Myocardial Changes Associated with Icterus Gravis of the Newborn

By

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(Received July 23, 1962)

Several factors may be at play in connexion with the sudden, unexpected death occurring before, during, or after, exchange transfusion. Such factors are:

(i) hyperpotassaemia
(ii) hypocalcaemia
(iii) hypervolaemia (resulting from excess transfusion)
(iv) cold blood (3)
(v) O_2 deficiency

While the first four factors, or the changes they may give rise to, can be eliminated with adequate care, the fifth factor is likely to occur more often.

In a previous paper (2) we have described in detail the circumstances that may give rise to hypoxia in newborns with icterus gravis, especially in patients with Rh incompatibility. Our observation of severe hydropic-vacuolar degeneration in the heart muscle in such cases agreed with the findings of other authors [1]. We think that hypoxia, in the first place is responsible for this degeneration.

The present investigations are part of a series of experiments carried out to lend support to the above view.

Methods

Thirty-two infantile rabbits weighing 210 to 400 g, and 2 adult rabbits weighing 2800 to 3300 g, were used. Seven of the infantile rabbits succumbed during treatment, 5 served as the controls.

The animals were tested for erythrocyte count and Hb concentration before every intervention. To induce haemolysis, phenylhydrazine was injected intravenously at 2 or 3-day intervals. On every occasion 0.01 g was injected, dissolved in 4 ml of physiological NaCl solution, pH 6.8 to 7.3. After a few treatments some animals died spontaneously, the survivors were killed by air embolism. The data for the animals involved in the experiments are shown in Table. I. The adult rabbits were treated with 0.03, 0.06 and 0.08 g of phenylhydrazine

Results

The intravenous injection of phenylhydrazine gave rise to significant haemolysis (Table I). Haemolysis developed faster in the smaller animals, than in the bigger ones. The control adult rabbits were treated with much higher doses, so as to produce haemolysis comparable in severity to that produced in the infantile rabbits.

I. Histological findings in the 20 infantile rabbits with haemolysis.

TABLE I
Experimental animals

No.	Weight in g	Erythrocyte count million		Hb value, g per 100 ml		Number and size of phenylhydrazine doses mg/kg	Duration of experiment, days	Killed by air embolism	Spontaneous death	Histological changes				
		initial	final	initial	final					Heart	Brain	Kidney	Spleen	Liver
1.	400	4.2	0.88	13.2	3.2	3 × 25	10	+	—	++	±	+	+	+
2.	340	2.8	1.7	12.0	3.0	3 × 29	10	+	—	++	±	+	+	+
3.	360	4.81	2.9	10.9	6.5	4 × 27	6	+	—	++	±	+	+	+
4.	400	4.04	1.26	11.2	3.4	4 × 25	6	+	—	++	±	+	+	+
5.	400	3.72	2.00	12.6	7.6	5 × 25	8	+	—	++	±	+	+	+
6.	390	3.03	2.0	11.8	9.7	5 × 25	8	+	—	++	±	+	+	+
7.	380	3.5	1.0	11.2	7.8	5 × 27	8	+	—	++	±	+	+	+
8.	350	3.0	1.4	13.2	9.4	5 × 28	8	+	—	++	±	+	+	+
9.	350	2.4	1.2	11.8	9.7	2 × 28	3	—	+	++	±	+	+	+
10.	250	4.0	1.0	11.2	8.8	2 × 40	3	—	+	++	±	+	+	+
11.	350	3.0	0.8	11.5	8.7	3 × 28	6	+	—	++	±	+	+	+
12.	360	2.8	0.5	12.0	10.0	3 × 28	4	—	+	++	±	+	+	+
13.	400	3.8	1.0	11.8	9.7	3 × 25	4	—	+	++	±	+	+	+
14.	210	3.9	0.9	10.9	7.3	3 × 47	4	—	+	++	±	+	+	+
15.	380	4.2	1.6	15.6	8.8	2 × 25	4	+	—	++	±	+	+	+
16.	400	4.0	1.46	14.4	9.1	2 × 25	4	+	—	++	±	+	+	+
17.	400	4.2	1.25	15.0	9.5	2 × 25	4	+	—	++	±	+	+	+
18.	350	3.6	1.19	14.7	7.2	2 × 28	4	+	—	++	±	+	+	+
19.	350	4.3	1.1	14.4	8.1	2 × 28	4	—	+	++	±	+	+	+
20.	280	3.9	1.2	15.0	8.3	2 × 35	4	—	+	++	±	+	+	+
Control animals														
1.	3300	4.0	2.0	14.1	10.6	3	4	—	+	±	—	±	±	+
2.	2800	3.9	1.4	12.9	7.9	3	4	+	—	±	—	+	±	++
1.	350	4.1	—	14.3	—	—	—	killed by stunning +	—	—	±	—	—	—
2.	300	3.8	—	14.0	—	—	—	killed by stunning +	—	—	±	—	—	—
3.	260	4.6	—	15.2	—	—	—	killed by stunning +	—	—	±	—	—	—
4.	320	4.0	—	14.6	—	—	—	killed by stunning +	—	—	±	—	—	—
5.	250	4.2	—	14.4	—	—	—	killed by stunning +	—	—	±	—	—	—

++ severe change
+ moderately severe change
± occasional change

Sections cut from the muscle of the right and left ventricle, as well as from the apex were examined. Most of the changes of considerable severity occurred in the subendocardiac area of the left ventricle. The subendocardial fibres showed vacuolization of varying severity, extending to the central one-third of the ventricular wall; the areas of these vacuoles were empty, showed no sudanophilia. The fibres immediately under the endocardium were fragmented and there were some areas showing homogeneous staining with eosin. In the area of the right ventricle slight vacuolization in the fibres was found exclusively in the subendocardial layer (Fig. 1, 2, 3).

The cerebral nuclei were not yellow in colour and showed only some oedema. In the kidneys hyperaemia, parenchymatous and vacuolar degeneration of the tubules were present; no haemoglobin casts were observed in the efferent ducts. In the spleen oedematous loosening of the pulp and hyperaemia were conspicuous; in the sinuses intra- and extracellular haemosiderin granules occurred. The liver showed hyperaemia, and in some areas microglobular fatty degeneration.

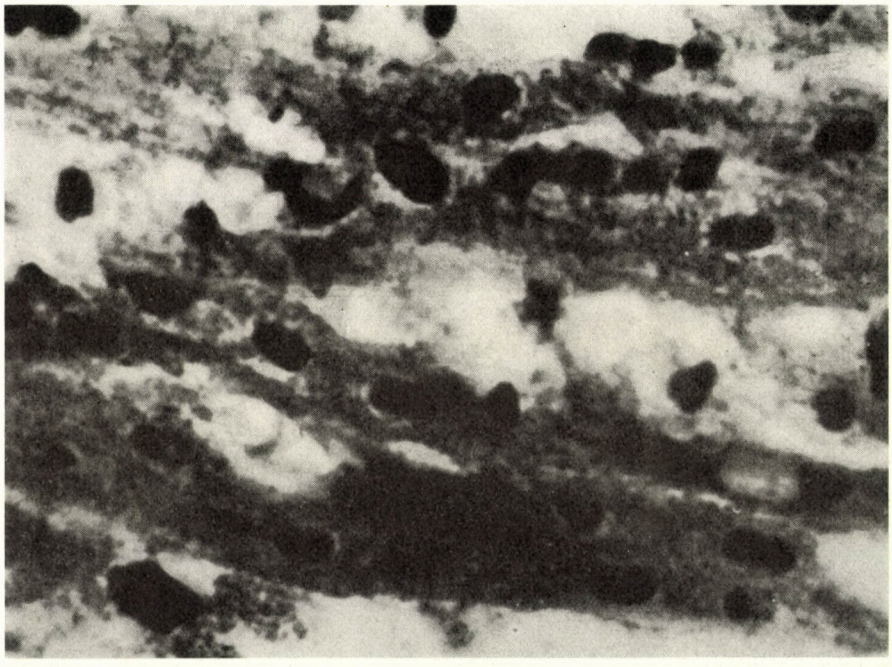

FIG. 1. Vacuolized, disintegrating fibres in the left ventricle (high-power view)

II. *a)* Histological findings in the first control adult rabbit.

There were a few vacuoles, but no disintegration of fibres in the subendocardial area of the left ventricle of the heart. Excessive hyperaemia was noted in the kidney, spleen and liver, where swollen liver cells with light cytoplasm were visible around the central veins.

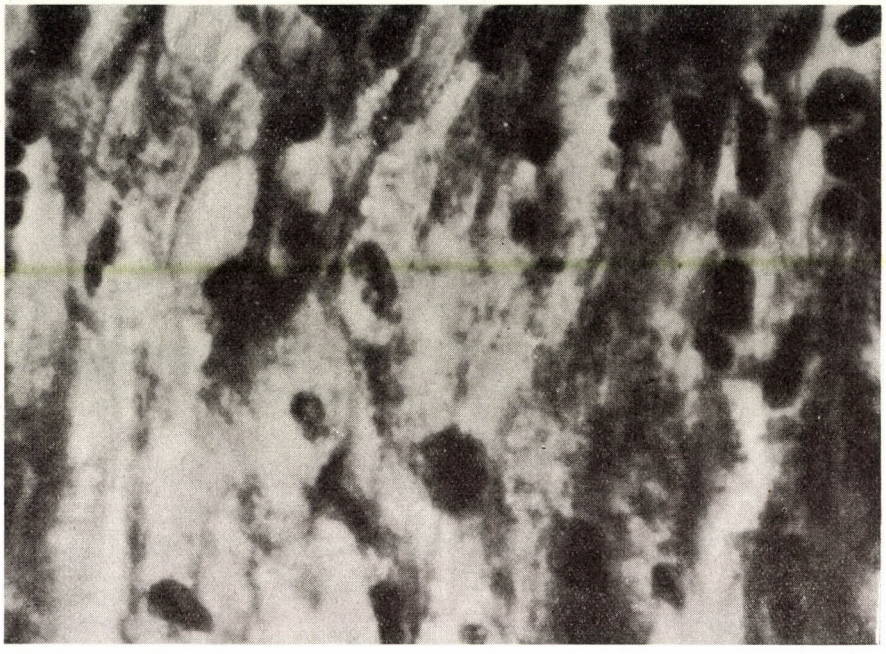

FIG. 2. Vacuolized myocardial fibres (high-power view)

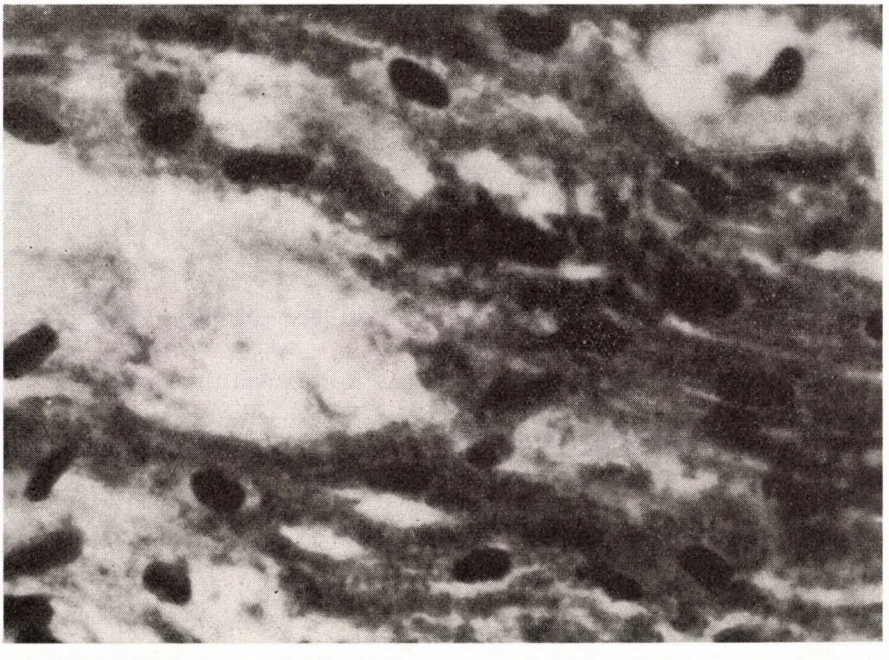

FIG. 3. Vacuolized, disintegrating myocardial fibres (high-power view)

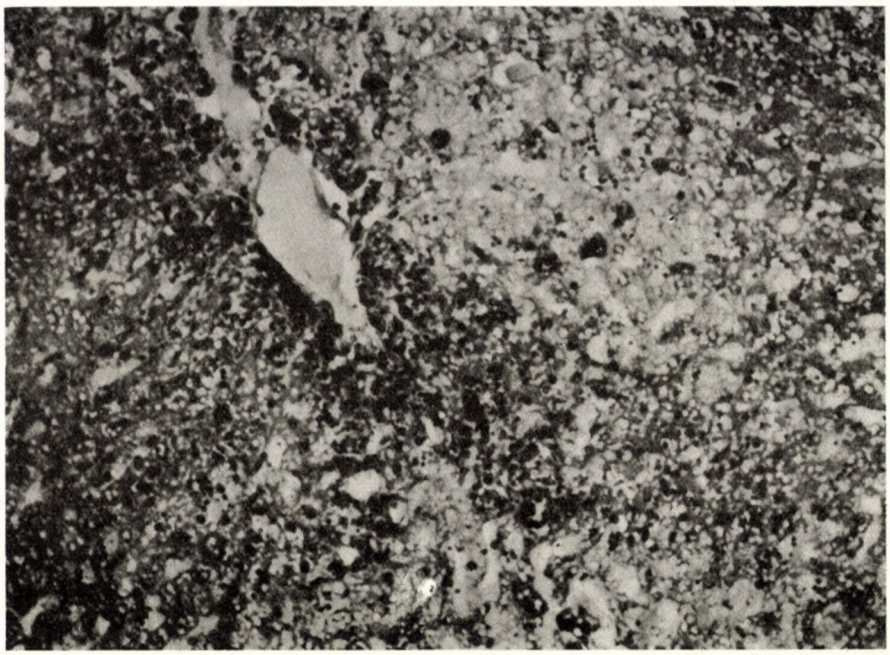

FIG. 4. Centrolobular necrosis with leucocytic infiltration in a liver lobule. Adjacent to the area of necrosis vacuolized liver cells are visible. (Medium-power view)

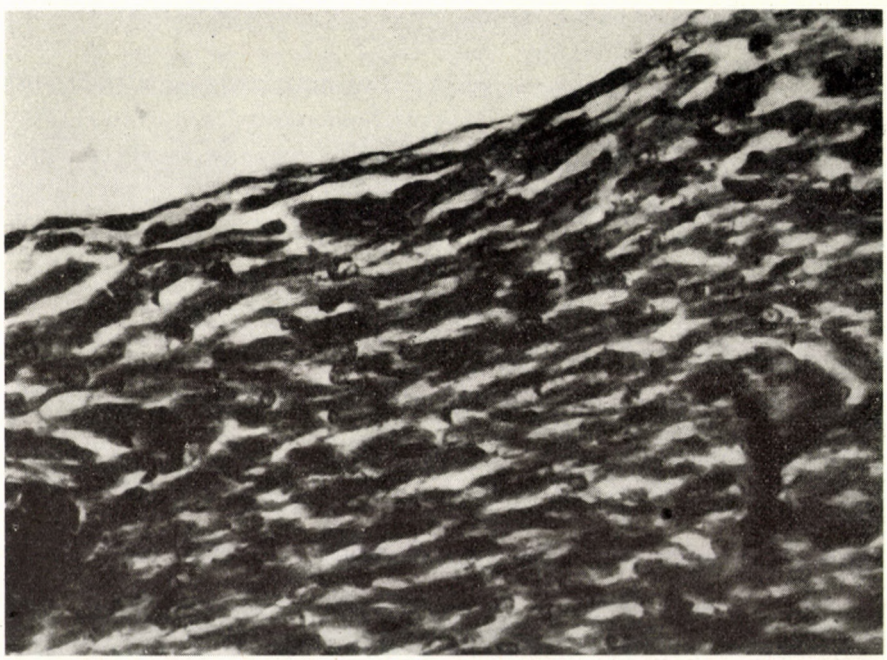

FIG. 5. Control infantile rabbit. Subendocardial layer of the left ventricle. Vacuolization, disintegration of fibres are not visible. (Medium-power view)

The brain showed no gross or microscopic changes.

b) Histological findings in the second adult control rabbit.

The changes in the heart were similar to those described above. The brain was oedematous. There was congestive hyperaemia in the spleen. In the liver, microglobular fatty degeneration, as well as acinocentral necrosis were visible, with leucocyticin filtration around the latter. In the kidney congestion and in some efferent ducts haemoglobin casts were found (Fig. 4).

III. Histological findings in the five control infantile rabbits.

The animals were killed by a blow to the occiput. The only change demonstrated in the liver, spleen and kidney was hyperaemia. There were haemorrhages on the leptomeninx and punctate haemorrhages in the subendocardial area of the left ventricle of the heart. These haemorrhages arose presumably at killing (Fig. 5).

Discussion

In infantile rabbits excessive haemolysis could be induced by treatment with phenylhydrazine. The resulting hypoxia gave rise to extensive and severe hydropic-vacuolar degeneration in the myocardium, especially in the left ventricle. The histological appearance of this vacuolar degeneration was exactly the same as that found in the heart muscle of newborns dead with icterus gravis. Our previous investigations have made it clear that the myocardium of infantile animals is highly sensitive to chronic hypoxia; it undergoes vacuolar degeneration rapidly while in the myocardium of adult animals there is at most a slight degeneration.

The obtained results support our view that myocardial vacuolar degeneration in icterus gravis is not a specific change, but a consequence of the hypoxia prevalent in that condition.

Further investigations are carried out in an effort to prevent the development of myocardial changes.

Summary

Haemolysis was caused by treatment with phenylhydrazine in infantile rabbits. The hypoxia resulting from haemolysis induced the same type of hydropic-vacuolar degeneration in the heart muscle, which is found in the hearts of newborns dead with icterus gravis. These observations lend support to the view that hypoxia alone is responsible for the vacuolar degeneration of the myocardium observed in icterus gravis.

References

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