space above the tongue, retracting ventrally, until they displace the tongue down and meet in the midline to form the roof of the mouth.

When palate closure was divided into seven arbitrary stages to make statistical analysis easier, he noted differences in the age at which closure occurred between different strains, but there was considerable variation in palate stage at a given chronological age, even within litters. This variation was greatly reduced when embryos were classified by their developmental rather than chronological age, using a scoring system based on the external characteristics of the embryo—a "morphological rating." When palate closure was scored against the morphological rating, the strain differences in stage of closure became much more apparent. In a companion paper we showed that cortisone caused cleft palate by delaying shelf movement and that there was more delay in the late-closing and susceptible (A/J) strain than the earlier-closing and resistant (C57BL/6) strain. The correlation between late closure and susceptibility was confirmed in various genotypes by Daphne G. Trasler. From these observations there emerged the idea of a threshold, beyond which delayed shelves could not close and cleft palate would result. They also showed how an embryo's susceptibility to environmenal "insults" could be altered by genetic differences in its normal developmental pattern that determined its distance from the threshold. This provided the most extensively defined experimental model for the multifactorial threshold concept as it relates to the common congenital malformations. Groups around the world are still exploring

1. Fraser F C & Fainstain T D. Production of congenital defects in the offspring of pregnant mice treated with cortisone. Pediatr. 8:527-33, 1951. (Cited 293 times since 1955.)