compensation of errors due to this factor and to differences in the completeness by which c is maintained by rephosphorylation at different ATP levels. It is of importance to emphasize the high value of $\Delta F°$ which, having been estimated before,[2, 3] is now obtained with more satisfactory precision and is found to exceed even the $\Delta F°$ and ΔH values of the hydrolysis of ATP.[8–10] It should be kept in mind that the value of k, notwithstanding its seemingly different mode of determination, is still essentially identical with a Michaelis-Menten constant. Hence it is a true association constant only if the velocity constants for combination and dissociation are considerably greater than that for the enzymatic decomposition. If this were not the case, k and $\Delta F°$ would have been underestimated.

Considering the excess of Mg over ATP in these experiments, it should be kept in mind that practically all ATP is in the form of the Mg complex[11, 12], so that the above derivation applies to this rather than to ATP as such.

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*RESULTS OF INVERSION OF NEURAL PLATE MATERIAL**

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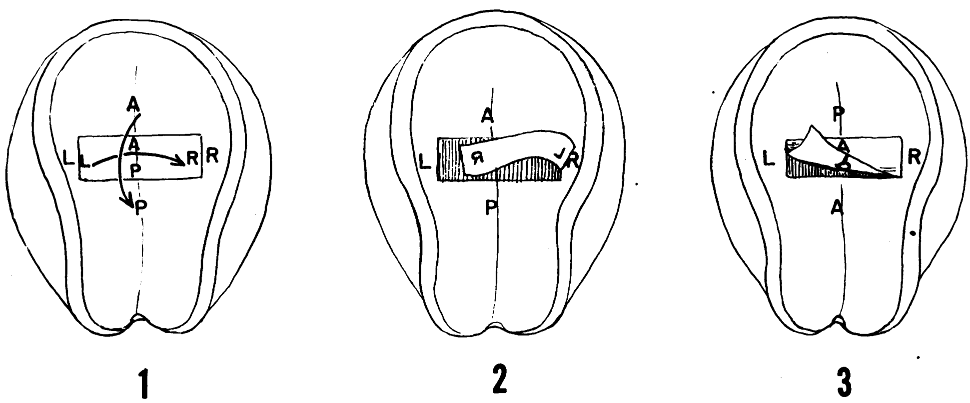
Capacities for differentiation have frequently been tested by transplanting or explanting parts of the embryonic nervous system. Experiments of this nature have contributed much information concerning the time of tissue determination, of regional determination, and specificity.[1–3] In the present investigation the ability of the medullary plate to form nervous system under varied conditions of autotransplantation has been studied.

It is well known that the chordamesoderm influences the overlying ectoderm to form nervous system. The present experiments were made to study development of the nervous system under conditions of inversion. A strip of medullary plate together with underlying archenteric roof was cut out of neurulae of the spotted salamander *Amblystoma punctatum* and replaced in all possible varying axial relations. The following questions were asked: (1) How do these reversals affect the nervous system and the mesodermal derivatives? (2) Will the structures formed adjust themselves to the level of the embryo as a whole? (3) Will the reimplanted structures be otherwise adjusted to their surroundings?

The operations performed are diagramed in Figures 1–3. Axes of the strips were reversed as follows: anteroposterior and mesiolateral (Fig. 1); mesiolateral and dorsoventral (Fig. 2); and anteroposterior and dorsoventral (Fig. 3). Stages used varied from Harrison's Stage 14 to Stage 16. The level of the strip was varied either anteriorly or posteriorly in the embryo to test its regional specificity.

Healing in all series occurred remarkably rapidly. The graft maintained its shape. In the operations involving dorsoventral reversal the graft remained sharply outlined because of the contrast between the lightly pigmented chordamesoderm and the fully pigmented neural plate surrounding it.



FIGS. 1–3.—Diagrams of the early neurula of *A. punctatum*, showing the field of operation and indicating the orientation of the strip of the prospective neural plate which was modified experimentally in its axial relations. Fig. 1, anteroposterior and mesiolateral axes reversed. Fig. 2, mesiolateral and dorsoventral axes reversed. Fig. 3, anteroposterior and dorsoventral axes reversed.

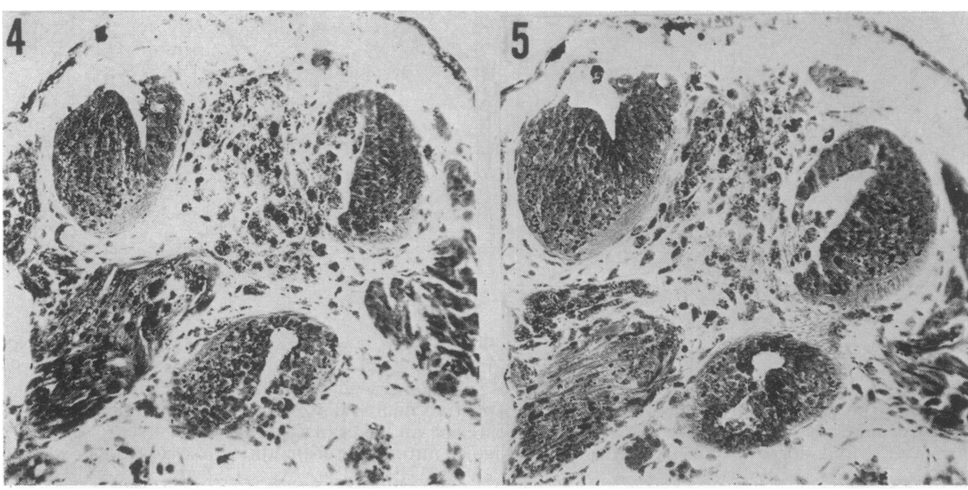
In the most favorable cases in the first series (as in Fig. 1), reversal without inversion, the closing of the neural folds was not retarded. The folds arched over the graft and obscured it from view. Subsequent development was fairly normal during the early stages, except for a thickening of the neural tube in the vicinity of the region of operation. As development progressed, the larvae were seen to have shortened bodies; it was suspected that this was due to defective development of the notochord, a suspicion later justified by study of the sections.

The nervous system in the first series (Fig. 1) has always developed regularly, irrespective of the level of operation. Marked deficits, however, have been found in the principal axial mesodermal structure, the notochord. In the less favorable cases, particularly those performed in the late neurula, the irregularities were chiefly those of blockage and malformation of the posterior head and trunk. The chordamesoderm evidently served as a partial block to one or the other of the enveloping neural folds.

In the second and third series (Figs. 2 and 3), where the dorsoventral axis was reversed, an entirely different course of development resulted. The nervous system from the graft was inverted. The only animals in which the transplanted nervous system showed any regularity were among the group operated at Stage 14. The inverted strip acted as a block to the nerve tube of the host; at the level of the graft it can be seen in sections that three nerve tubes are present (Figs. 4 and 5). Two lateral ones derive from the host medullary folds, a median one from the graft. In the case of the series (Fig. 2) in which the anteroposterior axis of the transplant was not reversed, the nervous structures induced in the graft proved to be of the appropriate level, as would be expected.

The chordamesoderm in inverted position is in most cases prevented from attaining its characteristic organization. It forms dissonant elements of unique cellular structure, as shown in Figures 4 and 5. In the third series, where the anteroposterior axis was reversed, the notochord appeared to form a more extensive indeterminate mass than in the second.

The chordamesoderm had already gastrulated normally before the operation and



FIGS. 4, 5.—The photomicrographs show the development of three typical nervous systems resulting from the operation shown in Fig. 3. The median nervous system has developed from the grafted strip; the two lateral ones, from regularly developing neural folds which were separated by cordamesoderm during the period of closing of the neural folds. The inchoate mass between the three nervous systems is composed of chordamesoderm which forms an indeterminate cellular mass lacking characteristic notochordal structure.

had performed its primary induction. Marx,[4] in Spemann's[5] laboratory, had shown that, under other conditions of transplantation, the notochord-forming region was the one region of the early gastrula able to realize its own potentialities. The most striking result of the present experiment has been to show that at a later stage, after the neural plate and the archenteric roof have started on the course of their differentiation, the notochord is far more dependent on its surroundings than is the nervous system.

Thus, in answer to the questions posed above, the following would appear to be true: (1) The nervous system maintains its identity under the various sorts of reversal imposed. The notochord fares less well. Even if left beneath the ectoderm, reversal of anteroposterior and transverse axes appears to disturb its elongation and its integrity. If differentiating notochord is placed dorsal to the medullary plate, it evidently ceases to develop as a structural entity, although cellular differentiation progresses. (2) The nervous system at the time of operation is capable of regulating, with regard to level, reversals of the anteroposterior and transverse axes but not reversals of the dorsoventral and anteroposterior axes imposed simultaneously. The notochord seems not to regulate anteroposterior reversal. (3) The archenteric roof and medullary plate retain their respective identities under conditions of reversal and do not adjust to their new position when the dorsoventral axis is reversed. In such a graft the chordamesoderm acts as an intrusive developmental block and separates locally the developing neural folds each of which forms a complete reduced nervous system characteristic of its original localization.

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