Myocardial Changes Associated with Icterus Gravis of the Newborn. II. The Effect of Steroid Treatment

By

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(Received July 21, 1963)

It has been shown that, on the one hand, grave extensive hydropic vacuolar myocardial degeneration occurs in newborns dead with icterus gravis, and, on the other hand, that this kind of degeneration can be reproduced in rabbits by inducing haemolysis [1, 2].

We have attempted to prevent the development of myocardial degeneration and thus the sudden death owing to central circulatory failure.

In cases of icterus gravis, in addition to exchange transfusion, corticoids have been applied with favourable results all over the world, owing to these drugs improving liver function, decreasing the antigen-antibody reaction and permeability, and their cholagogue effect. In the present investigations we have studied the histological pattern of the heart muscle following combined phenylhydrazine and corticoid treatment.

Material and Method

Thirty infantile rabbits ranging in weight from 220 g to 430 g were used. As a control, partly 5 untreated rabbits used in previous experiments, partly 4 which were treated only with 5 per cent dextrose in half strength Ringer's solution intravenously, and 6 animals subjected to combined treatment with 5 per cent dextrose in half strength Ringer's solution and prednisolone intravenously, were employed.

The experimental groups were as follows (see Table I).

Group I. Six rabbits (Nos 1 to 6) received 3 times 1 mg prednisolone together with 0.01 g phenylhydrazine (pH 6.8 to 7.3) in 6 ml 5 per cent dextrose, half Ringer's solution, intravenously, within 2 hours. One animal died at the end of the experiment, 5 were killed with air embolism.

Group II. Six animals (Nos 7 to 12) received 3 times 0.01 g phenylhydrazine in 5 per cent dextrose half Ringer's solution, intravenously, within 2 hours. Then all were killed with air embolism.

Group III. Six animals (Nos 13 to 18) received 3 times 1 mg prednisolone and 5 per cent dextrose half Ringer's solution, within 2 hours. Then all were killed with air embolism.

Group IV. Four animals (Nos 19 to 22) received 1 mg prednisolone intramuscularly, daily for 7 days and, subsequently, 1 ml prednisolone intramuscularly and 0.01 g phenylhydrazine in 6 ml 5 per cent dextrose half Ringer's solution intravenously, daily for 6 days, when all the animals died spontaneously.

Group V. Four animals (Nos 23 to 26) received 1 mg prednisolone intramuscularly daily for 3 days and, subsequently, 1 mg prednisolone and 0.01 g phenylhydrazine in 5 per cent dextrose half

TABLE I

No.	Group	Weight in g	Erythrocyte count (experiment) beginning	Erythrocyte count (experiment) end	Haemoglobin g (experiment) beginning	Haemoglobin g (experiment) end	phenylhydrazine, doses in g	prednisolone doses in mg	time of day	experiment hour	death by air embolism	spontaneous	Histological changes: heart	Histological changes: liver
1.	I.	410	4.2	2.6	15.6	14.1	3×0.01	3×1		2	+		+	
2.	I.	430	4.0	2.1	11.8	9.6	3×0.01	3×1		2	+		+−	
3.	I.	420	4.0	2.0	11.2	9.4	3×0.01	3×1		2	+		++	
4.	I.	235	5.8	4.6	9.4	5.5	3×0.01	3×1		2	+		+−	+
5.	I.	295	5.7	4.5	8.8	5.5	3×0.01	3×1		2	+		+−	
6.	I.	410	4.2	3.9	9.4	8.6	3×0.01	3×1		2			+	
7.	II.	400	4.3	1.2	13.2	9.0	3×0.01	—		2	+		++	+
8.	II.	295	5.3	3.6	8.2	5.8	3×0.01	—		2	+		++	
9.	II.	280	5.1	2.3	8.2	6.0	3×0.01	—		2	+		+	
10.	II.	330	5.4	2.1	9.1	6.0	3×0.01	—		2	+		+	
11.	II.	270	5.8	2.8	8.5	7.6	3×0.01	—		2	+		+	
12.	II.	250	5.1	2.5	7.6	5.4	3×0.01	—		2	+		+	
13.	III.	420	4.16		12.3		—	3×1		2	+		+−	
14.	III.	420	4.2		11.8		—	3×1		2	+		+	
15.	III.	320	4.2		16.5		—	3×1		2	+			
16.	III	260	3.3		16.0		—	3×1		2	+		+−	
17.	III.	250	3.0		11.0		—	3×1		2	+		+	
18.	III.	280	3.8		10.3		—	3×1		2	+		+−	
19.	IV.	350	4.8	2.1	10.9	8.3	4×0.01	13×1	14			+	+	+
20.	IV.	400	5.0	2.3	10.6	7.4	1×0.02	13×1	14			+	+	
21.	IV.	400	5.2	1.8	10.3	6.4	1×0.03	13×1	14			+	+−	
22.	IV.	410	4.9	2.2	11.2	5.4		13×1	14			+	++	
23.	V.	380	4.5	1.2	12.6	5.6	8×0.01	14×1	15		+		++	++
24.	V.	400	4.8	1.6	11.2	6.3	2×0.02	14×1	14			+	++	++
25.	V.	360	4.3	1.1	11.8	7.3	1×0.03	14×1	15		+		++	++
26.	V.	370	5.0	1.8	12.0	7.7		14×1	14			+	+	+
27.	VI.	350	4.0		9.1	—		—		2	+			
28.	VI.	380	4.0		14.7	—		—		2	+			
29.	VI.	420	4.24		12.9	—		—		2	+			
30.	VI.	410	4.16		13.5	—		—		2	+			

++ grave change + moderate change + — slight change

Ringer's solution, daily, for 11 days. Two rabbits died, two were killed in the usual way.

Group VI. Four animals (Nos 27 to 30) received 3 times 8 ml 5 per cent dextrose half strength Ringer's solution intravenously, within 2 hours, then were killed with air embolism.

Results

Histological studies of the heart muscle, liver, spleen, kidney and brain revealed the following.

Group I. In one animal (No. 3) marked vacuolization was seen in the subendocardial layer of both ventricles. In the other 5 animals vacuolization appeared only scarcely. The content of the vacuoles was not sudanophile (Fig. 1). Hyperaemia was observed in the other organs, being possibly the consequence of the destruction by air embolism.

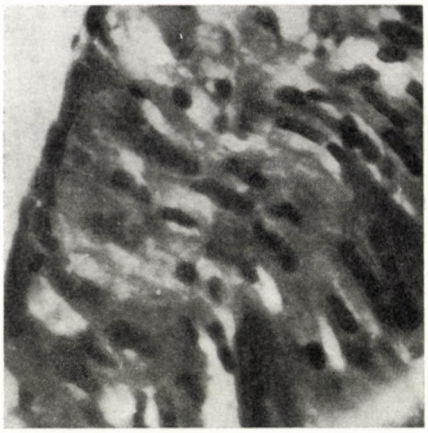

Fig. 1. Animal No. 6. Moderate myocardial vacuolization (in upper left quadrant of the picture)

Group II. In two animals (Nos 7 and 8) extensive vacuolization occurred in the heart muscle, in the subendocardial layer of both ventricles; vacuolization in 4 animals was moderate. No sudanophilia could be observed in the vacuoles (Fig. 2). Considerable hyperaemia was present in the other organs.

Group III. One animal (No. 14) showed definite vacuolization in the heart muscle; minimal or no vacuolization was observed in the heart muscle of the other animals.

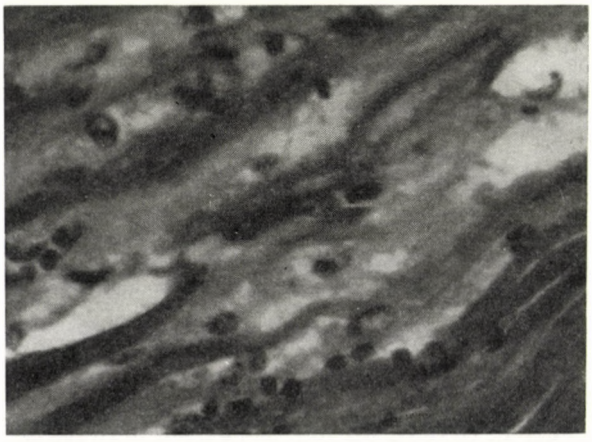

Fig. 2. Animal No. 7. Extensive myocardial vacuolization

Group IV. In one animal (No. 21) slight myocardial vacuolization was present. In the liver of the same rabbit, marked congestion, centrolobular necroses and leucocytic infiltration were present. Myocardial vacuolization in two other animals (Nos 19 and 20) was extensive, first of all in the subendocardial layer of the ventricles. In one of these animals (No. 19), the liver showed congestion and microglobular fatty degeneration. In one animal (No. 22), myocardial vacuolization in the subendocardial layer was considerable (Figs. 3 and 4).

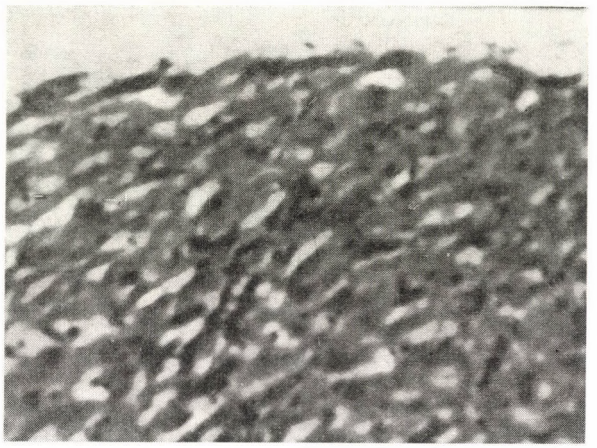

FIG. 3. Animal No. 21. Minimal subendocardial vacuolization

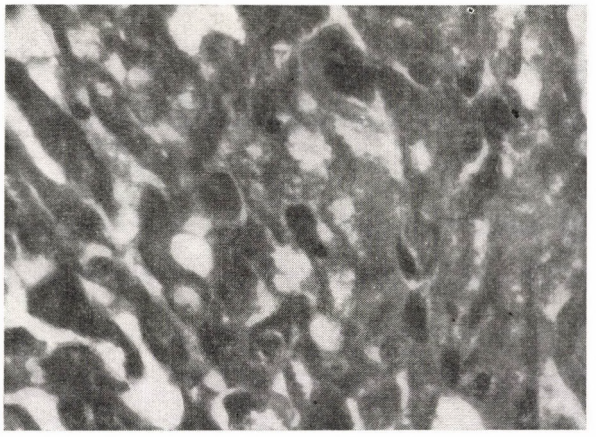

FIG. 4. Animal No. 23. Extensive myocardial vacuolization

Group V. In three animals (Nos. 23, 24, 25) definite myocardial vacuolization was found in the subendocar-

dial layer of both ventricles. In two animals (Nos 23, 24), next to microglobular fatty degeneration, centrolobular necroses were present in the moderate, microglobular fatty degeneration was seen (Figs. 5 and 6).

Group VI. All these animals had a normal heart. In one animal (No. 30)

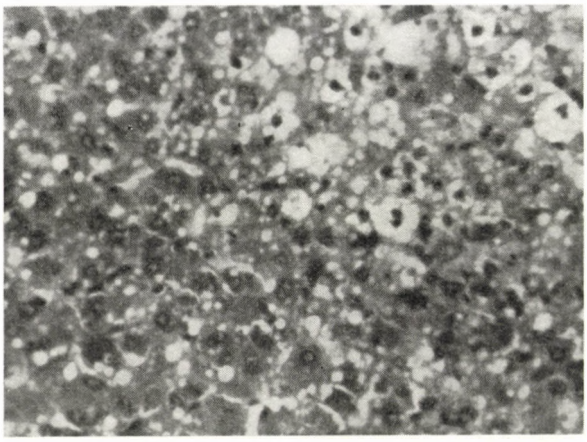

Fig. 5. Animal No. 23. Fatty degeneration in myocardium

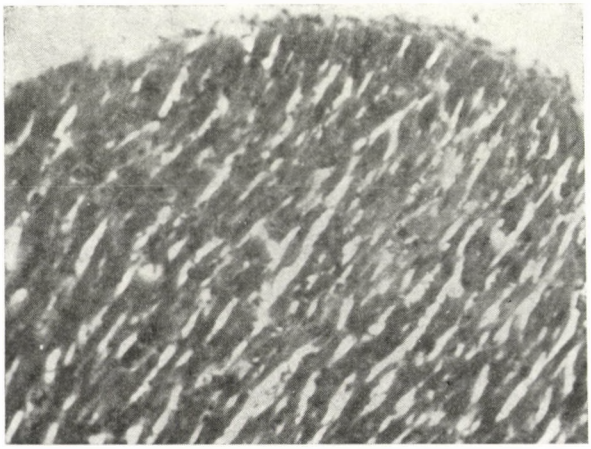

Fig. 6. Animal No. 29. No vacuolization in heart muscle

liver. In one of the animals (No. 23), however, coccidiodal infestation could be demonstrated in the intrahepatic bile ducts. In one animal (No. 25), congestion and marked fatty degeneration, and in one animal (No. 26) coccidiodal infestation was present in the liver.

Discussion

In the experiments lasting two hours, after administration of dex-

trose-Ringer's solution, no heart muscle lesion was found. On the administration of phenylhydrazine, myocardial vacuolization occurred. Simultaneous prednisolone treatment afforded a certain protection against the vacuolization.

In the experiments lasting 14 days, with the administration of similar quantities of prednisolone, there seemed to be a certain connection between the doses of phenylhydrazine, i.e. the rate of haemolysis and the myocardial vacuolization. The protective effect of prednisolone observed in this instance was not convincing, all the less since in the 2-hour experiment (Group III) myocardial vacuolization occurred after the administration of prednisolone alone, thus without haemolysis. (Detailed investigations would be needed to establish the kind of electrolyte shift ensuing in the myocardium after phenylhydrazine haemolysis and on administering prednisolone.)

We are aware of the fact that the present experiments are not in every aspect identical with human icterus gravis; they can probably be compared only as to haemolysis and anoxia. (Immune haemolysis might reveal some further points; such investigations are in progress.) We are, however, of the opinion that concerning the prevention of hypoxic injuries, experiments carried out in healthy rabbits may furnish some information.

Summary

Haemolysis has been induced in infantile rabbits by phenylhydrazine treatment and the effect of simultaneous administration of prednisolone on the heart muscle has been studied. No definite conclusions could be drawn as to the protective effect of prednisolone.

References

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2. Lukács, V. F., Gorácz, Gy., Simon, H.: Myocardial Changes Associated with Icterus Gravis of the Newborn. Acta paediat. Acad. Sci. hung. **3**, 271 (1962).

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