Reports

Congenital Malformations Produced by Amniotic-Sac Puncture

It has recently been reported (*1–3*) that the sex of the human fetus can be diagnosed with a high degree of reliability by examination of cells from amniotic fluid at any time from 8 weeks (*2*) to term. For this and other reasons (*4*), there are likely to be further experiments in which attempts will be made to obtain samples of amniotic fluid from women as early as possible in pregnancy. The theoretical possibility of harm to the fetus from such procedures has already been pointed out (*3*), and the present paper reports experimental evidence to this effect.

During studies in this laboratory, where attempts were made to inject substances into the amniotic sacs of mouse embryos (*5*), it was found that amniotic-fluid leakage caused teratalogical abnormalities. This was confirmed in further experiments (*6*). The uteri of pregnant mice were exposed through a midline abdominal incision, on day 13 of gestation (the day a vaginal plug was observed being day 0). A No. 26 hypodermic needle was inserted through the uterine wall and amniotic sac into the amnion of each embryo in one uterine horn, but nothing was injected. The embryos in the other horn were counted and acted as controls. The mother was then sewn up and reopened for examination of the embryos on day 18, just before term.

Of 14 treated mothers, six aborted or resorbed their litters. In the remaining eight litters, ten out of the 17 treated embryos that survived had cleft palates, whereas the palates of the 15 control embryos were closed. This is a highly significant difference ($p = 0.0003$ by Fisher's exact method). These cleft palates appear to have resulted from a loss of amniotic fluid, which constricted the embryo, pushing the head down on the chest and forcing the lower jaw upward. Thus the tongue was forced between the palatine shelves, which therefore could not fuse.

Our results with mice suggest that there may be a definite risk to the baby in inserting a needle into the amniotic sac in human beings, especially during the early stages of pregnancy when there is the danger of inducing abnormalities in the developing embryo. (*7*).

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7. Financial support from the National Research Council of Canada is gratefully acknowledged.

13 July 1956

Production of Increased Circulating Hemoglobin in Mice

An extract from the plasma of rabbits made anemic by phenylhydrazine, when injected subcutaneously into normal rats, has been found to produce increases in red-cell counts, in reticulocytes, in hemotocrit values, and in hemoglobin concentration (*1*). Extracts, previously tested on rats, have also been found effective in mice when they were given in larger doses. This result makes it appear likely that the polycythemic principle in anemic rabbit blood is effective generally in animals.

Preparation 2, Table 1, was made from a batch of plasma extract that gave a polycythemic response in rats. It was concentrated to one-half its original volume under reduced pressure at about room temperature. It was injected subcutaneously for 20 days into four Swiss albino mice of 33-g average weight. Each mouse was given 1 ml daily of the concentrate; this is equivalent to a dose of the unconcentrated material of 6 ml/100 g of body weight. When injecting rats, we used 2 ml/100 g. The dose ratios are shown in Table 1. Preparation 1, a control, was made in the same way as preparation 2, but from the plasma of normal rabbits. It was also injected into four mice, for 27 days, at three times the dose used for rats, calculated per gram of body weight. Preparations 1 and 2 were hypertonic. Preparation 3 was made from the same lot of plasma as preparation 2, first by concentration and then by dialysis at 4°C against distilled water to make the final concentration isotonic. It was injected into four mice in an amount corresponding to seven times the dose used for rats, per gram of body weight. Preparations 2 and 3 produced increases of hemoglobin; the control extract 1 had no effect. We have not found any activity in extracts of plasma from normal rabbits. As with rats, when the injection of active material is stopped, the hemoglobin concentration returns to its original normal value (*2*).

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2. This investigation was supported by research grant Nonr-220(09) from the U.S. Office of Naval Research.

4 June 1956

Table 1. Effect of different plasma preparations on mice. Average hemoglobin before and after injection (g/100 ml). The dose ratio was calculated as the amount of material injected per unit of body weight.

Preparation No.	No. of mice	Dose ratio (mouse/rat)	Days injected				
			0	7	14	20	27
1	4	3	15.7		15.6		15.5
2	4	3	14.3	15	17.5	18.2	
3	4	7	16.2	17.6	19.9		