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SHOCK ORGAN AND SHOCK TISSUE IN VARIOUS ANIMAL SPECIES

By

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Anaphylactic shock different in the various animal species is characterized by damage of one organ which is called for this reason the shock organ: such is classically considered the bronchopneumonic apparatus in the guinea pig, the circulatory system of the lungs in the rabbit, the liver in the dog, the peripheral circulatory system in the rat and in the mouse. The concept of tissue shock has been later added with the aim of better explaining the single features of the syndrome. Generally smooth muscle tissue is involved. Yet we still do not understand the different behaviour of this tissue in the organs of the various animal species.

With the aim of contributing to a clarification of the problem we have examined in this study, which represents the continuation and partly the synthesis of previous researches (*Melli et al.*, 1955; *Mazzei et al.*, 1957), the electrocardiographic and hemodynamic aspects of anaphylactic and histaminic shock in the guinea pig, rabbit and dog.

METHODS

Guinea pig—25 guinea pigs were sensitized by means of 2 subcutaneous injections of 1 cc of horse serum 1:10 every other day. The shocking injection (0.5 cc of the same solution) was done about 25 days after the second injection, 13 times in a jugular vein, 2 times intracardiac, 10 times in the right carotid artery (the needle was moved centripetally toward the aorta). Histamine shock was induced in 12 guinea pigs by means of an endojugular injection of histamine bichlorhydrate at the dose of mg 0.2 (9 cases), mg 0.3 (2 cases), mg 0.4 (1 case).

The six peripheral leads of the electrocardiogram were recorded in these animals during the development of anaphylactic and histaminic shock.

Rabbit—15 rabbits were sensitized by means of 4 subcutaneous injections of 1 cc of horse serum 1:10 every other day. The shocking injection (2 cc of the same solution) was done about 20 days after the last sensitizing injection through the marginal vein of the ear. Histamine shock was induced in 5 rabbits by means of intravenous injection of 1–2 mg of histamine bichlorhydrate.

An electrocardiogram and the pressures in the right ventricle, pulmonary artery, femoral artery were recorded in these animals during the shock either anaphylactic or histaminic. The pressures in the lesser circulation were recorded through a catheter; the pressure in the femoral artery was measured with a mercurial manometer.

Dog—An experimental study of anaphylactic shock, of histamine shock and of the hemodynamic changes consequent upon the ligation of the portal vein, was performed in 65 mongrel dogs.

33 middle-sized dogs (6 to 15 kg) were utilized for the study of anaphylactic shock. Sensitization was obtained in them by means of 14 daily subcutaneous injections of 1 cc/kg of horse serum 1:5. The production of antibodies was found constantly good (*Invernizzi et al.*, 1956). The shocking injection was done 15–25 days after the last sensitizing injection, 12 times through a catheter with the tip in the inferior vena cava, 21 times in a peripheral vein (generally the femoral vein). The experiment was performed in 2 animals under general anesthesia, otherwise in unanesthetized animals because of the antianaphylactic properties of narcosis (*Mazzei*, 1953; *Zanussi & Mazzei*, 1953).

In order to study the hepatic hemodynamics, a catheter was introduced under radioscopic control from a jugular vein into the inferior vena cava (13 cases) or into an hepatic vein (13 cases); a second catheter was pushed in the hepatic venous system until it occluded a vein; a pressure corresponding to that of the hepatic capillaries and very little below that of the portal vein was recorded through this catheter (*Myers & Taylor*, 1951). That the catheter in such a position was really arrested because it was occluding the catheterized vessel and not due to other causes (engagement against a bifurcation), was shown by the pressure there being clearly above that recorded in the hepatic veins and in the inferior vena cava.

The femoral arterial pressure was recorded in every experiment. The pulmonary arterial pressure was recorded in 6 animals.

Heparin was not added to the saline flowing to maintain the patency of the catheters, because it plays an important role in anaphylactic shock of the dog (*Jacques & Waters*, 1940, 1941).

The six peripheral leads of the electrocardiogram were recorded in every animal.

The experiment was interrupted at the acme of the shock in 5 cases with the sacrifice of the animal; the abdomen was rapidly opened so that a macroscopic examination of the liver could be done and specimens could be obtained for an

histological examination. After fixation in formalin and inclusion in paraffin the slides were either coloured with hematoxylin-eosin or impregnated with silver.

17 middle or large-sized dogs (10 to 35 kg) were utilized for the study of histamine shock; the experiments could be performed under a general anesthesia (injection of a solution of morphine and chloral into the peritoneum) as the narcosis does not interfere with the picture of histamine intoxication. The shock was induced by injecting histamine bichlorhydrate into a femoral vein at the dose of 0.1 mg/kg. The abdomen was longitudinally opened along the middle line in 11 among these animals, after placing a catheter to measure the hepatic venous pressure (7 cases) and hepatic "capillary" pressure (6 cases); a second catheter could then be guided under control from a large mesenteric vein to the portal trunk. The femoral artery was cannulated in all animals. An electrocardiogram was recorded in 6 animals in the 30 minutes following the injection of histamine.

In order to study the mechanism of the hemodynamic changes induced by anaphylactic and histamine shock in the dog we compared these changes with those following the ligation of the portal vein. The hepatic "capillary" pressure, the pressure in the portal vein, in an hepatic vein and in the femoral artery were measured in basal conditions and after ligation of the portal vein in 15 dogs, a variable number of times for each dog.

The hemodynamic changes observed during the experiments on the dog were analyzed statistically. The arithmetical mean, the standard deviation and the Student's *t* test were calculated; we called the differences, as usual, "non significant" when they could be due to chance with a probability greater than 5 per cent, "significant" when the probability was less than 5 per cent and "highly significant" when the probability was less than 1 per cent.

RESULTS

Guinea pig.—Anaphylactic shock was lethal in 12 cases, severe in 2, moderate in 4, light in 6; a shock was not observed in 1 case. The shock was lethal 6 times, severe once, moderate 3 times, light twice when the antigen was injected into a vein; the shock was lethal 5 times, severe once, moderate once, light 3 times when the antigen was injected into an artery. The shock was lethal in 1 animal, light in 1 after intracardiac injection of the antigen.

The injection of histamine induced a shock in all animals; death occurred in 8 among 12 experiments.

Dominating feature was in all animals with shock, either anaphylactic or histaminic, the well known asphyxia, which was not investigated further.

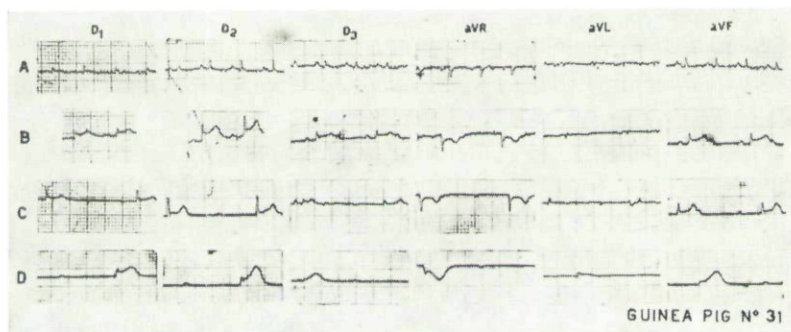


Fig. 1.

Lethal/anaphylactic shock. The paper speed is 50 mm/sec, instead of 25 mm/sec as usually. Immediately after the shocking injection (B) marked displacements of the ST segment appear with partial a-v block. The tracing C, recorded 90 sec after the shocking injection, shows total a-v block and almost complete regression of the ST segment changes. The tracing D shows premortal elevations of the ST segment.

Electrocardiographic observations. The electrocardiographic changes were alike in both types of shock. They are summarized in Table 1. Two kinds of them have been recognized: 1) arrhythmias, 2) changes of the ST segment and T wave.

1) Arrhythmias. Particularly important because of its frequency (15 in 25 cases of anaphylactic shock and 10 in 12 cases of histaminic shock) and because of its precociousness was the occurrence of an idioventricular rhythm; the idioventricular rhythm was sometimes tachycardic, but more frequently bradycardic; complexes originating from the left ventricle alternated frequently with complexes originating from the right ventricle; the shock was lethal or severe in any experiment with this arrhythmia; an initial short run of extreme tachycardia was followed by a progressive bradycardia in the most severe shocks. The idioventricular rhythm ceased within 1 to 2 minutes even in the lethal shocks and the sinus rhythm started again. Then usually premature beats, isolated escapes of nodal or ventricular centers, nodal or ventricular rhythms were recorded.

An atrio-ventricular block was observed in 19 cases: 18 of these were lethal shocks, 1 was a severe shock. Generally the atrio-ventricular block was at first sporadic, then partial, finally complete. (Fig. 1).

2) Changes of the ST segment and T wave. Displacements of the ST segment and changes of the T wave indicating subendocardial or subepicardial ischemia and lesion were commonly observed. The changes of the ST segment and T wave clearly indicated circumscribed impairment of the coronary circulation in 19 cases. They were precocious and transient in the majority of the cases. Changes of the repolarization and in particular high monophasic waves reappeared during the premortal stage in the lethal shocks. The premortal changes

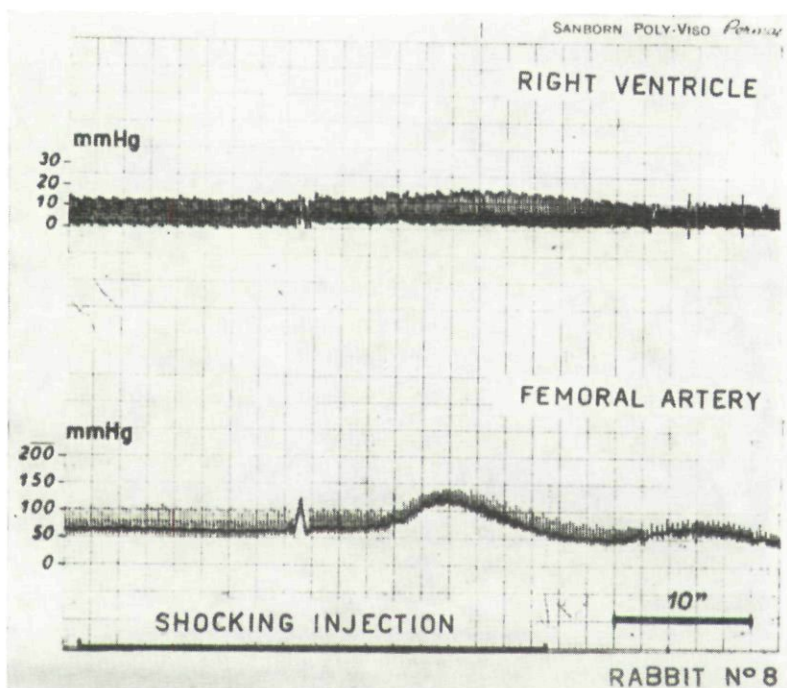


Fig. 2.

Lethal anaphylactic shock. Transitional rise of the right ventricular pressure. The femoral arterial pressure at first rises, then drops below the basal value.

could be distinguished from the initial ones not only because of an intermediate regression, but also because of a different localization. (Fig. 1).

A characterizing sequence of electrocardiographic abnormalities was the following in severe and lethal shocks, either anaphylactic or histaminic: precocious bradycardia, precocious signs of coronary impairment, almost complete regression of them, appearance of new changes of the repolarization.

Electrocardiographic changes have been absent only once among cases with light shock; altered repolarization and arrhythmias (nodal rhythm, ventricular rhythm, premature beats) have been observed in the others, without a close correspondence between evidence of the electrocardiographic abnormalities and degree of the shock. Neither the site of injection of the antigen was shown to be influential.

Rabbit.—The entity of the shock was hardly definable in our experiments due to the need of fixing beforehand the animal on the operative table. Sometimes convulsions and dyspnea were observed, sometimes muscular hypotonia was the only, though remarkable, sign. The anaphylactic shock was lethal twice, moderate 11 times; no signs of shock were produced in

TABLE 1
Frequency of the electrocardiographic changes during anaphylactic and histaminic shock in the guinea pig and in the rabbit.

		Inversion of the T wave	Ventri- cular rhythm	a-v block	Nodal rhythm	Pre- mature beats
<i>Guinea pig</i>	Anaphylactic shock (25 cases)	16	15	12	6	6
	Histaminic shock (12 cases)	9	10	7	3	9
<i>Rabbit</i>	Anaphylactic shock (15 cases)	6	4	2	2	5
	Histaminic shock (5 cases)	3	3	1	0	3

2 experiments. The injection of histamine was followed by lethal shock once, by severe shock twice, by light shock twice.

Remarks on pressor values. The systolic pressure in the pulmonary arteries rose during anaphylactic shock in 9 of 12 animals, by 5 to 13 mm Hg; no correspondence was recognized between entity of the shock and entity of the hypertension. No rise of the pulmonary arterial systolic pressure was observed in 3 cases; the shock was light in 2 of these cases, very light in one.

The systemic pressure was recorded in 9 experiments: no change in 2 cases, a fall of 20 to 50 mm Hg was observed in 7 cases. A noteworthy, though transient, rise preceded the fall of the systemic pressure in some experiments. (Fig. 2).

A remarkable rise of the pulmonary arterial pressure (respectively of 8, 10 and 12 mm Hg) was observed in the 3 animals presenting a severe or lethal histamine shock. The pulmonary arterial pressure was not recorded in the 2 animals in which the injection of histamine induced a light shock.

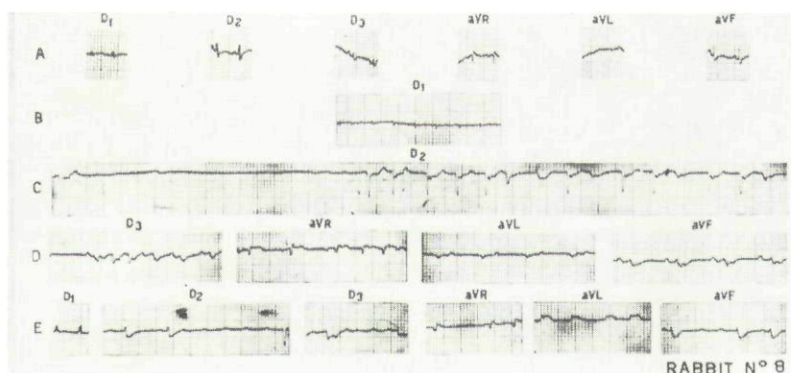


Fig. 3.

Lethal anaphylactic shock. A: basal electrocardiogram. B, C, D: electrocardiograms recorded between 30 sec and 1 min after the shocking injection. E: electrocardiogram recorded 3 min after the shocking injection. In C prolonged heart standstill followed by a ventricular rhythm; an isolated supraventricular beat is seen with a deep depression of the ST segment. In D sinus rhythm; the ST segment is deeply depressed in leads III and aVF. In E complete a-v block; the ST segment is depressed in leads II, III, aVF, elevated in aVL.

Electrocardiographic observations. They are summarized in Table 1. Clear displacements of the ST segment and changes of the T wave, the direction and diffusion of which were indicative of subendocardial involvement, were seen in the 2 animals in which the shock was lethal; moreover severe arrhythmias and finally ventricular fibrillation were noted in these 2 cases. (Fig. 3). Clear changes of the ST segment and of the T wave were recorded 3 times, isolated changes of the T wave 3 times, isolated premature beats once, no electrocardiographic abnormalities 4 times among the 11 experiments in which the shock was not lethal.

Changes similar to those recorded in the lethal anaphylactic shock were observed in the 3 animals in which histamine shock was severe or lethal; no electrocardiographic abnormalities were observed in the 2 animals in which the histaminic shock was light.

The electrocardiographic abnormalities seemed grossly proportional to the entity of the shock, either anaphylactic or histaminic; the abnormalities were precocious and their regression was simultaneous with the regression of the shock.

Dog.—28 among the 31 animals in which an anaphylactic shock was induced in absence of narcosis, showed signs of more or less severe generalized anaphylaxis. The most common symptoms were prostration, vomiting, dyspnea, defecation, urination; the first was constant, the others were less and less frequent. The vomited material was not hemorrhagic, in contrast with the common statements. We have never observed convulsive phenomena in the limbs. Only 2 dogs died in the 6 hours following the shocking injection. Neither the anaphylactic picture nor hemodynamic changes were observed in the 2 animals in which the shock was induced during narcosis. Injecting the antigen in the inferior vena cava or in the femoral vein was the same with regard to the anaphylactic picture or the pressor changes.

Dyspnea was constant, mild generalized muscular contractions were sometimes seen during histamine shock but no vomiting or diarrhoea.

Portal vein	$\bar{x}$								
	s								
	t								
	p								
Pulmonary artery	$\bar{x}$	16.5	16.0	-0.5					
	s	4.8	10.0	9.4					
	t			0.1					
	p			>0.05					
					n = 6				
Hep. "cap."-hep. v. gradient	$\bar{x}$	5.6	14.8	+9.2					
	s	4.3	7.1	3.8					
	t			7.6					
	p			<0.01					
					n = 9				
Hep. "cap."-v. cava gradient	$\bar{x}$	6.5	18.4	+ 11.9					
	s	5.8	8.3	7.3					
	t			5.1					
	p			<0.01					
					n = 10				

$\bar{x}$ = sample arithmetic mean.

s = sample standard deviation.

t = Student's t test.

p = probability (0.05 = non significant difference; 0.05 = significant difference; 0.01 = highly significant difference).

n = sample size (number of observations).

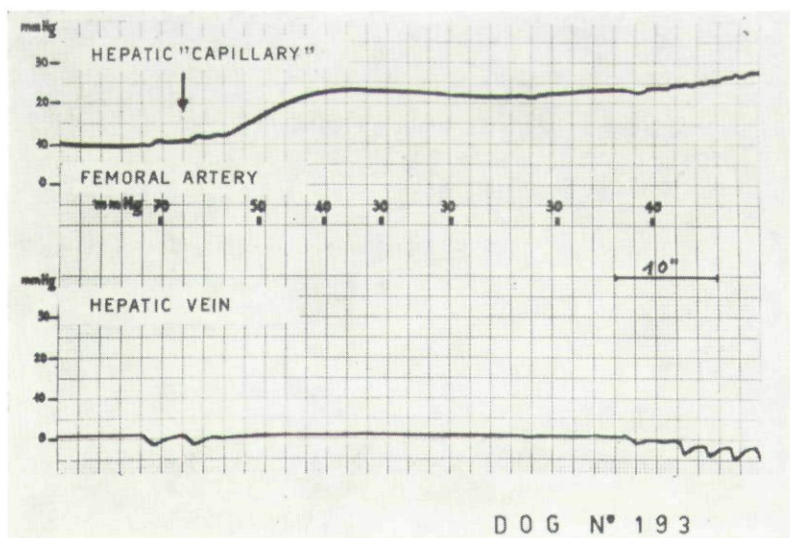


Fig. 4.

The administration of histamine (arrow) is followed by a steep rise of the hepatic "capillary" pressure, a drop of the femoral arterial pressure, a late drop of the hepatic venous pressure.

There was no general nervousness but a mild hyperpnea was noted in the animals in which, under narcosis, the vena porta had been ligated.

Remarks on pressor values. The data are summarized in Table 2.

1) Systemic arterial pressure. This value was determined in 18 unanesthetized animals during anaphylactic shock; the pressure dropped in 17; the only sign of shock was a mild portal hypertension in the single animal in which the systemic arterial pressure did not drop. The mean drop was 75.6 ± 13.9 . The variation is highly significant. The beginning of the pressor drop occurred always quite early (7" to 3'); the return to the basal values was gradual, generally 15' to 30' after the shocking injection.

The systemic arterial pressure was determined in 15 animals during histaminic shock; the drop was constant. (Fig. 4). The mean drop was 51.7 ± 24.7 . The variation is highly significant.

The systemic arterial pressure was determined 23 times after ligation of the portal vein; it remained unchanged 15 times (Fig. 5), it rose in 1 dog, it dropped in 7. The mean change was a drop of 6.7 ± 13.4 . The variation is not significant.

2) Hepatic "capillary" pressure. This value was determined during anaphylactic shock in 24 experiments. It rose in all but one experiment; the mean rise was 7.8 ± 6.3 . The variation is highly significant. The rise started 20" to 3' after the shocking injection, reached rapidly the maximum value and returned to the normal within 9' to 30'. (Fig. 6). The rise of the hepatic "capillary" pressure preceded always the appearance of vomiting and diarrhoea.

The hepatic "capillary" pressure was determined during histamine shock in 6 experiments. It rose in all (Fig. 4); the mean rise was 11.0 ± 7.3 . The variation is highly significant.

The variations of the hepatic "capillary" pressure were not statistically significant after ligation of the portal vein; no change was observed 5 times, there was a slight drop 9 times, there was a slight or moderate rise 10 times. The mean change was a rise of 0.7 ± 3.8 .

3) Pressure in the hepatic veins. This pressure was determined in 13 experiments during anaphylactic shock; there was a rise in 2, a drop in 10, no change in 1. (Fig. 6). The mean

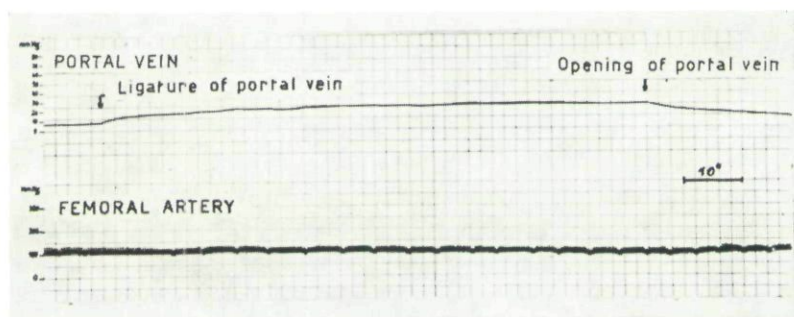


Fig. 5.

The ligation of the portal vein is not followed by a drop of the femoral arterial pressure.

value of the variations was -2.9 ± 4.2 . This variation is significant. The drop started 20'' to 4' after the shocking injection and disappeared within 15'.

There were no significant changes of the pressure in the hepatic veins during histamine shock; this pressure decreased in 5 experiments, rose in 1, remained unchanged in 1. (Fig. 4). The mean variation was -1.8 ± 2.4 .

Not even after ligation of the portal vein were significant variations of the pressure in the hepatic veins observed; a drop was recorded in 2 experiments, a rise in 2, no change in 5. The mean variation was -0.2 ± 3.3 .

4) Pressure in the inferior vena cava. The pressure changes in the inferior vena cava (recorded only during anaphylactic shock) corresponded to those described in the hepatic veins. The record was done in 13 experiments; no changes were observed in 3 cases, a rise in 1, a drop in 9. The mean variation was -3.1 ± 3.3 . This is highly significant. Even the time of appearance and of return to the normal were similar to those described for the hepatic veins.

5) Pressure in the portal vein. This pressure was not recorded during anaphylactic shock because the animals were not anesthetized. It was recorded during histamine shock in 9 experiments; the pressure rose in all; the mean rise was 13.8 ± 7.5 . It is highly significant.

After ligation of the portal vein the mean rise proximal to the ligation was 20.8 ± 10.4 . (Fig. 5). It is highly significant. This value was determined in 16 cases.

6) Pressure in the pulmonary artery. It was recorded in 6 experiments during anaphylactic shock; there was a drop in 4, a moderate rise in 2. The mean variation was -0.5 ± 9.4 . It is not statistically significant.

7) Quantitative relations among the various phenomena of anaphylactic and histamine shock. The entity of anaphylactic shock, as it could be evaluated from the exterior symptoms, was not clearly related to the entity of the various hemodynamic changes. So beside animals presenting in severe shock and slight hemodynamic changes, there were animals in which a

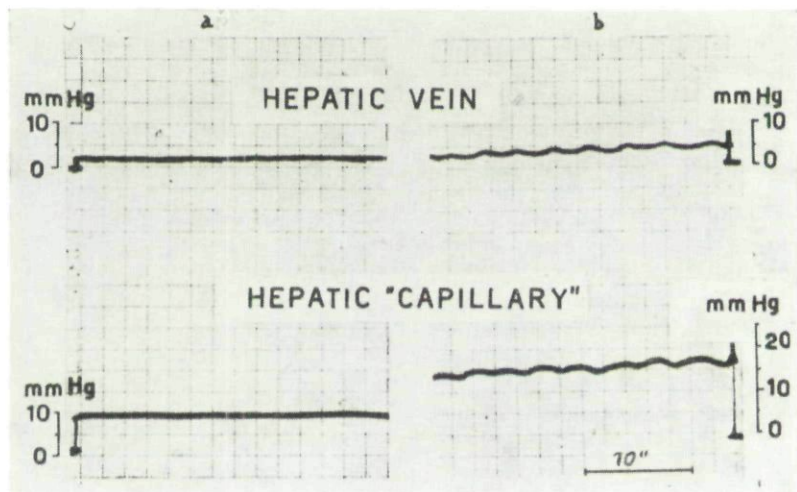


Fig. 6.

a: basal tracings. b: tracings during anaphylactic shock. The gradient between the hepatic "capillary" pressure and hepatic venous pressure rises from 6 to 13 mm/Hg.

severe circulatory collapse or a sharp hepatic "capillary" hypertension were not apparently accompanied by severe shock.

The gradient between the hepatic "capillary" and the hepatic venous pressure, studied in 9 experiments with anaphylactic shock, constantly rose (Fig. 6); the mean rise was 9.2 ± 3.8 . It is highly significant.

The gradient between the hepatic "capillary" pressure and the pressure in the inferior vena cava was studied in 10 experiments with anaphylactic shock; there was a mean rise of 11.9 ± 7.3 . It is highly significant.

The gradient between the hepatic veins and the inferior vena cava, examined in 3 experiments with anaphylactic shock, did not change.

The gradients between the hepatic "capillary" and the hepatic venous pressure, between the hepatic "capillary" pressure and the pressure in the inferior vena cava were not examined during histamine shock in experiments numerous enough to allow a statistical evaluation. (Fig. 4).

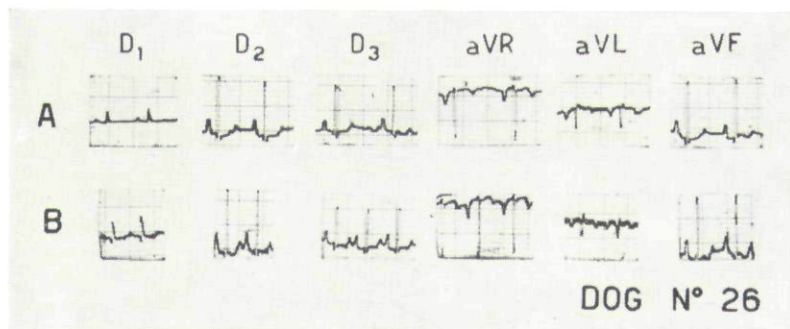


Fig. 7.

A: basal electrocardiogram. B, electrocardiogram 2 min after the shocking injection; severe tachycardia without evident change of the repolarization.

As to the pressor changes in the femoral artery they were absolutely unrelated to those in the hepatic circulation during both anaphylactic and histamine shock.

8) Time relations among the various phenomena of the anaphylactic and histaminic shock. The drop of the systemic arterial pressure started after the rise of the hepatic "capillary" pressure only in 1 experiment, simultaneously with this in 4, before this in 7. The changes of the portal venous, of the hepatic "capillary", of the hepatic venous pressure and of the pressure in the inferior vena cava were generally simultaneous.

The same time relations were observed during histamine shock. In particular the drop of the systemic arterial pressure started after the rise of the hepatic "capillary" or portal venous pressure in 3 experiments, simultaneously with this in 4, before this in 6.

Electrocardiographic observations. The electrocardiogram was studied in 12 experiments during anaphylactic shock, in 6 experiments during histamine shock. Tachycardia, sometimes of high degree, was noted. There were no conduction defects, no exaggerated myocardial excitability or signs of evident coronary impairment. (Fig. 7). Sometimes mild changes of the T wave, in all probability secondary to the tachycardia, were noted.

Pathologic observations. An examination was done of the liver in 5 animals sacrificed at the acme of the shock. Its volume was considerably increased, the color was bright, the capsule was stretched; when cut a lot of hematic fluid flowed out.

Microscopically cellular swelling, electively localized in the external two thirds of some lobules, was observed. The sinusoids showed essentially two types of changes, even in a single slide: the collapse of the walls, especially where the cellular swelling was predominant, or severe congestion, particularly in the centrolobular region. Both the cellular swelling and the congestion of the sinusoids participated in characterizing the macroscopic aspect of the liver.

DISCUSSION

Guinea pig (37 experiments). The electrocardiographic study, confirming our previous researches, has shown that severe and complex changes of the cardiac rhythm (atrio-ventricular blocks, sustained or isolated escapes of nodal and ventricular centers, premature beats) and changes of the ST segment and T wave, index of subendocardial or subepicardial lesion-ischemia, occur in association with both the anaphylactic and histamine shock of the guinea pig. The electrocardiographic changes were precocious and correlations could be recognized between type and entity of the electrocardiographic changes on the one hand and the entity of the shock on the other.

Of particular interest is the observation that signs of lesion-ischemia could be present when the spasm of the bronchial muscles was to be considered slight. These are experiments that make us think that the sharing of the coronary circulation in anaphylactic and histamine shock of the guinea pig is primary and sometimes apparently localized. On the other hand we have shown in other experiments that asphyxia per se does not imply electrocardiographic changes except when extreme and in the premortal stage (*Melli et al.*, 1955).

These experiments confirm that the picture of the anaphylactic shock is the same if the shocking injection is done in the aorta, a carotid artery or a vein. The prevalence of respiratory and cardiac phenomena is not due to a technical artifice, such as the lungs coming precociously in touch with the antigen, but to their peculiar characteristics. We confirm therefore that the "shock organ" of the guinea pig (this term meaning an organ particularly reactive and dominating the morbid picture and not exclusively the reactive organ) are the respiratory apparatus and the myocardium. The "shock tissue" is to be considered in this animal the bronchial and coronary musculature.

Rabbit (20 experiments). We have shown, by means of the cardiac catheterization, that anaphylactic and histamine shock in the rabbit occur in association with an important rise of the right ventricular and pulmonary arterial pressure, while the systemic arterial pressure, after a very short but considerable rise, undergoes a remarkable drop. The right ventricular and pulmonary arterial hypertension are to be considered apparently due to a rise of the pulmonary resistances.

We have observed during anaphylactic and histamine shock changes of the ST segment and T wave referable to involvement of the coronary arteries. The type of the electrocardiographic changes and the lack of correlations between the hemodynamic changes in the lesser circulation and the electrocardiographic abnormalities make us to believe that these are not secondary to pulmonary hypertension and right ventricular load. Thus the lungs and myocardium behave as "shock organ", while the smooth musculature behaves as "shock tissue". The coronary muscle fibers are apparently involved as in the guinea pig. A difference exists in the two experimental animals as far as the respiratory apparatus is concerned: while the bronchial musculature is involved in the guinea pig, the musculature of the arterial tree is involved in the rabbit.

Dog (65 experiments). No electrocardiographic abnormalities to be ascribed to involvement of the coronary circulation have been shown during anaphylactic and histamine shock.

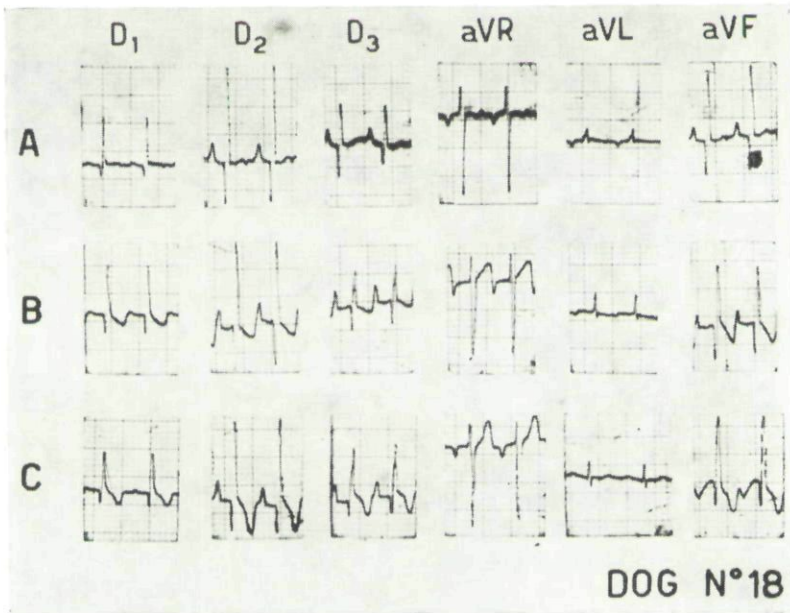


Fig. 8.

A: basal electrocardiogram. B, electrocardiogram 2 min after administration of Polyvinylpyrrolidone; inversion of the T wave in leads I, II, III, aVF. C, electrocardiogram 6 min after administration of Polyvinylpyrrolidone; the inversion of the T wave in the same leads is deeper.

This lack of evident signs of coronary impairment during anaphylactic and histamine shock has been a surprise to us, because we had shown them in the dog after administration of Polyvinylpyrrolidone (Folli *et al.*, 1955) and have recently confirmed after further research on Polyvinylpyrrolidone and the histamine releaser 48/80 (unpublished data) (Figs. 8, 9). As far as we know this difference between anaphylactic and histamine shock on the one hand and the effects of histamine releasers on the other is not known and is one instance of the few differences between the two experimental procedures.

Arterial systemic hypotension and portal hypertension are the most evident hemodynamic consequences of anaphylactic and histamine shock. The portal hypertension has been directly

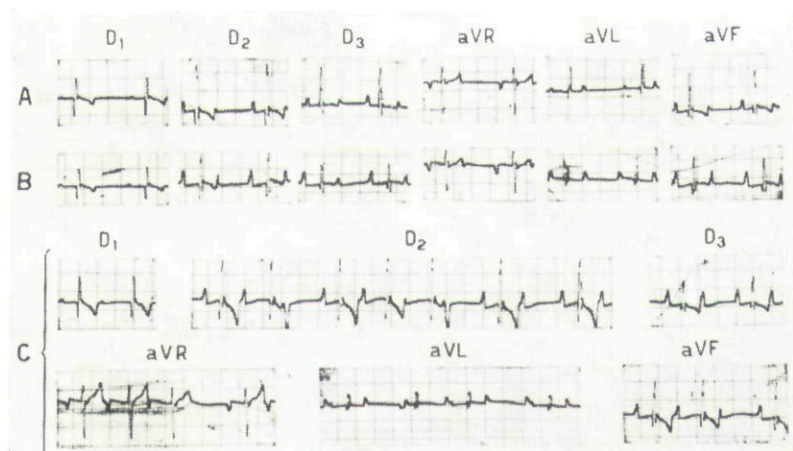


Fig. 9.

A: basal electrocardiogram. B, electrocardiogram 2 min after administration of 48/80; a-v block 2:1. C, electrocardiogram 4 min after administration of 48/80; a-v block and dissociation, deep inversion of the T wave in leads I, II, aVF.

measured through a catheter during the histamine shock, has been indicated by the hepatic "capillary" hypertension during anaphylactic shock; there is no need to emphasize that a close relationship between the hepatic "capillary" pressure and the portal pressure has been shown by *Myers & Taylor* (1951).

No hypertension in the hepatic veins and in the inferior vena cava have accompanied the portal hypertension; a drop of the pressure in the hepatic veins and in the inferior vena cava was on the contrary observed in some experiments. The classic hypothesis which refers the hepatic changes occurring in the shock of the dog to a spastic contraction of a muscular ring (sphincter of *Maunther & Pick*) in the wall of the hepatic veins (*Wells*, 1911; *Simonds*, 1919; *Simonds & Brandes*, 1927 a, b) is shown therefore to be incorrect. As the hepatic "capillary" and portal hypertension is not reflected in the hepatic venous system we can state that an obstruction is established at the level of the portal capillaries or of the hepatic venules.

Some authors (*Weil et al.*, 1924, *Simonds & Brandes*,

1927 a, b) have referred the systemic arterial hypotension, typical of anaphylactic and histamine shock, to the hepatic barrage. This hypothesis is no longer tenable after our experiments. The drop of the systemic arterial pressure is simultaneous with or precedes the pressor changes in the hepatic circulation except in 1 experiment. Moreover we emphasize that while the systemic and the hepatic pressor changes are both remarkable in some experiments, they are unrelated in others. On the other hand the data obtained after ligation of the portal vein show that a barrage in the portal circulation does not provoke either a systemic collapse, or just significant changes of the systemic arterial pressure. It is true that the portal barrage was not at the level of the intrahepatic ramifications in this experimental model; this however ought not to make a difference. We conclude that the hepatic barrage doesn't play a determinant role in provoking the systemic collapse characteristic of anaphylactic and histaminic shock in the dog. Probably the two phenomena are independent signs of shock. The centralizing of the morbid phenomena in the liver is certainly due to the peculiar features of this organ in the dog and not to experimental artefacts. In fact our experimental method did not carry an accumulation of the noxious agent in the liver, it should be the lungs that would be first and prominently involved. We have not observed dyspnea or hypertension in the lesser circulation. Therefore the liver is the "shock organ" (in the restrictive meaning stated above) in the dog.

The "shock tissue" in this animal remains unsettled. In fact clarifying the basis of the hepatic barrage is impossible on the basis of our experiments. A vascular spasm, either at the level of the post-capillary venules or at the opening of the capillaries into the venules, or an extrinsic compression of the capillaries by interstitial edema could be a possibility. Only in the first case the smooth musculature could be considered "shock tissue" even in this experimental animal. Otherwise the liver cells, the mastzellen or blood cells are to be taken into consideration as "shock tissue".

CONCLUSIONS AND SUMMARY

The electrocardiographic and hemodynamic study of anaphylactic and histamine shock has allowed us to reach the following conclusions.

1) Severe myocardial lesions, which we regard as related to coronary spasm because of their early development and evolution, are shown in the guinea pig both in anaphylactic and histamine shock.

2) The coronary-myocardial changes are primary like the bronchial constriction: they are conspicuous and appear simultaneously with asphyxia, they can be quite prominent when the bronchial constriction is moderate. Severe mechanical obstruction of the airways does not lead to analogous electrocardiographic changes (except in the premortal stage).

3) The pulmonary apparatus and the myocardium are therefore to be considered the "shock organ" of the guinea pig. The smooth musculature of the bronchi and of the coronaries is the "shock tissue". As the picture of the shock appears absolutely identical wherever the antigen is injected (a vein, a carotid, the aorta, the left ventricle) we have to admit that this morbid centralization is a peculiar feature of this animal species and not an experimental artefact. We cannot rule out a contributory role of spasm in other vessels.

4) Constant, early and quite marked (though less than in the guinea pig) electrocardiographic abnormalities related to coronary spasm, are seen during anaphylactic and histamine shock in the rabbit.

5) Right ventricular and pulmonary arterial hypertension appear simultaneously in this animal during shock. They appear to be due to a rise of the pulmonary resistance ("pulmonary barrage"). A noteworthy, though transient, systemic arterial hypertension occurs which is followed by severe hypotension. The pulmonary arterial tree and the coronaries are to be considered the "shock organ" in the rabbit. The participation of other vascular territories is not ruled out even in this

experimental animal. The smooth musculature is the "shock tissue".

6) No significant electrocardiographic abnormalities or dyspnea have been observed in the anaphylactic or histamine shock in the dog, not even when the antigen, injected through the inferior vena cava, was brought into immediate contact with the lesser circulation and afterwards with the myocardium.

7) This lack of electrocardiographic abnormalities is in contrast with the effects of histamine releasers and is one instance of the few differences between the two experimental procedures.

8) Anaphylactic and histamine shock of the dog are followed by hepatic "barrage" and portal hypertension, while the pressure in the hepatic veins and in the inferior vena cava remain unchanged or decrease.

9) A barrage in the portal circulation is therefore established during anaphylactic and histamine shock of the dog. The barrage however is not, as classically stated, due to contraction of a sphincter at the junction between the hepatic veins and the inferior vena cava; it is to be localized inside the liver at the level of the capillaries or venules.

10) A remarkable drop of the systemic arterial pressure occurs simultaneously with the above mentioned phenomena or sooner. This hypotension cannot be a consequence of cardiac failure, nor is it due to the hepatic barrage and diminished venous return; in fact no arterial systemic hypotension follows the ligation of the portal vein. The arterial systemic hypotension is to be considered a direct consequence of the shock.

11) Certainly the picture of the anaphylactic shock in the dog is dominated by the hepatic strain and therefore the liver is the "shock organ" of this animal. The "shock tissue" remains undecided.

12) The reason why the responsiveness of the different organs varies according to the animal species and also the reason why the same "shock tissue", namely the smooth musculature, is responsive in one rather than in the other is not known.

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