PATHOMORPHOLOGIC CHANGES OF THE CARDIOVASCULAR SYSTEM IN TWINS

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The author reports on primary diseases and on secondary reactions of adaptation in fetal hearts of twins. Cases of fibroelastosis endocardica, cases of hypertrophy of the heart, and the circulatory reactions following feto-fetal transfusion in twins, are discussed.
Using histochemical methods, several enzymes of the myocardium in deceased twins have been investigated.

Adequate growth and sufficient oxygen supply for the cell metabolism of the fetus do not only depend on the function of the placenta but on cardiac output and circulation in the fetal blood flow system, too.

In the fetal heart, as in that of the adult, from the viewpoint of the pathologist, one may separate (1) primary diseases, from (2) secundary reactions of adaptation.

This short report will show macroscopic and microscopic changes, including enzyme-histochemical findings in human fetal twin hearts.

How can the pathologist see causes and consequences of disorders of the cardiovascular system? Cardiac hypertrophy, or fibroelastosis endocardica, develops within weeks and can be recognized macroscopically. Morphologic changes originating by lack of oxygen can be established after some hours; they may be seen by conventional or fluorescence microscopy. Very acute disorders, beginning within minutes, can only be recognized by means of electron microscopy and enzyme histochemistry.

1. *Primary fetal heart diseases*, except malformations, are very rare. Only myo- and endocarditis due to viruses, protozoa, and bacteria, come into question. Fibroelastosis endocardica combined with hydrops congenitus in deceased twins has hitherto been described only thrice (Stadler 1961, Hoenicke 1963, Nora et al. 1967). The cause of this fetal fibrous endocardial thickening has been clarified just as rarely. During the last five years we found one stillborn twin with hydrops and fibroelastosis endocardica of the right ventricle among 10 selected deceased MZ pairs of twins, properly examined. The cause might be looked for in a chronic hypoxic damage of the heart (Figs. 1 and 2). Virologic examinations of the heart were negative. The twins had the same blood group and sex.

2. *Morphological reactions of adaptation of the fetal heart* confirm the statements (Dawes 1969) on blood flow in the fetal experimental animal (lamb), stating that both sides of the heart work parallelly. The right heart mainly provides the lower region of the body over the

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patent ductus botalli and the placenta parallel with the fetal circulation. The left heart mainly supplies the coronary arteries and the brain.

As in the adult, cardiac hypertrophy demonstrating adaptation can be seen in the fetus. The fetal myocardium also reacts to an increased stress following hemodynamic and metabolic pathological influences by hyperplasia caused by a more rapid succession of the mitotic division (Thomas 1962). Whereas the hypertrophy of the right heart — e.g., in erythroblastosis with chronic anemia and placental hyperplasia or in arteriovenous vascular anastomoses in the brain with hypervolemia of the vena cava superior — is known in the singleton, still further possibilities come into account in the MZ twin.

In our autopsies we observed:

1. Chronic hypervolemia and polycythemia following chronic feto-fetal transfusion in vascular anastomoses in the placenta. Generally, the heart of the hypotrophic anemic donor is normal or only slightly enlarged, whereas that of the recipient is strongly increased in comparison with normal weights of the fetal hearts (Teichmann 1968).
2. Hypertonia and disordered circulation following placental vascular anastomoses between parts A and B in vitium cordis congenitum (Fig. 3) of one twin. There was a cor biloculare in other multiple malformations (cyclopy, agyria, dysmelia).
3. A " third " circulation, parallel with the fetal organism and the placenta, through an acardius amorphus anencephalus, leading to a volume hypertrophy of the twin in case of a monochorionic twin placenta (Figs. 4 and 5).

In 11 further preponderantly heterozygotic liveborn twins, who died withins 7 days, we moreover carried out histochemical examinations of the heart immediately post mortem. The prenatal ages of the twins stood at 28 to 35 weeks. Corresponding to the duration of pregnancy, their birth weights were stated within the scope of the 50% percentile of a normal weight curve for dichorionic twins, except one case of hypotrophy (Fig. 6). Three pairs of twins were examined. In these cases the occurrence of 19 different enzymes in the newborn myocardium was examined and changes into perinatal hypoxia and acidosis were found out.

Experiments were carried out on human autopsy material. After freezing by carbon-dioxide snow (the time for autolysis was not longer than 40-120 minutes), 10-14 μ thick general section of the left and the right heart were made in the cryostates (system Dittes-Duspiva) and were brought to reaction in the various incubation media according to regulations. Control slides were incubated without the respective substrates.

RESULTS

1. Histochemical changes following acute disorders in the fetal myocardial cell predominantly occur in the right ventricle also in twins deceased few hours post natum. Loss of glycogen is markedly stronger in the right ventricle, but occurs in both ventricles after a longer survival time. In severe hypoxemic damages, glycogen is consumed in the subendocardial conduction system last of all.
2. In more progressive gestational age, changes of the enzyme activities can be also stated in the histologic section. In the examined twins, less activities of enzymes could be stated at the gestational age of 28 weeks and much more at 35 weeks.

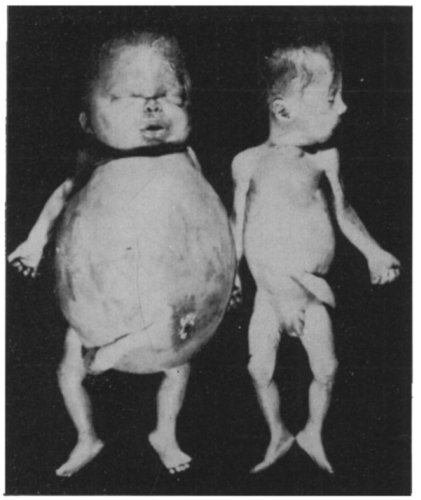

Fig. 1. Twin I with hydrops congenitus, the abdomen enlarged by 1300 cc ascites, birht weight 3200 g.
Twin II with 1120 g birth weight, gestational age 32 weeks. (No. V 225-226/66).

Fig. 2. Twin I with fibroelastosis endocardica; view into the right ventricle with a porcellaneous whitish thickening of the endocardium. Autopsy preparation. (No. V 225/66).

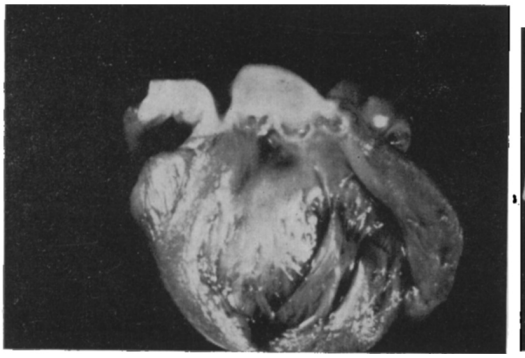

Fig. 3. Muscular cardiac hypertrophy and hyperplasia of the monochorionic male twin I; gestational age 24 weeks, birth weight 1000 g Weight of the heart 12 g (standard weight 6 g). Autopsy preparation. (No. V 707/66).

Fig. 4. Monochorionic twin placenta with female acardius amorphus anencephalus (twin II); birth weight 280 g.
Female twin I, 660 g birth weight, with cardiac hypertrophy and hyperplasia caused by circulatory stress due to additional supply of the acardius by vascular anastomosis. (No. V 819-820/66).

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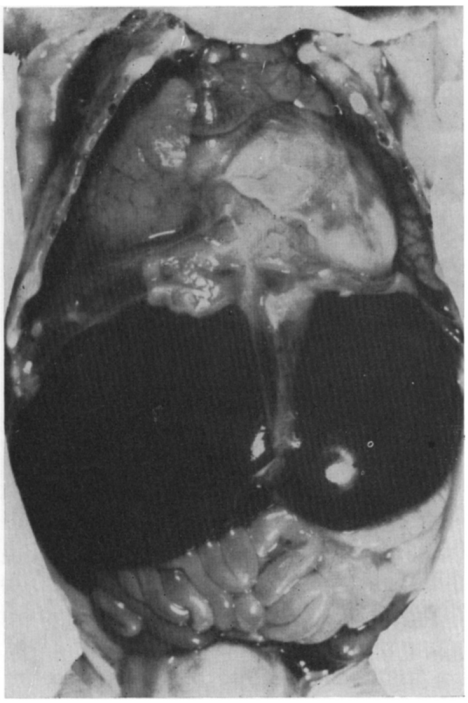

Fig. 5. Situs of the thorax and the abdomen of twin I (see Fig. 4). Gestational age 24 weeks. Hypertrophy and hyperplasia of the heart and the liver. Weight of the heart 9 g, and of the liver 60 g. (No. V 819/66).

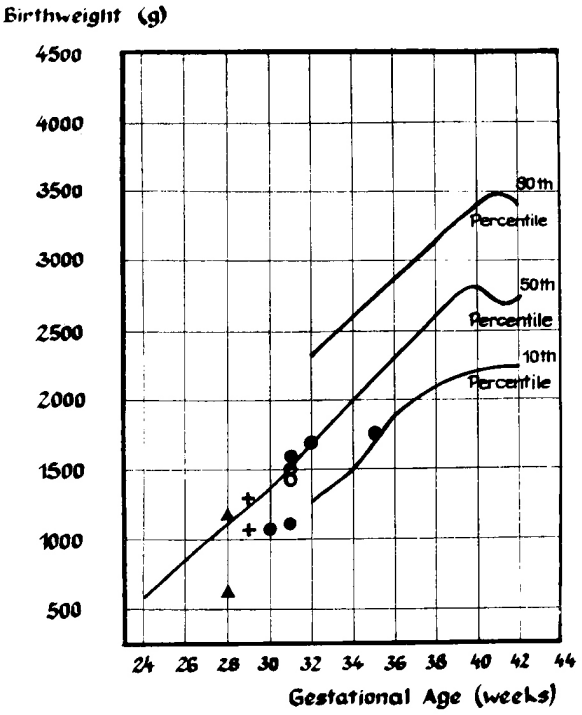

Fig. 6. Intrauterine growth standard for dichorionic twin (—) weights of twin sets (+ , ▲ , ○) and single twins (●), observed by the author concerning their enzyme activities.

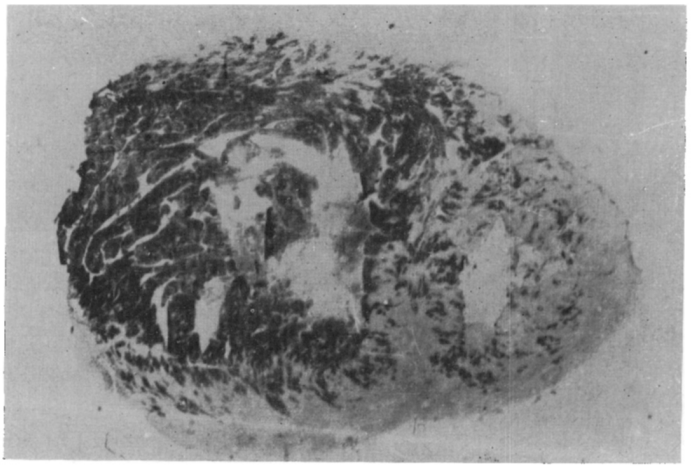

Fig. 7. Histochemical demonstration of phosphorylase *a* in the heart of a newborn twin. Microscopic slide; the reaction is more intense in the left ventricle then in the right. The histochemical study has been carried out through Lojdas method. (No. Su 262/72).

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Table. *Enzymes in the Human Newborn Myocardium* (Gestational age 28-35 weeks)

Enzymes of carbohydrate metabolism	Activity
1. Lactate dehydrogenase	+++
2. Glucose-6-phosphate dehydrogenase	++
3. α-Glycerophosphate dehydrogenase	++
4. Phosphorylase *a*	+
5. Glucose-6-phosphatase	∅
Enzymes of aminoacid metabolism	
6. Glutamate dehydrogenase	+
7. Leucine aminopeptidase	∅
Enzymes of lipid metabolism	
8. β-Hydroxybutyrate dehydrogenase	++
9. Nonspecific esterases	+
Enzymes of citric-acid cycle	
10. Succinate dehydrogenase	++
11. Isocitrate dehydrogenase	++
Other enzymes	
12. Monoamino oxidase	(+)
13. Cytochrome oxidase	+++
14. Adenosintriphosphatase	+++
15. Alcaline phosphatase	∅
16. Acid phosphatase	∅
17. NADH-tetrazolium reductase	++
18. NADPH-tetrazolium reductase	++

∅ = none; (+) = very low; + = low; ++ = moderate; +++ = high

3. In the fetal period, the following enzymes are not present in the myocardium: alcaline and acid phosphatase and glucose-6-phosphatase. There is little aminoacid metabolism with low activities of the glutamate dehydrogenase. Monoamino oxidase in the histologic section could be demonstrated with very low activities in traces in the twins from the 28th week. The quantity of monoamino oxidase increases strongly with age. The myocardium doesn't produce leucine aminopeptidase.

4. Among the enzymes of carbohydrate metabolism, lactate dehydrogenase is predominantly present, becoming most traceable and showing an increased hypoxydotic myocardium.

5. Independent on the glycogen contents of the myocardium, phosphorylase *a* proves to be a sensitive indicator for lack of oxygen. In experimental myocardial infarction this enzyme has also been of interest for the statement of the disordered metabolism of the myocardium. A predominant absence of phosphorylase *a* in the right myocardium partly

supports the conception of anatomic dextrocardiac failure (Fig. 7). In severe hypoxydotic conditions, both ventricles are affected by a reduction of phosphorylase *a*. In hypoxia, there are small drops of fat in the myocardium; less frequently, necroses could as well be stated histologically by routine stainings.

6. Dichorionic twins with a normal weight of the heart do not differ, essentially, from a control group of singletons in their myocardial metabolism.
7. Twin partners did not show any difference in their myocardial fermental patterns, even with hypotrophy of one of them.
8. The activities of enzymes in the human newborn myocardium are shown in the Table.

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