

PERMEABILITY OF THE PLACENTAL BARRIER TO HEMOLYTIC STAPHYLOCOCCI AND TRYPAN BLUE

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Intravenously injected staphylococci and trypan blue first enter the amniotic fluid, from which they pass by the enteral route into the fetal blood.

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The penetration of bacteria through the placenta during normal pregnancy has been the subject of conflicting reports in the literature [8].

In the present investigation the permeability of the placental barrier to hemolytic staphylococci and trypan blue (molecular weight 990) was studied during normal pregnancy.

EXPERIMENTAL METHOD

Two series of experiments were performed on rabbits at different periods of pregnancy. Permeability of the placental barrier to hemolytic staphylococci was studied in the experiments of series I, and its permeability to trypan blue in series II. The hemolytic staphylococci were injected intravenously in doses of 2-3 billion bacterial cells. At various time intervals after injection of the staphylococci (2-3 h and 2-3 days), caesarian section was performed. Under sterile conditions, maternal blood (from the heart), fetal blood (from the heart) and liver, were taken for seeding on Petri dishes with meat-peptone agar. Embryos at different stages of intrauterine development were ground up completely. The amniotic fluid and the maternal and fetal parts of the placenta were also taken for seeding. The Petri dishes with the seeding material were incubated for 24 h at 37°, after which they were examined for the presence of colonies of hemolytic staphylococci. Trypan blue (1% solution) was injected into a vein of the ear as a single dose of 2 or 4 mg/kg, 2-3 h and 1-2 days before caesarian section, after which two doses, each of 2 mg/kg, were given at intervals of 1-2 days. At operation the presence of trypan blue in the maternal plasma, the amniotic fluid, and the gastric contents was investigated. Further evidence of permeability of the placental barrier to trypan blue was given by staining of the embryos or fetus itself.

EXPERIMENTAL RESULTS

In the experiments of series I, performed on 28 rabbits, starting from the 11-12th day of pregnancy, i.e., from the time of formation of the placenta, and continuing until the end of normal pregnancy, the placenta was found to be impermeable to hemolytic staphylococci during the second and last thirds of pregnancy. Only in two (of 28) cases were staphylococci observed to pass through the placenta from the maternal to the fetal blood. In the same series of experiments changes in permeability of the placenta associated with maternal disease resulting from intravenous infection with staphylococci were studied. In these experiments a culture of hemolytic staphylococci was injected intravenously 2-3 days before caesarian section in doses of between 2 and 10 billion bacterial cells. The diseased rabbits were investigated in the second and last thirds of pregnancy. Altogether 23 animals were used in the experiments. In all animals staphylococci were observed to pass through the placental barrier if injected before the 25th day of pregnancy, i.e., at a time when growth and development of the placenta was still continuing. Large numbers of staphylococci were found in the amniotic fluid, the fetal blood and liver, or the ground embryonic tissues. The staphylococci first penetrated into the amniotic fluid, and not through the capillary walls of the umbilical vessels, and infection of the fetus took place only later as a result of aspiration of amniotic fluid.

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In the experiments of series II, on 24 rabbits at different periods of normal pregnancy, trypan blue was injected in a dose of 2 and 4 mg/kg 2-3 h before caesarian section. In all the experimental rabbits, regardless of the period of pregnancy, the placenta was found to be impermeable to trypan blue. In the same series of experiments, trypan blue was injected into 32 rabbits during the second and last thirds of pregnancy, 2-3 days before caesarian section, in a dose of 2 and 4 mg/kg. When injected in a dose of 2 mg/kg, the trypan blue did not pass through the placental barrier, although it was present in the maternal blood plasma. If trypan blue was injected in a dose of 4 mg/kg, or into two doses of 2 mg/kg at intervals of 1-2 days, the dye passed through the placental barrier. In this case trypan blue also was found initially in the amniotic fluid, after which it entered the fetal blood through the enteral route by aspiration of amniotic fluid. Consequently, both staphylococci and trypan blue, if they passed through the placenta, entered the fetal blood as a result of preliminary penetration through the wall of the chorionic villi into the amniotic fluid, and then by an enteral route into the blood, and not through the capillary endothelium of the umbilical vessels.

The results demonstrate that during normal pregnancy staphylococci do not pass through the placental barrier. When, however, the intravenously injected staphylococci produce a disease, the normal permeability of the placental barrier is disturbed, and it becomes permeable to staphylococci. Results obtained in our laboratory show that any unusual form of stimulation (especially one causing a disease in the pregnant female) inhibits the "gestation dominant" [1-3], with an accompanying disturbance of the normal permeability of the placental barrier.

In the light of these concepts the results obtained in the experiments with trypan blue can be understood and the contradictions found in the literature can be explained. Repeated injection of trypan blue, or injection of a large dose, acts as a stress stimulus, causing inhibition of the "gestation dominant." According to some workers [4, 7, 10], for instance, trypan blue does not pass through the placental barrier (a single injection of the dye was given). According to other authors [5, 6, 9], however, trypan blue passes through the placental barrier, and may accordingly play the role of teratogenic factor (the dye was injected repeatedly).

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