little attention has been given to the osmotic activity of cells of fixed tissues. Readily observed hemolysis soon showed that red corpuscles were isotonic with solutions of which the ionic concentration approximates that of blood plasma and it was assumed that these solutions, namely, physiological salt solution or Ringer's fluid, were most favorable for the preservation of mammalian tissues generally. Those who have used manometric methods for the study of supravital phenomena have seldom questioned this assumption.

The osmotic pressure maintained by cells or interstitial tissue may be measured by immersing weighed slices of tissue in solutions of sodium chloride or other electrolytes immediately after the removal of the tissue from the body (1, 2). The changes of weight that occur during the first few minutes of immersion indicate the concentration that is isotonic with the tissue. By this procedure liver has been found to be isotonic with solutions of sodium chloride with molar concentration more than twice that of plasma or of red blood corpuscles. Kidney cortex is isotonic with similar solutions with somewhat less than twice the same molar concentration.

The aims of the present study have been to learn if the osmotic pressure of tissues determined by their isotonicity in solutions of electrolytes is a measure of the osmotic pressure they maintain during life and to determine some of the conditions under which this pressure is kept constant or impaired.

Method

Slices of tissue from white rats or other mammalian species have been cut with a razor blade and have been approximately 0.5 mm. in thickness and 5 by 1.5 mm. (1). They have been weighed on a torsion balance and then immersed in solutions of sodium chloride usually varying in concentration from 0.1 to 0.5 molar. They have remained immersed during 10 minutes at room temperature varying from 20–25°C. In later experiments the temperature has been kept constant at 20°C., but the rate of water exchange has not been obviously modified. Immediately after removal from its immersion fluid each slice has been applied gently

* This study was conducted with the aid of grants from The Jane Coffin Childs Memorial Fund for Medical Research and The Anna Fuller Fund.

to cotton gauze and turned three times in order to remove adherent fluid. The slices have been again weighed and the per cent change in weight determined.

Isotonicity of Rat Tissues

Water exchange of parenchymatous tissues, of the rat, namely liver, kidney, pancreas, and submaxillary gland, maintains an approximately linear course when plotted in relation to the concentration of the solutions and the point at which this line crosses the abscissa marks the level of isotonicity.

The changes that follow similar immersion of dense fibrous tissue, for example that of corium of the skin, tendon, tendinous fascia of muscle and wall of the aorta, do not pursue the same course but take up water in strong as well as weak solutions and fail to reach a level of equilibrium (2, 3). These tissues immersed in solutions of sodium chloride exhibit the same water exchange as gelatin.

It is probable that several factors may modify the water exchange of liver tissue immersed in solutions of sodium chloride. Though the animals have been killed by bleeding and the vena cava has been cut the quantity of blood that remains in the liver doubtless varies somewhat. The successive slices that are used, though cut as far distant as possible from the hilum of the lobe, may contain a variable quantity of fibrous tissue and the wall of a moderately large blood vessel included in the section may increase the intake of water in the stronger solutions (2). Deviation from the linear relation of water exchange to concentration when it occurs, suggests that osmotic relations of the parenchymatous cells have been disturbed by these or other factors. Nevertheless an almost constant average of isotonicity indicates that the errors which occur tend to balance one another.

Liver:

The average of 10 determinations of the osmotic pressure of liver tissue measured by its isotonicity with solutions of sodium chloride (1) has been that of a solution of 0.34 molar. When liver tissue protected from evaporation has been kept at 37°C. during 100, 120, and 180 minutes, sliced and immersed in solutions of sodium chloride, molecular concentration as the result of autolysis has increased so greatly that its isotonicity is uniformly greater than that of 0.4 molar sodium chloride and it draws water from solutions of this concentration (1). At lower temperatures the change is much delayed. When measurements of isotonicity by the procedure described are grouped (Table I) with reference to the time interval at room temperature between the death of the animal and the immersion of the tissue, the average level of isotonicity has been the same for determinations made within 1 hour and those made between 1 hour and 1½ hours. The tissue has been in both instances, isotonic with sodium chloride 0.34 molar. After a longer interval there may have been some elevation of the level of isotonicity but the observed change is not significant.

These figures indicate that the ionic concentration within the tissue remains essentially unchanged during a period of almost 1½ hours after somatic death.

In later experiments it has been possible to reduce to 5 minutes the time interval between death of the animal and immersion of the tissue. Possible causes of delay have been avoided and estimation of isotonicity has been limited to the results of immersion of liver slices in 0.3 and 0.4 molar sodium chloride. After from 4½ to 5½ minutes following death the average isotonicity of liver tissue from 3 rats has been at the level of 0.30 molar sodium

TABLE I

Isotonicity of Liver Tissue with Molar Solutions of Sodium Chloride at Intervals after Death

No. of animal	Up to 60 min.		60 up to 90 min.		More than 90 min.	
	Time interval	Molar solution	Time interval	Molar solution	Time interval	Molar solution
	min.		*min.*		*min.*	
1	21	0.244	68	0.265		
2	25	0.383	86	0.272		
3	45	0.481	83	0.400		
4	49	0.350				
5	56	0.292	77	0.294		
6	56	0.322	76	0.361		
7	60	0.312	81	0.367		
8			61	0.400	104	0.356
9			63	0.350		
9			84	0.369		
10			66	0.291	116	0.400+
11			67	0.339	116	0.350
12			68	0.342		
12			89	0.329		
13			76	0.442	97	0.388
14					93	0.227
Average.....		0.341		0.344		0.355+

chloride. The corresponding figures obtained with slices of liver from the same animals have been, after 25 minutes, 0.27 molar and, after 50 minutes, 0.31 molar.

Kidney:

Kidneys from four rats, as stated in a former publication (1), were isotonic with solutions of sodium chloride which averaged 0.25 molar. Isotonicity of kidneys from normal rats examined later have varied from 0.2 to 0.29 and have averaged 0.23 molar (Table II). Kidney slices immersed 1 and 2 hours after death have had, with about the same range of variation, the same average

isotonicity; that is, the molecular concentration of the tissue has remained approximately unchanged during 2 hours at room temperature.

TABLE II

Isotonicity of Kidney Cortex with Molar Solutions of Sodium Chloride at Intervals after Death

Up to 60 min.			60 up to 90 min.			More than 90 min.		
No. of animal	Time interval	Molar solution	No. of animal	Time interval	Molar solution	No. of animal	Time interval	Molar solution
	min.			*min.*			*min.*	
1	25	0.20	8	63	0.21	12	97	0.26
2	33	0.20	9	82	0.20	13	113	0.27
3	38	0.23	10	89	0.27	14	114	0.21
4	50	0.20	11	89	0.24	15	117	0.26
5	52	0.29						
6	58	0.26						
7	59	0.22						
Average.....		0.23			0.23			0.25

TABLE III

Isotonicity of Pancreas with Molar Solutions of Sodium Chloride at Intervals after Death

No. of animal	Up to 30 min.		30 up to 60 min.		More than 60 min.	
	Time interval	Molar solution	Time interval	Molar solution	Time interval	Molar solution
	min.		*min.*		*min.*	
1	16	0.32				
2	16	0.31	40	0.30		
3	19	0.21				
4	24	0.25			110	0.40+
5	25	0.25	46	0.40+		
6	26	0.37			110	0.40+
7	27	0.27				
8			34	0.50+	110	0.54
9			39	0.47		
10			45	0.42		
11			49	0.33		
12			53	0.44		
13					66	0.60+
Average.....		0.28		0.41+		0.49+

Pancreas:

Pancreas immersed within 30 minutes after death has been found isotonic with solutions of sodium chloride varying in concentration from 0.21 to 0.37, the average being 0.28 molar (Table III). Pancreas that has remained during

30 to 60 minutes after removal at room temperature has in 5 instances been isotonic with similar solutions from 0.3 to 0.47 molar and in two instances the tissue has drawn water from all solutions tested up to 0.4 to 0.5 molar. After 60 minutes pancreas in all instances has drawn water from solutions with concentration of 0.4 to 0.5 molar (indicated in Table III by +). Pancreas does not maintain its first level of isotonicity as long as liver or kidney.

Submaxillary Gland:

Isotonicity of the submaxillary gland in tests made within the 1st hour after removal from the body (Table IV) has varied considerably. After intervals of 1 to 2 hours isotonicity under the same conditions has varied through a wider

TABLE IV

Isotonicity of Submaxillary Gland with Molar Solutions of Sodium Chloride at Intervals after Death

No. of animal	Up to 60 min.		More than 60 min.	
	Time interval	Molar solution	Time interval	Molar solution
	min.		*min.*	
1	36	0.30		
2	46	0.40		
3	47	0.28		
4			67	0.50+
5			73	0.36
6			93	0.28
7	52	0.33	120	0.37
Average.....		0.33		0.38+

range and in one instance the tissue has drawn water from all solutions of concentration up to 0.4, 0.5, or 0.6 molar (indicated in Table IV by +). With the submaxillary gland as with the pancreas the level of isotonicity may increase after an interval greater than 1 hour following removal from the body.

Isotonicity of Tissues of Mouse, Guinea Pig, Rabbit, and Cat

Tests have been undertaken to determine whether tissues of several available species of animals exhibit osmotic changes similar to those of the rat. The isotonicity of slices of liver, kidney, and pancreas determined by immersion in solutions of sodium chloride is recorded in Table V.

The level of isotonicity in the animals examined has been consistently smaller for kidney than for liver.

Isotonicity of Tissue from Cortex and Medulla of the Kidney:

Slices of kidney cortex of the rat, cut somewhat less than 1 mm. in thickness and concentric with the surface of the organ, have been compared with those

from a lower level. Microscopic examination shows that the outermost slice consists of cortex characterized by the presence of glomeruli and convoluted tubules whereas the slice below is in large part the outer zone of the medulla, recognized microscopically by loops of Henle and collecting tubules. The inner part of the medulla is characterized by its gray-white color. Slices limited to

TABLE V

Isotonicity of Liver, Kidney, and Pancreas from Several Mammalian Species

	Liver	Kidney	Pancreas
	molar	*molar*	*molar*
Mouse	0.33		
"	0.33	0.25	
"	0.36	0.30	
"	0.35	0.29	
"	0.33	0.31	
Average	0.34	0.29	
Guinea pig	0.42	0.21	0.36
" "	0.33	0.21	0.43
" "	0.33	0.22	0.29
" "	0.43	0.25	0.23
" "	0.40	0.24	
Average	0.38	0.23	0.33
Rabbit	0.35	0.29	0.28
"	0.33	0.29	0.20
"	0.28	0.25	0.17
"	0.33	0.25	0.27
Average	0.32	0.27	0.23
Cat	0.37	0.29	

these different parts of the kidney are more accurately prepared from animals larger than the rat; namely, from guinea pig, rabbit, or cat.

The levels of isotonicity found in cortex on the one hand, and outer zone of the medulla on the other, have not differed significantly (Table VI) though the figures suggest that higher levels may be reached in the outer medullary zone. Graphs prepared for the two zones of each animal to show water intake plotted in relation to the concentration of sodium chloride solutions have pursued an approximately linear course which crosses the abscissa at the point of equilibrium. Those representing water changes in immersed pieces of the inner zone of the medulla have shown so much fluctuation that the point of equilibrium is uncertain (indicated in Table VI by question marks).

The Effect of Pathological Changes on the Osmotic Pressure Maintained by Liver and Kidney Tissue

Earlier studies (4) have shown that certain substances that injure the cells of the liver when administered to animals, namely chloroform and carbon tetrachloride, reduce the osmotic pressure of liver tissue so that it falls to the level of the blood serum but is promptly restored when recovery ensues. Similar changes occur in the cortex of the kidney when cells of the contoluted tubules are injured by potassium chromate. The effect of various injuries on the osmotic pressure normally maintained by liver and kidney has now been

TABLE VI

Isotonicity of Kidney Tissue from Cortex and Medulla Tested with Solutions of Sodium Chloride

	Cortex	Outer zone of medulla	Inner zone of medulla
	molar	*molar*	*molar*
Rat	0.20	0.28	0.32 (?)
"	0.20	0.18	0.31 (?)
"	0.23		0.24
Average	0.21	0.23	
Guinea pig	0.22	0.22	0.20 (?)
Rabbit	0.29	0.38	0.40+
"	0.29	0.25	0.42
"	0.25	0.28	0.22
"	0.25	0.30	0.26 (?)
Average	0.27	0.30	
Cat	0.29	0.28	0.21 (?)

studied. The injurious agencies selected have been withdrawal of food, injury by low protein diet, ligation of the common bile duct, and ligation of one ureter.

Withdrawal of Food:

Experiments on rats have shown that withdrawal of food with free access to water during at least 7 days has had little effect upon the osmotic pressure maintained by liver tissue as determined by immersion of slices in solutions of sodium chloride (Fig. 1). During successive days the average figure representing isotonicity has not varied significantly from that obtained with liver tissue of well fed animals (Table I). Similarly the average concentration of salt solution isotonic with the kidneys of fasted animals (Fig. 2) has remained almost identical with that of kidneys of normal animals (Table II).

Pancreas and submaxillary gland tissue undergo within 30 minutes after

removal from the body changes which modify their water exchange when in solutions of sodium chloride (Table III) and in all instances slices of tissue from fasted animals have been immersed within this interval. Observations have been few (Fig. 3) but with tissue from both organs the level of isotonicitv has

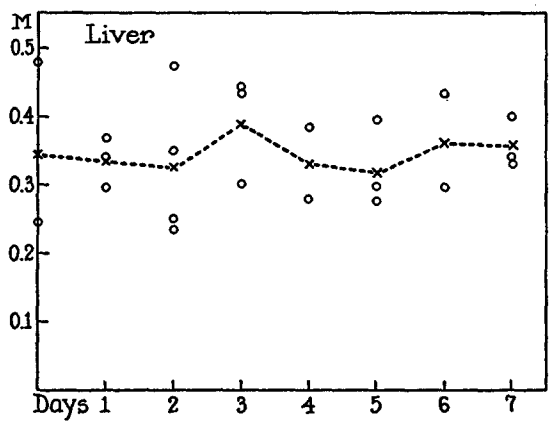

FIG. 1. Showing the isotonicity of slices of liver from rats that have received water but no food during 7 days. The average isotonicity on sucessive days is indicated by the broken line.

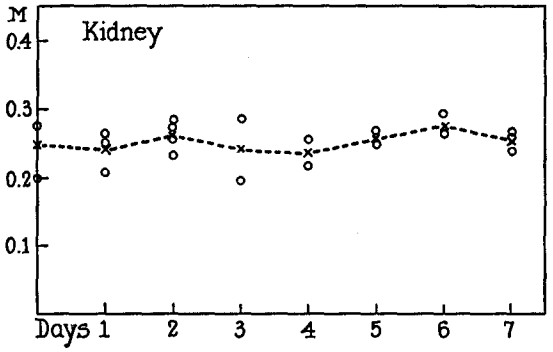

FIG. 2. Showing the isotonicity of slices of kidney from rat with food withdrawn (as in Fig. 1).

risen during the 2nd and 3rd day of fasting. It is possible that in some instances this change accompanies inactivity of these two glands.

Protein Deficiency:

Experiments have been undertaken to determine the relation between osmotic pressure maintained by liver parenchyma and the injuries to liver tissue caused by a diet with low protein content. The diets administered have been similar to those used by György and Goldblatt (5) and have contained, in addition to

vitamins and salts, protein as casein in the proportion of 5 per cent, carbohydrate (cerulose), 89 per cent, and cod liver oil, 2 per cent. Fat, as visible globules, appears promptly in liver cells and is abundant after from 2 to 3 weeks. Nevertheless it is not uniformly distributed throughout the organ and may be much more abundant on the left side, that is in the large left lobe, the left central, and the caudate lobes, than in the right upper and right central lobes. The quantity of fat in the small right lower lobe usually conforms with that on the left side. The lobes on the left side during the early period of diet administration may have a uniform bright yellow color whereas those on the right may be brownish red and normal in appearance. The deposition of fat in greater quantity on the left side has been observed by Glynn, Himsworth, and Lindan (6). After about 100 days cirrhosis appears and tends to advance more rapidly

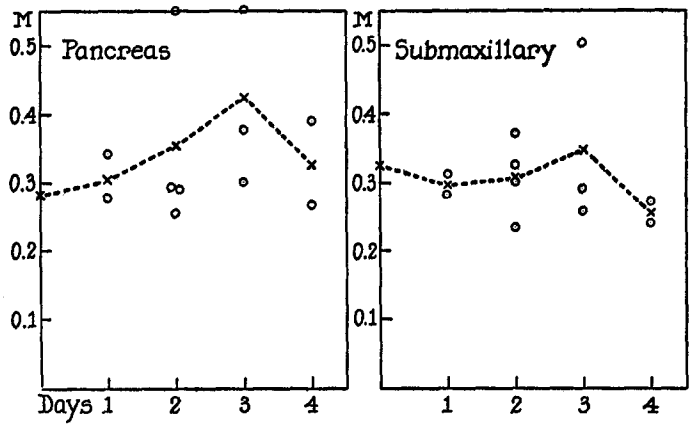

FIG. 3. Showing (*a*) the isotonicity of slices of pancreas of rats with food withdrawn (as in Fig. 1); (*b*) the isotonicity of submaxillary gland of the same animals.

on the left side in the lobes where deposited fat had been more abundant. When a diet containing 8 per cent of protein (casein) and 36 per cent of fat (Crisco) is administered to rats visible fat is deposited in the liver cells in great abundance and is uniformly distributed throughout the organ.

The progress of changes in the level of isotonicity measured by immersion of liver slices in salt solutions of differing concentration has been studied in animals given the diet containing 5 per cent of protein and only 2 per cent of fat (cod liver oil) and killed at intervals of about 2 weeks during the first 251 days of dieting (see Fig. 3). In most of the animals two determinations have been made, one with tissue from the right central lobe or right upper lobe and the other from the left lobe. The level of isotonicity has varied in the same animal and in different animals but during the period from 30 to 90 days of diet administration has been uniformly below the average for normal animals. There has been no constant relation between the level of isotonicity and fat deposition in liver cells but when accumulation of fat has been conspicuously greater in the

left lobe its level of isotonicity has been somewhat higher than that in the right lobe that has been examined. In the period between 90 and 126 days wide fluctuations in the level of isotonicity have occurred. These are perhaps referable to profound liver injury on the one hand or regenerative changes on the other. Regenerative changes are in part new formation of fibrous tissue and in part regeneration of liver cells.

A second group of animals has been given the same diet and killed for examination, in part after about 100 days, and in part after about 160 days

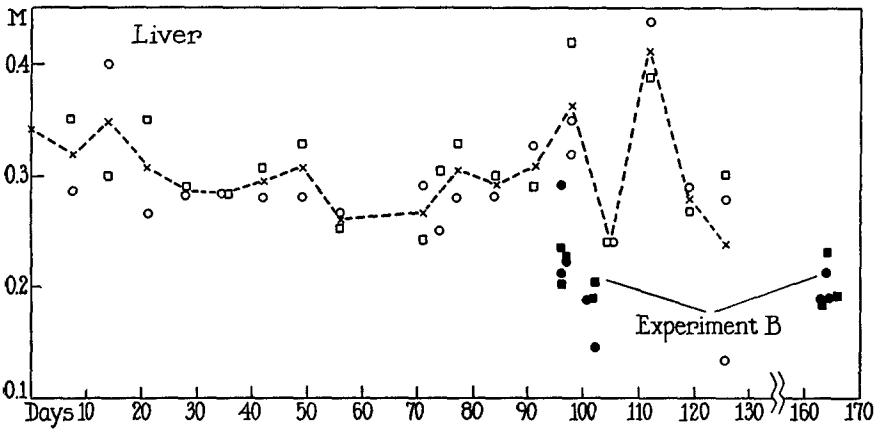

FIG. 4. Showing the isotonicity of slices of liver from rats that have received a low protein and low fat diet during a prolonged period. Determinations are in duplicate from each liver, one indicated by a circle from the right side of the organ and the other indicated by a quare from the left side. One group of animals represented by open circles and squares weres killed at intervals of 2 weeks or more. A second group indicated by solid black circles and squares were killed between 96 and 102 days of diet administration and between 163 and 165 days (Experiment B).

(indicated in Fig. 4 by solid black circles and squares). The level of isotonicity in these animals has been uniformly low.

Results of Ligation of the Common Bile Duct:

Experiments have been undertaken to determine the effect of ligation of ducts upon the water equilibrium of slices of liver or of kidney immersed in solutions of sodium chloride. Ligation of the common bile duct is promptly followed by increase of pressure within the duct, by jaundice, and by injury to liver cells. Following ligation the level of isotonicity of liver tissue (Fig. 5) has fallen gradually from the normal level of 0.35 molar to approximately 0.25 molar after 6 days and has later tended to rise to its former level though jaundice persists. The determinations have not been multiplied because the liver has shown evident ability to maintain a level considerably above that of the blood in spite of the injury which it has sustained. During the period of

continued jaundice at the time when osmotic pressure of liver tissue has been depressed the isotonic level of kidney tissue has been unchanged (Fig. 5).

Results of Ligation of One Ureter:

Observations concerning the osmotic changes in the kidney after ligation of its ureter (Fig. 6) have the advantage that they can be controlled by similar

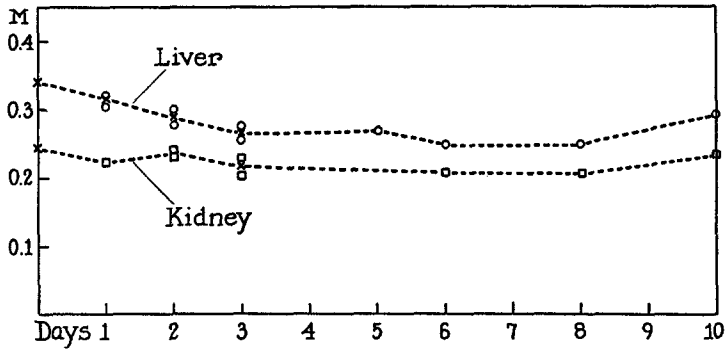

FIG. 5. Showing the isotonicity of slices of liver and of kidney from animals killed at intervals after ligation of the common bile duct. Circles indicate liver and squares, kidney.

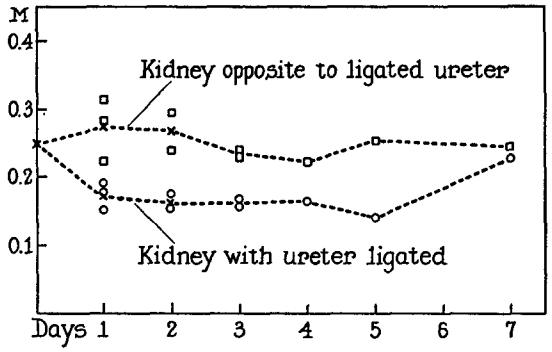

FIG. 6. Showing the isotonicity of slices of kidney from animals killed at intervals after ligation of one ureter. Circles indicate kidneys with ureter ligated; squares indicate kidney opposite to that with ligated ureter.

examination of the other kidney. With experimental ureteral occlusion pressure rises within the ureter, hydronephrosis with compression of both cortex and medulla ensues, and there are atrophy and fatty change of the cells of the convoluted tubules of the cortex.

During 1 week osmotic pressure of tissue from the relatively normal kidney remains essentially unchanged at about the normal level, namely 0.23 molar, whereas that of tissue of the kidney with ureter ligated falls within 24 hours to a level only slightly higher than that of the blood. This pressure has been little

changed during the next 5 days and has then risen to its former level. Restoration of the level of osmotic pressure occurs in the presence of profound changes in the tissue and requires further investigation.

RECAPITULATION AND DISCUSSION

Earlier publications (1, 2) have shown that slices of liver or kidney tissue when immersed in solutions of sodium chloride maintain an osmotic pressure much higher than that of blood and are in water equilibrium with solutions much more concentrated than those isotonic with red blood corpuscles. These observations have been confirmed by Robinson (7, 8). Little attention has been given to similar observations made long ago. Filehne and Biberfeld (9) weighed pieces of liver and kidney of the rabbit after immersion in solutions of sodium chloride and in a brief note state that the tissues took up water in 1.5 per cent solutions. Hirokawa (10) found that kidney cortex of pig, cow, rabbit, and cat was in water equilibrium with solutions of sodium chloride between 1 and 2 per cent.

It may be suspected that changes of molecular concentration within the cytoplasm of cells occur as the immediate result of injury or death of cells and bear only indirect relation to the osmotic pressure maintained by living cells. Evidence contrary to this assumption is the fall of osmotic pressure which occurs when the functional activity of liver or kidney is impaired by injurious agents administered parenterally as, for example, chloroform or carbon tetrachloride in case of the liver and potassium chromate in case of the kidney. Osmotic pressure exhibited by these tissues then falls to a level approximating that of blood but returns to its former level if recovery occurs. Another instance of diminished osmotic pressure in association with impaired functional activity is that which occurs when hepatomas (2) are formed from liver cells by the action of butter yellow; osmotic pressure maintained by the tumor cells which have lost the functional characteristics of liver cells is approximately that of the blood.

The present study has shown that the osmotic pressure found with slices of normal liver and of kidney under the conditions of these experiments remains unchanged during at least 1½ hours following their removal from the body when they are kept at a temperature of 20–25°C. Changes indicating increase of the intracellular molecular concentration occur after a longer period and may be hastened by the autolysis which occurs when tissues are kept at a temperature approximating 38°C. Slices of pancreas are less resistant to the changes that follow their removal when kept at 20–25°C. but have shown no change within ½ hour.

In the present study the greater number of measurements of relative osmotic pressure have been made with tissues of the rat and the number of those made with tissues of other mammals has been small. No exact numerical relations are definable but the average ratio of isotonicity of tissue from liver or kidney

of several mammalian species to the approximate isotonicity of red blood corpuscles with 0.15 molar sodium chloride has been as follows:—

	Liver	Kidney
Mouse	2.3	1.9
Rat	2.3	1.6
Guinea pig	2.5	1.5
Rabbit	2.1	1.5
Cat (one only)	2.5	1.5

These ratios are fairly constant within the limitations imposed by the procedure employed.

Adverse agencies have been studied in order to determine how they affect the osmotic pressure maintained by tissues of some parenchymatous organs of the rat. Withdrawal of food with free access to water has produced during 7 days at least no change in the level of isotonicity of liver (Fig. 1), or of kidney (Fig. 2) tissue. Nevertheless the isotonicity of two glands, namely pancreas (Fig. 3) and submaxillary gland (Fig. 4) has reached in some instances an unusually high level on the 2nd and more conspicuously on the 3rd day of food withdrawal. From the observations on the two glands no conclusion can be drawn but it is possible that glandular inactivity may favor this temporary change.

A low protein diet (casein, 5 per cent, and fat, 2 per cent) continued through a period of 150 days (Fig. 4) has been accompanied during approximately 90 days by diminution of the osmotic pressure maintained by liver tissue, followed in the later period of observation by great fluctuations which are as yet unexplained but perhaps referable to regenerative changes in the injured liver. In the early period of low protein diet fat has accumulated in great quantity in liver cells, usually in greater abundance in the left lobes of the liver, but no relation between the intensity of fatty change and the level of osmotic pressure has been demonstrable.

Following ligation of the common bile ducts pressure within the duct increases and dilatation of its branches throughout the liver occurs. Pressure within the obstructed duct reaches 250 to 300 mm. of water in the dog and cat and is maintained in the latter without diminution during 6 days (Mitchell and Stifel (11)). It is somewhat less in the rabbit (Hering and Simpson (12)). Well known changes ensue; there is moderate accumulation of fat droplets in the parenchymatous cells about the portal spaces with some atrophy of cells, foci of necrosis in most instances, proliferation of ducts at the periphery of the portal spaces, and scant new formation of fibrous tissue at the same site. Increase of pressure within the duct is accompanied by jaundice. In the presence of these changes the osmotic pressure maintained by slices of liver tissue (Fig. 5) has fallen gradually during 5 days from the normal level, in equilibrium

with 0.34 molar sodium chloride, to that of a 0.25 molar solution. Later it tends to return to a higher level. The isotonicity of kidney tissue notwithstanding the presence of jaundice has shown little change (Fig. 5).

Study of the changes which occur in the kidney following ligation of one ureter (Fig. 6) is well controlled by observations made on the other kidney. With ligation of the ureter increases of pressure within it does not stop until it has reached 50 to 70 mm. mercury (Cushny (13)) and is accompanied by dilatation of ureter and of renal pelvis with hydronephrosis. Both cortex and medulla are compressed, tubules are dilated, and renal cells particularly those of the convoluted tubules undergo atrophy. Following ligation of the ureter isotonicity of the hydronephrotic tissue has fallen in some instances to the level of that of blood (Fig. 6) whereas pressure of the opposite kidney has remained almost unchanged. These relations have persisted during 4 days. Later the isotonicity of the kidney with ureter ligated tends to reach a higher level (present also after 13 days but not shown in Fig. 6).

SUMMARY AND CONCLUSION

Osmotic pressure maintained by liver or kidney tissue measured by its water equilibrium with solutions of sodium chloride remains unchanged from 5 minutes up to 1½ hours following removal of the tissue from the body. Then with autolytic increase of molecular concentration within the cytoplasm of cells it reaches a higher level. Osmotic pressure maintained by pancreas or submaxillary gland, as ascertained in the same way, remains unchanged during ½ hour and later increases.

Liver tissue of rat, mouse, guinea pig, rabbit, and cat maintains an osmotic pressure greater than twice that of the blood, and kidney tissue maintains an osmotic pressure somewhat less than twice that of blood.

Fasting throughout a period of 7 days has little influence upon osmotic pressure maintained by cells of liver or kidney.

Low protein diet has been found to depress osmotic pressure of liver cells after about 4 weeks, and with degenerative changes in the parenchyma, notably fatty infiltration, this pressure has remained at a diminished level during approximately 90 days.

Increase of pressure within the common bile duct and the changes following biliary obstruction are accompanied by depression of the osmotic pressure maintained by liver tissue and ligation of the ureter diminishes the osmotic pressure maintained by kidney tissue. In both instances osmotic pressure tends later to rise to its former level.

The osmotic pressure maintained by liver or by kidney tissue preserves an approximately uniform level under normal conditions and may be little changed by conspicuous injury to the organ. When this osmotic homeostasis is impaired by severe injury the pressure maintained by the tissue returns to its former level with recovery from the injury.

BIBLIOGRAPHY

1. Opie, E. L., *J. Exp. Med.*, 1949, **89,** 185.
2. Opie, E. L., *J. Exp. Med.*, 1949, **89,** 209.
3. Opie, E. L., and Rothbard, M. B., *Arch. Path.*, 1950, **50,** 800.
4. Opie, E. L., *J. Exp. Med.*, 1950, **91,** 285.
5. György, P., and Goldblatt, H., *J. Exp. Med.*, 1942, **75,** 355.
6. Glynn, L. E., Himsworth, H. P., and Lindan, O., *Brit. J. Exp. Path.*, 1948, **29, 1.**
7. Robinson, J. R., *Proc. Roy Soc., London, Series B*, 1950, **137,** 378.
8. Robinson, J. R. *Proc. Roy Soc., London, Series B*, 1952, **140,** 135.
9. Filehne, W., and Biberfeld, H., *Arch. ges. Physiol.*, 1902, **91,** 569.
10. Hirokawa, W., *Beitr. Chem. Physiol. u. Path.*, 1908, **11,** 458.
11. Mitchell, W. T., and Stifel, R. E., *Bull. Johns Hopkins Hosp.*, 1916, **27,** 78.
12. Hering, P. T., and Simpson, S., *Proc. Roy. Soc., London, Series B*, 1907, **79, 517.**
13. Cushny, A. R., The Secretion of Urine, London, Longmans, Green and Co., 2nd edition, 1926.