DISTURBANCES OF WATER-ELECTROLYTE BALANCE OF THE BLOOD AND TISSUES IN PULMONARY EDEMA CAUSED BY DIPHOSGENE AND ADRENALIN

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The few scattered items of information concerning the changes in the water-electrolyte balance of the blood and tissues in certain types of experimental edema of the lungs [1-4] demonstrated the importance of these changes in the development of pulmonary edema.

A systematic investigation has been made of the distribution of water and the main electrolytes in blood, edema fluid, and in many organs during rapidly developing adrenalin edema of the lungs (19 rabbits), and during edema developing over a period of many hours following diphosgene poisoning.

TABLE 1. Water-Electrolyte Balance of the Blood and Edema Fluid in Diphosgene and Adrenalin Edema of the Lungs

Index	Control	Diphosgene edema		Adrenalin edema	
	$M \pm m$	$M \pm m^1$	P^2	$M \pm m$	P
Hematocrit index (in % erythrocytes)	31±0,67	40±1,47 43±2,34	0,001 0,001	32±2,08	
Dry residue of blood (in %)	16,50±0,36	20,02±0,68	0,001	16,35±0,64	
Na (in mg%) of plasma	347±2,43	320±9,7 333±4,45	0,001 0,01	343±4,06	
Na of edema fluid	—	349±6,35		343±4,87	
Cl (in mg%) of plasma	348±3,85	320±3,40 323±5,36	0,001 0,001	330±4,50	<0,01
Cl of edema fluid	—	368±7,96	0,05 0,001	346±4,25	<0,02
K (in mg%) of plasma	17,9±0,37	21±2,81 41,7±3,05	0,001	29,5±2,40	<0,001
K of edema fluid	—	28,2±1,55	0,001	30±3,10	<0,01
Na of erythrocytes (in mg%)	56,0±3,40	48,5±5,82 42,6±1,46	0,02	52,47±3,13	
Cl of erythrocytes (in mg%)	165±8,05	216±13,10 227±9,30	0,01 0,001	190±13,30	
K of erythrocytes (in mg%)	372±12,00	364±19,00 357±1,10		360±6,65	

Numerator—at the height of development of edema, denominator—after death of the animal.

The values of P are given only when their differences from the control group are significant. For the edema fluid P in the numerator gives the significance of the difference from the plasma of normal blood, and in the denominator—from the plasma after the development of edema.

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TABLE 2. Weight Factors and Water-Electrolyte Composition of Certain Organs and Tissues of Healthy Rabbits and Rabbits with Diphosgene and Edema of the Lungs

Tissue	Control					Diphosgene edema		
	Weight factor	Dry residue (in %)	M±m (content per dry weight in mg%)			Weight factor	Dry residue (in %)	M±m (content per dry weight in mg%)
			Na	Cl	K			Na
Lungs	0,37±0,01	20,40±0,27	774±18,60	793±38,60	1 304±29,40	1,24±0,06 $P<0,001$	13,35±0,49 $P<0,001$	2 110±7,70 $P<0,001$
Kidneys	0,75±0,03	20,08±0,38	972±50,30	990±69,40	1 150±17,40	0,60±0,04 $P<0,001$	22,75±0,52 $P<0,001$	806±41,7 $P<0,05$
Liver	5,21±0,46	24,40±0,46	451±24,60	360±20,80	1 038±25,40	3,98±0,36 $P<0,05$	24,20±0,41	412±22,20 $P<0,05$
Spleen	82,6±13,80	21,00±0,20	554±17,50	657±108	1 800±65	47,9±3,61 $P<0,05$	21,28±0,13	637±28 $P<0,05$
Muscles	—	23,35±0,18	179±10,90	164±17,65	1 810±46,80	—	24,80±0,47 $P=0,01$	180±11,50
Skin	—	32,62±1,80	558±46,50	660±41,00	472±26,60	—	35,60±1,22	530±22,70

Tissue	Diphosgene edema		Adrenalin edema				
	M±m (content per dry weight in mg%)		Weight factor	Dry residue (in %)	M±m (content per dry weight in mg%)		
	Cl	K			Na	Cl	K
Lungs	2 005±79,50 $P<0,001$	920±50,0 $P<0,001$	0,84±0,04 $P<0,001$	15,20±0,28 $P<0,001$	1 570±124 $P<0,001$	1 470±47,50 $P<0,001$	1 047±32,80 $P<0,001$
Kidneys	571±40,60 $P<0,001$	1 031±22,6 $P<0,001$	0,62±0,02	20,70±0,55	940±67,0	850±60,5	1 120±37,0
Liver	325±20,80	1 135±39,60 $P<0,05$	4,05±0,22 $P<0,05$	24,42±0,52 —	368±26,40 $P<0,05$	282±17,00 $P<0,01$	1 109±37,80
Spleen	585±57,50	1 590±59,5 $P<0,05$	56,0±5,50 $P<0,05$	20,50±0,23	599±34,50	646±76,50	1 684±86,0
Muscles	148±9,90	1 716±49,00	—	23,30±0,42	179±12,70	132±0,91	1 705±66,0
Skin	404±55,40 $P<0,02$	422±67,0	—	30,42±1,27	677±83,0	612±52,5	397±41,0

Note. The weight factors of the lungs, liver, and kidneys are given in g/100 g, the weight factors of the spleen in μg/100 g. The value of P is given when the difference from the control group is significant.

EXPERIMENTAL METHOD

Diphosgene edema (16 rabbits) was produced by poisoning for 15 min (0.8-1.2 mg/liter). Adrenalin was injected into the femoral vein of 19 rabbits in a dose of 0.4-1.2 mg/kg. Twelve healthy rabbits were used as controls. The water content of the blood and tissue was determined by drying them to constant weight. The concentration of sodium and potassium was determined by flame photometry, and the chloride concentration by Rusniak's method. Their concentration in the tissues are expressed per unit weight of dry substance. The weight factors of the organs were determined. Before the experiment and after the development of edema the hematocrit ratio and the content of water and electrolytes in the erythrocytes and plasma were determined.

EXPERIMENTAL RESULTS

The results given in Table 1 show that in both forms of edema changes took place in the blood in the same direction, but they were much more marked in the case of diphosgene poisoning. The obvious hemoconcentration detected in diphosgene edema by the increase in the hematocrit index and in the dry residue of the bood, did not take place in the animals with adrenalin edema. This is not surprising, because, as shown by the weight factor and dry residue of the lungs (Table 2), the severity of the adrenalin edema was much less than that of the diphosgene edema. The concentration of sodium and chloride in the plasma was lowered. The decrease in the concentration of chloride was particularly marked. The sodium concentration also fell in the erythrocytes, i.e., sodium was lost from the blood into some other medium.

The concentration of chloride in the erythrocytes rose strongly, indicating its partial migration from the plasma into the erythrocyte. This type of change is characteristic of the respiratory acidosis accompanying pulmonary edema. The increase in the concentration of bicarbonate in the plasma in this state causes the transfer of corresponding amounts of chloride into the erythrocyte [2]. The potassium concentration in the plasma rose sharply, whereas in the erythrocytes it showed a slight decrease, evidently because of movement of the potassium into the plasma. Because of the fact that the potassium concentration in the blood cells is 20 times greater, a considerable release of potassium into the plasma and an increase in its concentration there need not necessarily be accompanied by any significant decrease in the potassium concentration in the erythrocytes. A high hyperkaliemia in rabbits with adrenalin edema has also been observed by Utiyama [4].

The electrolyte composition of the edema fluid, which is a filtrate of the blood plasma, differed from the original composition of the plasma and from its electrolyte composition after the development of edema. As Table 1 shows, these differences were much greater in the case of diphosgene poisoning. The fact must be noted that, against the background of the decrease in the sodium concentration in the plasma, its concentration in the transudate was in fact slightly higher than in the plasma before the experiment. This is true to an even greater degree of the chloride. The impression was gained that both electrolytes accumulated in the lung tissues and then passed out into the transudate. The concentration of potassium in the edema fluid in diphosgene edema was much higher than its initial concentration in the plasma, but did not reach the concentration in the plasma at the end of the experiment. It may, therefore, be concluded that the development of edema reached a considerable degree before the maximal change in the potassium concentration took place in the plasma.

Both investigated forms of pulmonary edema were accompanied by changes in the weight factors of certain organs. The weight of the kidneys, liver, and spleen showed a decrease (Table 2).

The absence of changes in the dry residue of the liver and spleen suggested that the decrease in their weight during diphosgene and adrenalin poisoning took place mainly, not because of loss of water, but because of release of stored blood from these organs into the general bood stream. The significant decrease in weight of the kidneys in the rabbit with diphosgene edema was combined with a significant decrease in their water content. As is clear from the changes in the dry residue of the other tissues, a possible source of supply of water for the blood in this edema was its mobilization from the muscles and, to a certain extent, from the skin. The less severe adrenalin edema was not accompanied by any appreciable disturbances of the water balance.

Changes took place in the electrolyte composition of the investigated tissues. Most of them showed a decrease in the concentrations of sodium and chloride, which were significant in the kidneys and skin in diphosgene poisoning and in the liver after injection of adrenalin. The concentration of sodium and chloride in the lungs was increased very considerably: the sodium concentration by 2.7 and 2.5 times and the chloride concentration by 2.0 and 1.9 times respectively in diphosgene adrenalin edema

A small but significant increase in the sodium concentration was found in the spleen in diphosgene edema. The decrease discovered in the chloride content of various organs and its increase in the lungs were in agreement

with A. M. Charnyi's findings [1] in diphosgene edema. The increase in the concentration of sodium and chloride in the lungs may be attributed, at least in part, to the considerable excess of extracellular fluid in these organs associated with the development of edema. Meanwhile, the decrease in the sodium concentration in the plasma and erythrocytes, with the decrease in this level in most other tissues, suggested the possibility of the redistribution of sodium chloride in the body and its accumulation in the lungs even before its release into the edema fluid. This was confirmed by the higher concentration of sodium chloride in the edema fluid than in the blood. The excess of sodium chloride in the lungs was therefore not only the result of the development of edema, but also one of the factors contributing to its appearance.

The potassium concentration fell in nearly all the investigated tissues in both types of edema. The fall in the potassium level was particularly great in the lungs (by 39 and 17%). Besides the potassium leaving the erythrocytes, another possible source of the excess of potassium in the plasma was that lost by the lung and other tissues.

In connection with the changes in the water and electrolyte balance of the tissues and blood described above, the significant increase in the weight of the adrenals, by 150% in diphosgene and adrenalin edema respectively, which is characteristic of the stress syndrome, deserves attention. Very probably the redistribution of electrolyte and water discovered in the two types of pulmonary edema reproduced in these experiments is directly dependent on the change in the secretion of the adrenal cortex, resulting from the stressor action of those factors producing the pulmonary edema.

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