ANOMALOUS ALAR PLATE REGULATION IN THE EARLY CHICK NEURAL TUBE

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In previous studies attention has been given to numerous problems concerning regulatory mechanics and proliferation control mechanisms in the chick neural tube. In a number of instances studies were made of the regulative development, including proliferation patterns, occurring in response to induced neural tube defects (Birge and Hillemann, 1953; Birge, 1959a; 1959b; 1960; 1962). However, most attention has been given to the mesencephalic alar plate system of the early chick brain.

Subsequent to the removal of one mesencephalic alar plate, cells soon migrate into the deficient area from the opposite intact alar plate. Twelve to twenty-four hours after the operation, mitotic rate has increased throughout the intact alar plate tissue to 30-35% above normal. Proliferation continues at an accelerated rate, giving rise by day 7 to an optic tectum with a cell population approaching that of two normal mesencephalic alar plates of comparable development. By day 8 an *over-shoot* occurs in the growth of the regulating system, and this condition is sustained through day 9. During this period of *over-growth* the cell population averages 10% greater than that of two normal alar plates. Coincident with this *over-shoot,* mitotic activity drops below normal. Accordingly, the cell population decreases on day 10, showing a slight *under-shoot* before leveling off at the normal value (for two plates) by day 12.

The mechanism controlling proliferation, presumably a feedback system, appears quite sensitive to the size and/or density of the cell population, compensating for increases or decreases therein, by concomitant shifts in mitotic rate. Apparently the alar plate system is normally *self-limiting* or *self-regulating* in the control of proliferation. The regulative responses to hemilateral alar plate ablation are summarized in Table 1.

Though it has been well established that the regulatory pattern noted above is the usual response to early hemilateral alar plate ablation, a few exceptions to this pattern have been noted. They will be treated in this paper, as they bear on the subject of proliferation control.

Methods and Materials

This study concerns three chick embryos out of 138 which underwent hemilateral alar plate ablations during 28-38 hours of development. After each operation the embryo was reincubated and they were subsequently sacrificed at 2 to 20 days of development.

The three specimens in question were sacrificed at 4-5 days of development. In each instance the brain lesion was less complete than usual, leaving a significant amount of damaged tissue intact. All operations

TABLE 2.—Extent of alar plate regulation occurring subsequent to hemilateral ablation.

Age of Embryos	No. of Embryos Sacrificed	Overall Range of Regulative Growth	Average Extent of Regulative Growth	% size of Intact Alar Plate Area Compared With 2 Normal Plate Regions
Days		%	%	%
2	8 (8)	0-3	..	..
3	7 (4)	-16	10	55
4	5 (4)	18-38	28	64
5	5 (4)	35-52	44	72
6	7 (4)	47-68	54	77
7	4 (4)	60-72	70	85
8	8 (4)	102-120	116	108
9	6 (4)	108-123	120	110
10	10 (4)	75-93	86	93
11	7 (0)	.....	....	....
12	8 (4)	76-123	98	99
13	4 (0)	.....	....	....
14	8 (4)	96-109	102	101
15	8 (0)	.....	....	....
16	8 (4)	97-104	100	100
18	6 (4)	97-112	106	103
20	5 (2)	91-101	96	98

The extent of regulative growth is given as the percentage volume of tissue produced in excess of that normally formed by one alar plate. The number of embryos used in each age group for volumetric studies is given in parenthesis. (From Birge, 1959a.)

were performed as previously described (Birge, 1959a). Also, all other experimental procedures were maintained as previously noted.

RESULTS

Histological examinations of the three embyros in question revealed excessive infoldings of the dorsal half of the mesencephalon, including the alar plate system. In each case, the extensive infolding nearly filled or occluded the mesocoele, rendering the mesencephalon essentially solid in appearance. Also in each instance, the cellular population of the alar plates greatly exceeded that normally found to occur during the post-operative period.

Estimates of the population size, based on methods previously used (Birge, 1959a), indicated a five to eight-fold overproduction of cells, as compared to normal embryos of corresponding development. As noted above, cell production normally bears a distinct relationship to population size and/or density. When modest over-production results, cell division rate normally declines, presumably in response to such proliferation control mechanisms as are discussed above.

However, in the three instances noted herein, proliferation rate apparently was not subjected to such limitations or restrictions. It would seem that the mechanisms which normally limit proliferation in such systems were inoperative in these three cases, at least in part. This suggests that in a low percentage of cases, proliferation control mechanisms normally operative in the mesencephalic alar plate system of the chick may, under certain circumstances, break down, at least to some extent. As a consequence excessive over-proliferation may result. The three cases in point bear at least a superficial resemblance to carcinogenetic systems in this respect.

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