COXSACKIEVIRUS INFECTION DURING GRAVIDITY ENHANCES THE PATHOPHYSIOLOGICAL PROCESS IN PUPS AFTER CHALLENGE INFECTION WITH THE SAME VIRUS

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Introduction

Enteroviruses are distributed worldwide. Very often infections caused by these viruses go unnoticed due to subclinical course. In a pregnant woman such infections remain frequently undiagnosed because of mild and non-specific manifestations. In neonates, however, coxsackie B virus (CVB) infections can cause the sepsis syndrome, sometimes followed by severe disease and death. Moreover, seroepidemiological studies relate CVB infections during pregnancy with increased risk for childhood-onset type 1 diabetes.

Aim

The objective of this study was to follow-up the pathophysiological process after coxsackievirus infection in offspring born to dams infected with the same virus in the first, second and third week of gravidity.

Materials and methods

- Virus: Coxsackievirus B4-E2
- Mice: CD1 outbred mice
- Infection: Pups were challenged orally with coxsackievirus B4-E2 at a dose of 0.2 x 10^6 $TCID_{50}$/ml on day 25 after birth.
- Mock infected (with PBS parallel to the virus infection) mice served as controls. Pups were sacrificed on days 5, 12 and 21 post infection (p.i.).
- Collected material: Heart, pancreas
- Quantitative measurement of genome copies: RNA isolation, Real-time RT-PCR
- Histopathology: Sections of heart and pancreas tissue, haematoxylin and eosin staining

Results

Independent of the copies of RNA which were observed in the heart and pancreas of the challenged offspring, we observed histopathological changes only in the pancreas of the challenged pups. After oral infection we observed inflammation of the islets of Langerhans, the endocrine tissue of the pancreas for the first time. The inflammation was present in the offspring of the mice infected in the third week of gravidity.

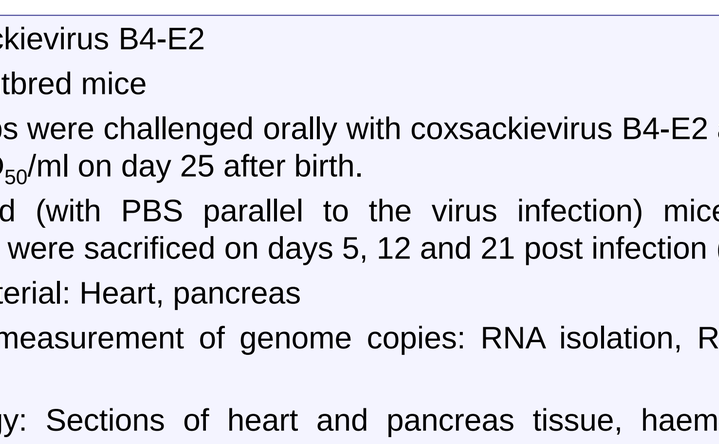

Fig. 1. Quantitation of viral load in heart and pancreas tissues of virus-challenged pups on day 5 p.i.
Day 4 = dams infected in the 1st week of gestation (on day 4); Day 10 = dams infected in the 2nd week of gestation (on day 10); Day 17 = dams infected in the 3rd week of gestation (on day 17); +/+ mother and pup infected; -/+ mother mock infected and pup infected; (P) = pancreas; (H) = heart.

Results

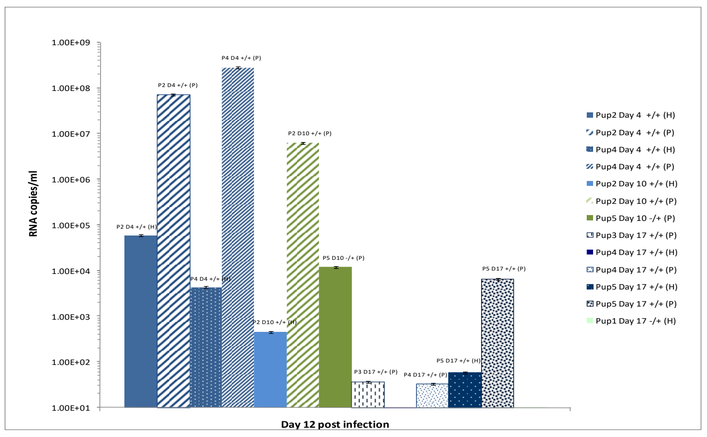

Fig. 2. Quantitation of viral load in heart and pancreas tissues of individual virus-challenged pups on day 12 p.i.
+/+ mother and pup infected; -/+ mother mock infected and pup infected; P = pup; 1, 2, 3, 4, 5 number code of individuals per category; D = day; (P) = pancreas; (H) = heart.

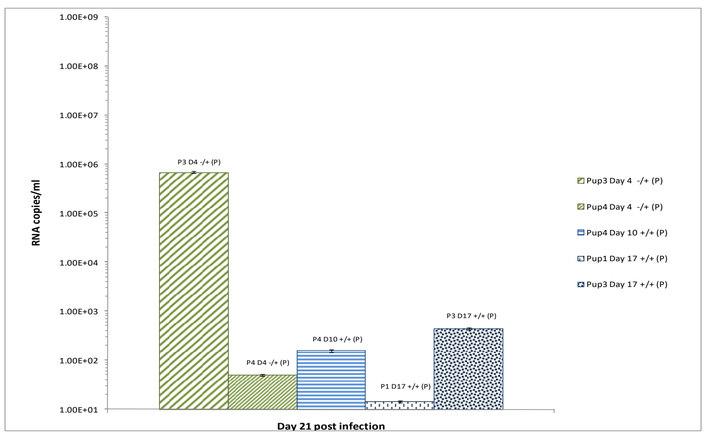

Fig. 3. Quantitation of viral load in heart and pancreas tissues of individual virus-challenged pups on day 21 p.i.
+/+ mother and pup infected; -/+ mother mock infected and pup infected; P = pup; 1, 2, 3, 4, 5 number code of individuals per category; D = day; (P) = pancreas; (H) = heart.

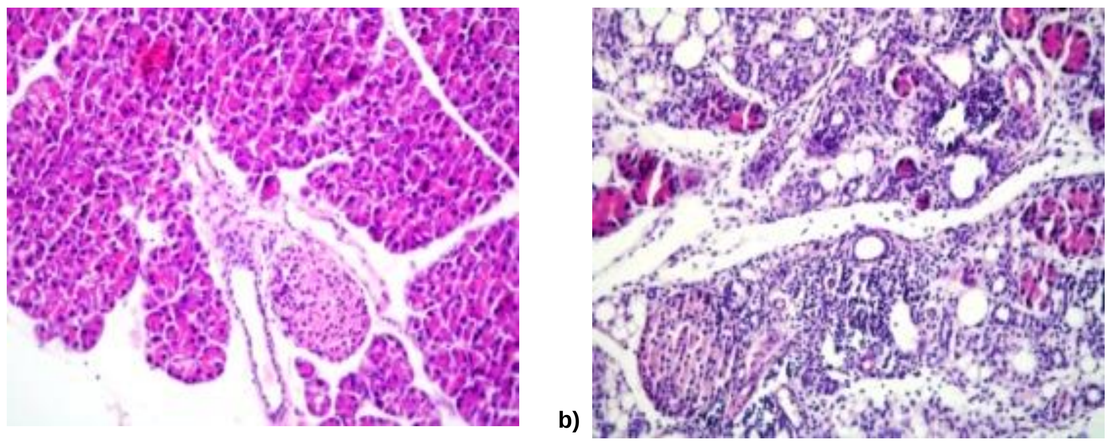

Fig. 4. Histopathological observations in the pancreas of challenged pups.
a) Control pancreas (20x)
b) Chronic pancreatitis and lymphocytic infiltrates in the islets (20x)

Discussion and Conclusion

We conclude that infection during gravidity enhances the pathophysiological process especially in the pancreas, and the time of infection during gravidity may also rule the intensity of the infection, which may be enhanced by the innate and adaptive immune responses.

The study was approved by the Ethical Committee of the Slovak Medical University and the State Veterinary and Food Control Authority of the Slovak Republic.
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