observed ionospheric peak might be an *F1* region produced by solar ultraviolet radiation. It is still plausible in this case that no *F2* peak will develop, and the thermal structure is not likely to differ importantly from that shown in Fig. 2 (*18*).

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15. With a decay time scale of only a few minutes, the E region in the morning will have an electron density well below the upper limit of 5×10^3 electron/cm^3 set by the Mariner.
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19. This article is contribution No. 148 of the Kitt Peak National Observatory. The observatory is operated by the Association of Universities for Research in Astronomy, Inc., under contract with NSF. We are indebted to D. M. Hunten, R. M. Goody, and T. M. Donahue for many helpful discussions during the course of this work.

Inductive Processes in Embryonic Development

Most organs form as a result of gradual cumulative effects of interactions among embryonic tissues.

A. G. Jacobson

During development the cells of a multicellular organism become different from one another although they are presumably endowed with identical genomes. The mechanisms of cell differentiation present some of the most provocative problems of modern biology. In many animal embryos one such mechanism is embryonic induction. In general terms, embryonic induction is an interaction between one tissue (the inductor) and another responding tissue as a result of which the responding tissue takes a course of differentiation it would not have followed had the interaction not occurred.

It would be well if we knew when, or even if, induction begins and ends, as it is very difficult to untangle induction processes from other processes that occur before and after them or concurrently with them. Embryonic induction is part of a continuum of developmental processes. But the concept of induction, once separated out and named, has suffered reification. A number of papers imply or refer to "the moment of induction," and attention has prematurely shifted from study of the *process* of embryonic induction to a search for "the inductor substance." Induction has been studied for more than 60 years, but only recently have any inductive tissue systems been reasonably well defined with respect to their timing and spatial arrangements. The purpose of this discussion is to describe some of these inductive systems.

Programming for developmental events begins as early as oögenesis (*1*),

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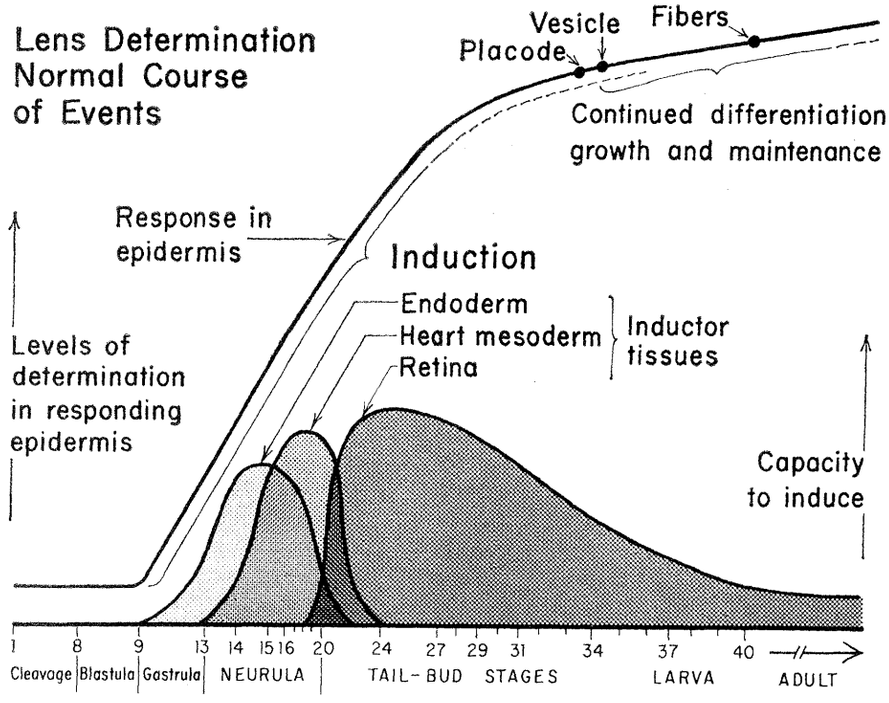

Fig. 1. A graphic model of lens induction in a salamander. The abscissa represents time and is marked off in arbitrary stage numbers and names (*19*). The relative amount of time between stages is illustrated; actual time varies greatly with the temperature. At 17°C, the time between stage 9 and stage 40 is 3 weeks in the west coast newt. The ordinate for the response curve is logarithmic, the level of response being a function of the sum of all past indication. The ordinate representing the capacity of inductor tissue to induce is linear. Values on the ordinates were deduced from experiments such as those illustrated in Figs. 2–8.

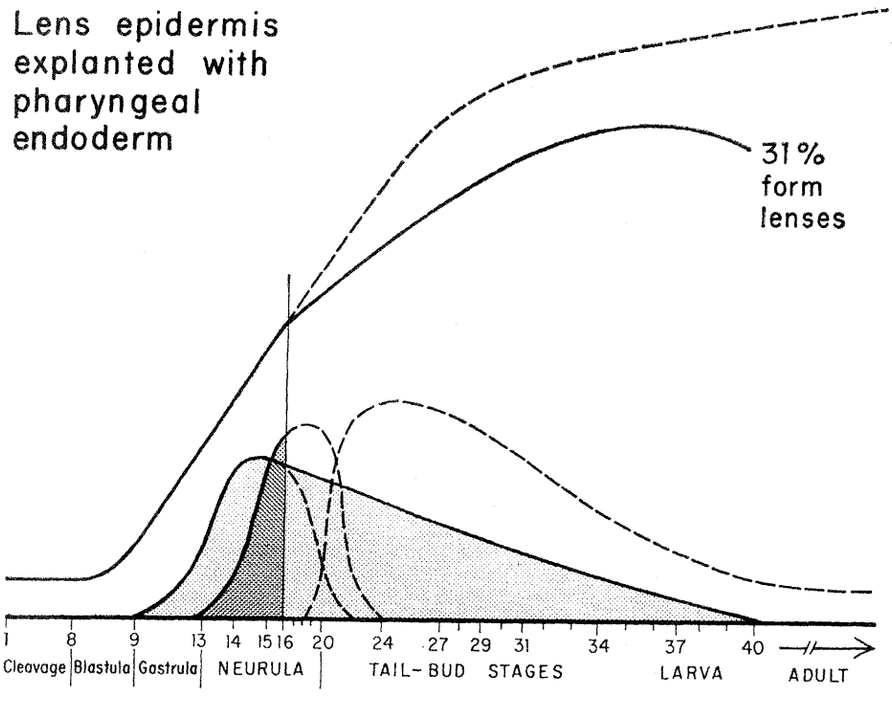

Fig. 2. Lens induction by pharyngeal endoderm is sufficient and persistent enough to produce lenses in nearly one-third of the cases in which lens epidermis and endoderm are artificially forced to continue their association in explants (solid curve). The dashed lines indicate the levels of induction capacities and response in normal development. Refer to Fig. 1 for comparison with normal development.

and the cells of an embryo differ from one another at their earliest delimitation. The action of a particular group of embryonic cells as a particular sort of inductor is related to regional differences in the egg cytoplasm from which the cells are derived, and the capacity of cells to respond to inductors in a certain way also traces, in part, to the conditions established in the egg cytoplasm during oögenesis. Thus these very early determinative events cannot be ignored in studies of embryonic induction. For convenience in referring to them, let us use the term "predetermination."

Some induction potentialities have been localized in uncleaved eggs. Curtis (*2*) has been able to transplant cortical cytoplasm in early amphibian embryos and zygotes. One important result of his work is the demonstration that the organizer tissue of Spemann—the primary inductor in the embryo—traces back to the position of some properties of the cortical cytoplasm of the gray crescent region of the uncleaved zygote. Soon after fertilization, these properties spread through the cortical cytoplasm and are incorporated into the cells cleaving from that region of the cytoplasm, apparently imparting to them the ability to induce the main axial organs.

Since response and inducing capacities are forming during oögenesis, it is nearly impossible to say when induction begins. It is just as difficult to distinguish the end of an induction process. Induction does not end with the first appearance of a tissue or an organ primordium. Further association between a forming organ and the properly oriented tissues that have induced it is essential if the organ is to differentiate and grow normally. These "formative influences" are not easily distinguishable from continued induction. Some organs, such as the lens, will atrophy if their inductor tissues are removed, even after the organ is fully formed, and such "sustaining factors" are also difficult to distinguish from continued induction.

Adding to the analytical burden, morphogenetic movements rearrange cell groups before, during, and after induction, and indeed some morphogenetic movements result from induction.

Most studies of embryonic induction have been with amphibians, and most of the present discussion will refer to

work with salamanders. Of the three germ layers of the vertebrate embryo, the ectoderm is the most dependent upon induction for the emergence of the various organs it forms. The central nervous system is the first set of ectodermal organs to appear, and Spemann's organizer, the chordamesoderm, is the responsible inductor tissue in a normally developing animal. As the central nervous system develops, it in turn participates as an inductor in the determination of other ectodermal organs, including the nose, lens, and ear.

Although more attention has been given to the induction of the central nervous system than to any other system, I think it may be one of the least likely systems finally to yield an understanding of induction. The central nervous system is one of the most strongly predetermined of the ectodermal derivatives and therefore requires the least subsequent induction. The ease with which the central nervous system can be induced by any number of odd treatments or substances is a principal block to an understanding of this induction system.

The nasal sac, the lens of the eye, and the inner ear structure are far more amenable subjects for study of embryonic induction than the central nervous system, for their induction requires more time and induction is more important in their determination. They are much less predetermined than the central nervous system, and they are relatively simple, discrete organs.

Induction of the Lens

Understanding of any induction system requires knowledge of the complete history of the responding cell group. Potentially a lens could be induced from any group of cells derived from the animal (upper) hemisphere of the amphibian egg, but normally only two small groups of ectodermal cells form lenses. These are the two groups of cells that have been successively exposed to the most potent lens inductors.

As tissue relationships change during development, different lens-inductor tissues are utilized. The ectoderm that will later form the lens is underlain in gastrula stages by the endodermal wall of the future pharynx, and this endoderm is the first inductor of the lens. As gastrulation proceeds, the mesodermal mantle extends forward from the blastopore, and its anterior edge comes to lie just posterior to the future lens ectoderm. This edge is the future heart, and it too is an inductor of the lens (*3*).

At the open-neural-plate stage of de-

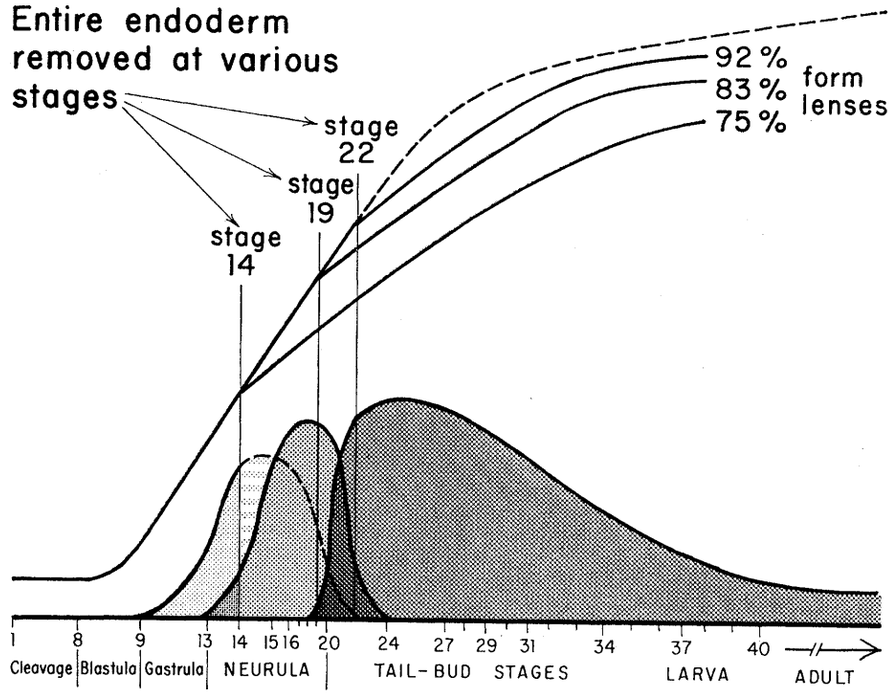

Fig. 3. The pharyngeal endoderm participates in lens induction at least from stages 9 to 23. Removal of the entire endoderm during this period results in failure of some embryos to form lenses. The longer the endoderm is present, the greater the percentage of cases that form lenses.

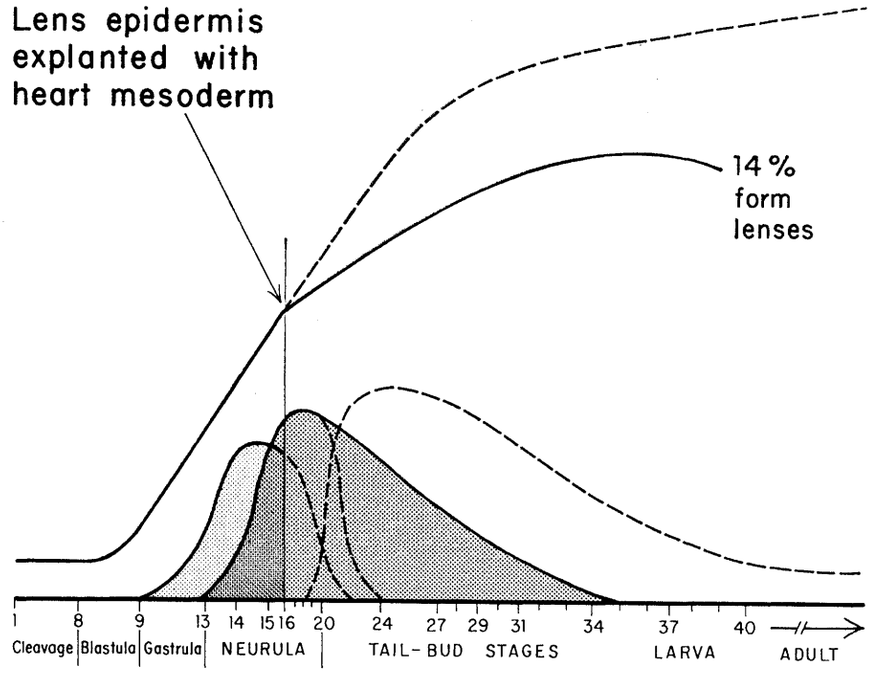

Fig. 4. Future heart mesoderm induces lenses in some of the cases in which heart mesoderm and lens epidermis are isolated together. The capacity to induce lenses does not last as long in the heart mesoderm as it does in the endoderm.

velopment, the future lens cells are located in two areas of the epidermis that lie just lateral to the anterior brain plate. As the neural plate rolls up into a tube, the future retinal cells evaginate from the prospective brain as part of the optic vesicle. The lifting up of the epidermis as the neural folds rise and the bulging out of the optic vesicle bring the future retina into contact with the future lens cells. From then on the retina is the inductor of the lens. Unlike the earlier inductors, the retina retains the ability to induce lenses as it itself differentiates into its adult form. Interactions between retina and lens continue even into adult stages.

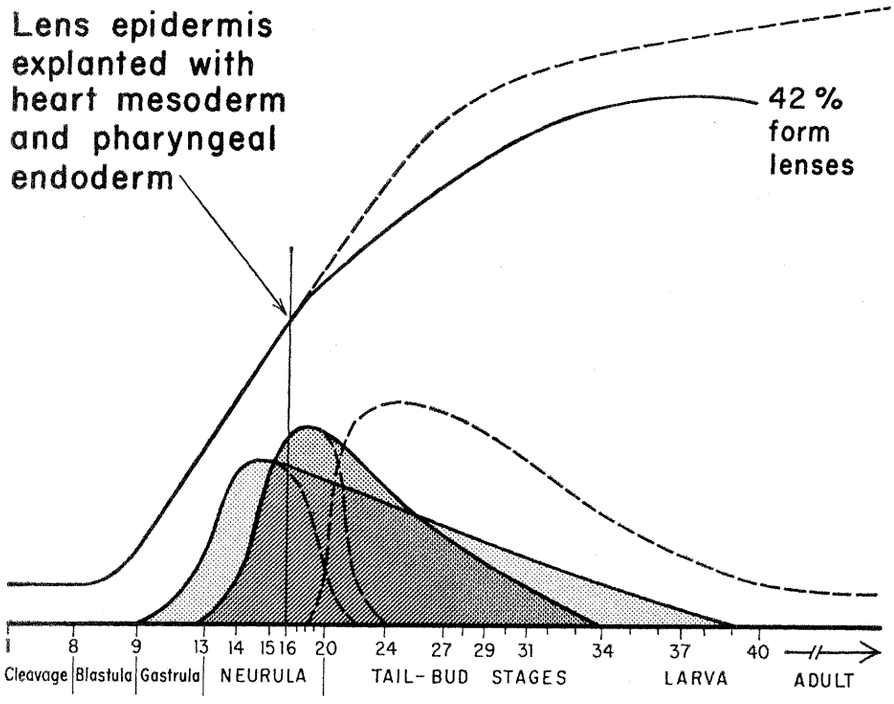

Fig. 5. When both heart mesoderm and pharyngeal endoderm are isolated together with the prospective lens epidermis, their lens-inducing effects are additive. Compare with experiments in Figs. 2 and 4.

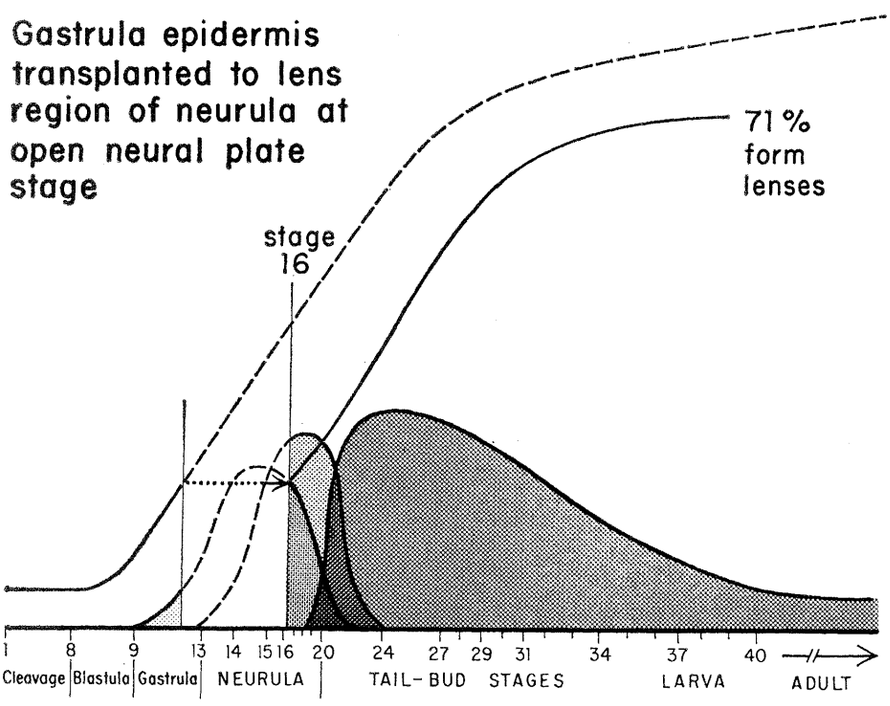

Fig. 6. When the epidermis skips association with endoderm and mesoderm from gastrula to middle neurula stages no lenses are formed in 29 percent of the cases. This failure of induction occurs despite the fact that the epidermis experiences the entire course of lens induction by the retina.

From many experiments and observations on the origin of the lens (*3*, *4*) I have constructed a graphic model of the process of lens determination (Fig. 1). The model is not accurate in every detail because all necessary quantitative information is not yet available. Although the information for this model comes from my work of the past 13 years with the west coast newt, *Taricha torosa*, I believe the general pattern of lens determination to be the same in all vertebrates. There are, however, variations in the timing of responses among species and hence, apparently, in degree of dependence on the retina as a lens inductor. Some of the experiments from which the normal course of lens determination was deduced are illustrated in the same graphic form in Figs. 2–8.

The curves in these figures represent the changing influences of three different inductor tissues on ectoderm that produces lenses. They are derived from experiments in which the lens-inducing capacity of tissues was measured by the percentages of cases in which lenses were produced in experimental combinations of tissues. The spatial distribution of lens-induction capacity throughout the animal will be considered later.

At least two factors influence the amount of induction as described by these curves. First, there are changes in the intrinsic capacities of inductor tissues to induce lenses. For example, the capacity of the pharyngeal endoderm to induce lenses is persistent but gradually diminishes as the endoderm itself differentiates. Second, the normally changing spatial relationships between the prospective lens ectoderm and its inductors modify the effectiveness of lens induction on that ectoderm.

For example, the effective induction by endoderm increases as the endoderm moves beneath the prospective lens epidermis at early gastrula stage 9. Induction continues at a high level through those stages when endoderm underlies the lens epidermis and then decreases as the lens epidermis is lifted away when the neural folds rise in late neurula stages. The endoderm does not lose

its capacity to induce lenses at that time, it is merely removed from the scene.

The levels of determination in responding epidermis, shown in the response curve of Fig. 1, have been derived from measurements of the amount of additional induction needed for lens elicitation at various stages of development. The response in the epidermis is a function of the sum of all past induction, provided induction was continuous. The amount of effective induction is determined by the strength of the inductors, the length of exposure to inductors, and the number of inductors. When more than one inductor is acting at the same time, the effects are additive.

In the salamanders I study, the first visible sign that a lens is forming is the clustering of the epidermal cells into a lens placode at a late tail-bud stage. The placode rounds up into a vesicle and detaches from the epidermis. Differentiation into lens epithelium and lens fibers is evident in early larval stages. These three events are marked on the response curve of Fig. 1.

In the gastrula and neurula stages, long before there is any visibile sign of lens formation, lens induction proceeds very rapidly. The combined induction by endoderm and mesoderm makes lens induction particularly intense at neurula stages, more so than at any other time in development. In no case, however, is the lens epidermis at these stages sufficiently determined that it can form a lens without subsequent induction. Explanting the prospective lens epidermis at mid-neurula stages into isotonic salt solution removes the epidermis from any further lens induction, and in no case does a lens form. This sort of experiment will not yield a lens unless the epidermis is isolated shortly before placode formation or later.

Explantation Experiments

If prospective lens epidermis of an embryo in the open-neural-plate stage is explanted together with its underlying pharyngeal endoderm, artificially forcing continued association of these two tissues, the endoderm provides sufficient subsequent induction to cause lenses to be produced in 31 percent of the cases (Fig. 2). The lenses that form, however, are not as fully differentiated nor as large as normal, and in the absence of continuing induction, which only the retina normally provides, they ultimately regress.

The importance of the endoderm as a lens inductor can be beautifully illustrated by removing the entire endoderm at various stages of development. The longer the endoderm remains in the embryo, the greater the probability that lenses will form (Fig. 3).

When lens epidermis of an embryo

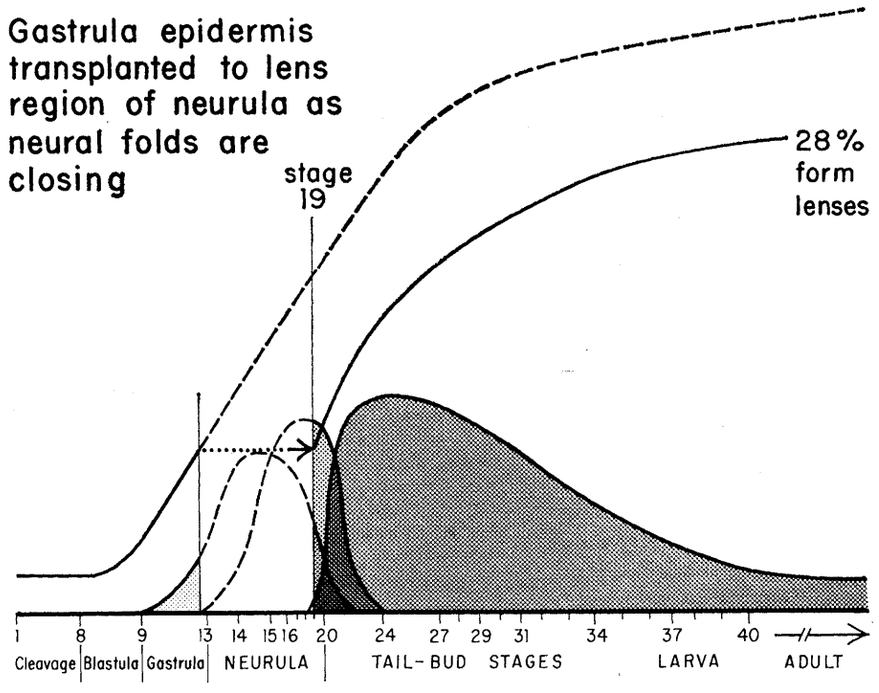

Fig. 7. This experiment differs from the one in Fig. 6 only in that induction by endoderm and mesoderm does not occur between stages 16 and 19 in these cases. When induction does occur between these stages, as in Fig. 6, lenses are formed in 43 percent more cases.

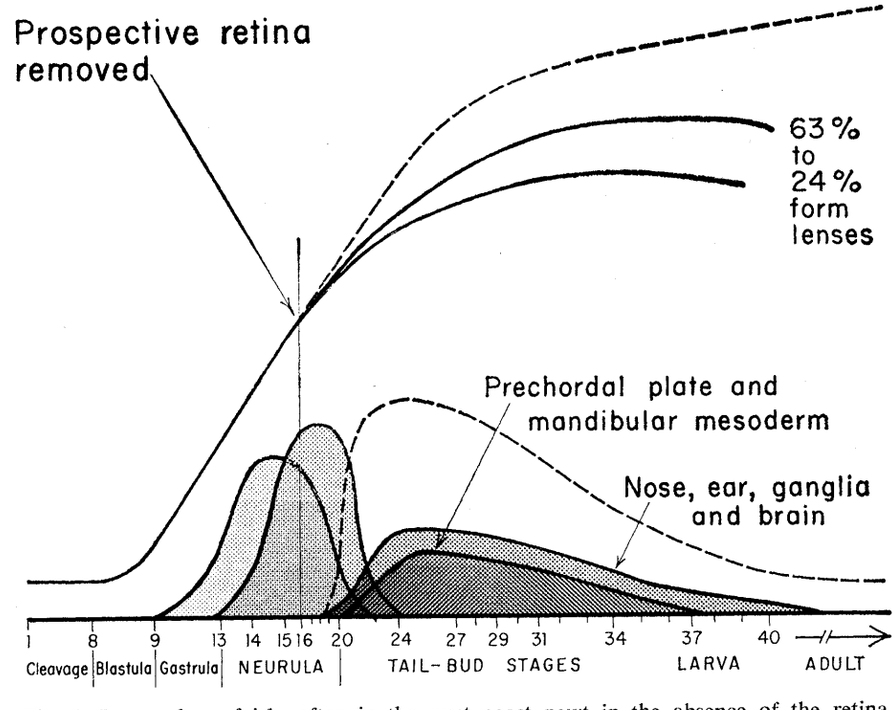

Fig. 8. Lenses form fairly often in the west coast newt in the absence of the retina, being formed most frequently when the embryos are reared at 16°C prior to the operation. Fewer lenses are produced when the embryos are reared at lower or higher temperatures. In the absence of the retina, the lens epidermis experiences some lens induction from head tissues that it does not normally encounter.

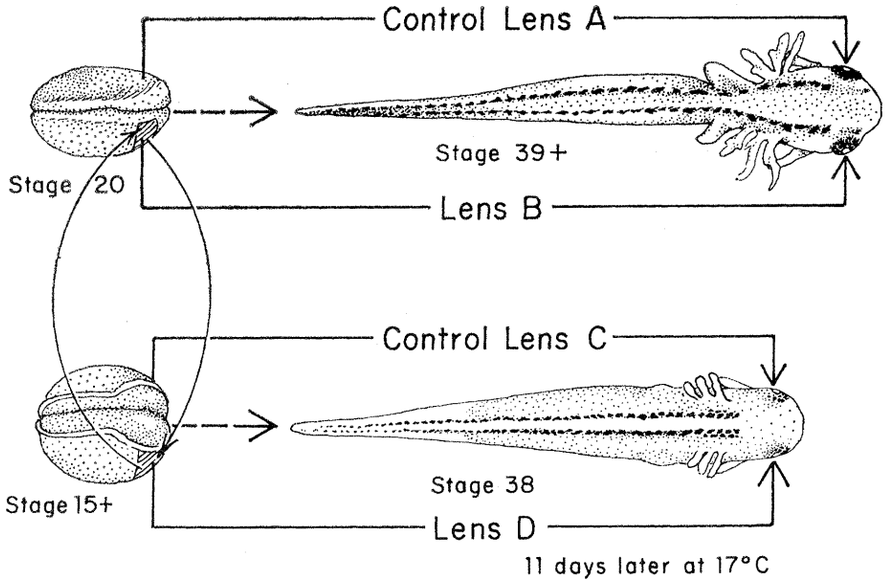

Fig. 9. By reciprocal transplantation the period of lens induction between stage 15+ and stage 20 is skipped in lens B and repeated in lens D. The unoperated sides produce lenses A and C that serve as controls. After 11 days, the larvae were fixed and sectioned and the lens volumes were calculated from area measurements. The volumes of the lenses (10^{-3} mm^3) were: A = 1.75, B = 0.55, C = 1.26, D = 2.02.

in the open-neural-plate stage is explanted together with the prospective heart mesoderm, lenses form (Fig. 4), but less often than in the similar experiments with endoderm.

In 1920, Ross Harrison, using late neurulae of *Ambystoma maculatum*, transplanted epidermis in which lenses had already been partially induced to the ventral heart site and obtained beautifully formed lenses (*5*). It seems clear now that the heart mesoderm provided the continued induction and that the endoderm that induces lenses in the neurula stages also continued to be involved, since it is displaced posteriorly and ventrally following neurula stages (*6*). The lens-inducing effects of endoderm and heart mesoderm are additive when these two tissues are explanted together with prospective lens epidermis (Fig. 5).

Lens induction for the important period between mid- and late-neurula stages was measured in two sets of experiments. Prospective lens epidermis of late gastrulas was transplanted to the future lens site of older, neurula-stage hosts, replacing the host's lens epidermis. The transplanted epidermis therefore missed lens induction between late gastrula stages and the neurula stage of the host at the time of implantation, and the incidence of lens formation was considerably less than 100 percent. The two sets of experiments differed only in that one group (Fig. 6) had the benefit of lens induction between mid-neurula stage 16 and late-neurula stage 19, and the other (Fig. 7) did not. Lens induction by endoderm and mesoderm between these two stages resulted in 43 percent more cases of lens formation. In other experiments in which all endoderm and mesoderm was removed at stage 16 in one set and at stage 19 in another, a similar difference (44 percent) was obtained.

The experiments cited, and others as well, indicate that the endoderm and mesoderm are at least equal to the retina in importance as lens inductors. Together, the pharyngeal endoderm and the heart mesoderm usually account for more than half of the total induction necessary for lens formation.

In a classic sort of lens-induction experiment first performed by Spemann in 1912 (*7*), the area of the open neural plate containing the prospective retina is removed by microsurgery from one side of the embryo. Will a lens form later on the side that lacks a retina? There is a long history of different results with this experiment (*8*). When the operation is done under similar conditions, some species of amphibians produce lenses in the absence of the retina and others do not. Furthermore, in a given species, if the embryos are kept at certain temperatures prior to the operation, lenses often develop later in the absence of the retina, whereas if they are kept at other temperatures lenses seldom or never form.

In experiments with the west coast newt (Fig. 8), embryos kept at 16°C prior to removal of the prospective retina produced the highest percentage of lenses in the absence of the retina. Fewer lenses were produced after embryos had been kept at higher or at lower temperatures (*3*). Lower temperatures greatly increase the length of time spent in early stages of development and therefore increase the length of exposure of responding epidermis to early lens inductors. But lower temperatures should also decrease the rate of chemical processes that have been presumed to underlie induction. These two antagonistic temperature effects could account for the optimum temperature found for lens production, but probably the situation is more complex.

One could imagine that the endoderm, mesoderm, then retina, normally acting in that order, have qualitatively different effects on the responding tissue, but I have found no evidence at all for such differences. The effects of each of the lens-inductor tissues is the same; one inductor may substitute for the other, and lenses will form in the absence of any one of the three.

The timing of the inductive interactions between these three inductor tissues and the responding lens epidermis is not critical. Lens formation occurs in experiments in which the responding tissue is moved to older or younger hosts. Periods of induction can be repeated or skipped with results that can be related only to the total amount of induction. A description of such an experiment follows.

Just prior to the time when the retina becomes effective as a lens inductor is the important period of induction during neurula stages when both endoderm and mesoderm are inducing lens. An experiment was done to determine the effects of repeating this period of induction on the one hand, or skipping it on the other. This was accomplished by reciprocal transplantation of the prospective lens epidermis between embryos at early and late neurula stages (Fig. 9). The embryos were fixed and sectioned 11 days after the operation, when they had reached larval stages. There were then four lenses, each with a different inductive history. Lenses on the untreated sides of the experimental embryos had undergone normal courses

of induction. Of course the younger animal had a younger normal lens. The lenses that formed in the transplanted epidermis ought to differ from both the normal lens in the host and the normal lens in the donor. One would predict that the lens that forms in the epidermis transplanted from the older to the younger neurula, which repeats the period of induction between the two stages, would be more developed than either normal lens, even though it is in the younger host. The lens which forms in the epidermis transplanted from the younger to the older neurula and thus skips that period of induction ought to be less developed than any of the others. The results of this experiment (Fig. 10) are in accord with these predictions.

These experiments not only support the idea that induction by the endoderm and mesoderm is equivalent to induction by the retina, but they bear on another matter as well. This is the continuing effect of the retina on the developing lens. It has been known for years that removal of the lens from association with the retina at various stages of development of the lens has deleterious effects on the continued differentiation and growth of the lens and that such lenses ultimately regress (*9*). That this stimulating and sustaining effect of the retina is indeed continued induction, and not some qualitatively different effect is strongly suggested by the fact that adding or subtracting the much earlier endodermal and mesodermal influences has similar effects on lens growth and differentiation.

Nose and Ear Induction

The developmental histories of the nasal sac and the inner ear are similar to that of the lens. The normal courses of nose and ear determination, respectively, are illustrated in Figs. 11 and 12. At least three inductor tissues act successively, from gastrula through larval stages, to induce each of these organs. A portion of the central nervous system is the final inductor in nose and ear determination, as it is in lens determination. In gastrula and neurula stages, portions of the endoderm and mesoderm are inductors of the nose, and two regions of the mesoderm are inductors of the ear. Experiments similar to those with the lens provided the data for this picture of nose and ear determination (*4*).

Competence

The propensity of a tissue to form a particular organ in response to induction has been called competence. Predetermination establishes a pattern of competence in the ovum and zygote. Decreasing competence is the result of intrinsic changes that take place within the responding tissue when inductive influences diminish or are removed. Increasing determination during early development has been described as an intrinsic change in competence, but in every case is probably due to induction by previously unrecognized early inductors.

In the case of the lens, the determination of head ectoderm to form a lens steadily increases after gastrulation as a result of induction by the endoderm and mesoderm during gastrula and neurula stages. The capacity to induce lenses is greatest in the endoderm that underlies the prospective lens ectoderm and in the heart mesoderm and other nearby mesoderm, but lens-induction capacity is also present in diminishing amounts, distributed in gradient fashion, throughout the rest of the endoderm and mesoderm. Similarly, in neural tissues the capacity to induce lenses is greatest in the retina but is present to lesser degrees in the rest of the eye and in the diencephalon and other brain parts. These gradients of inductive capacity result in the spatial distribution of lens competence described so often in the past.

If sufficiently exposed to lens-inducing tissues, any part of the early ectoderm can form a lens. Early mesoderm

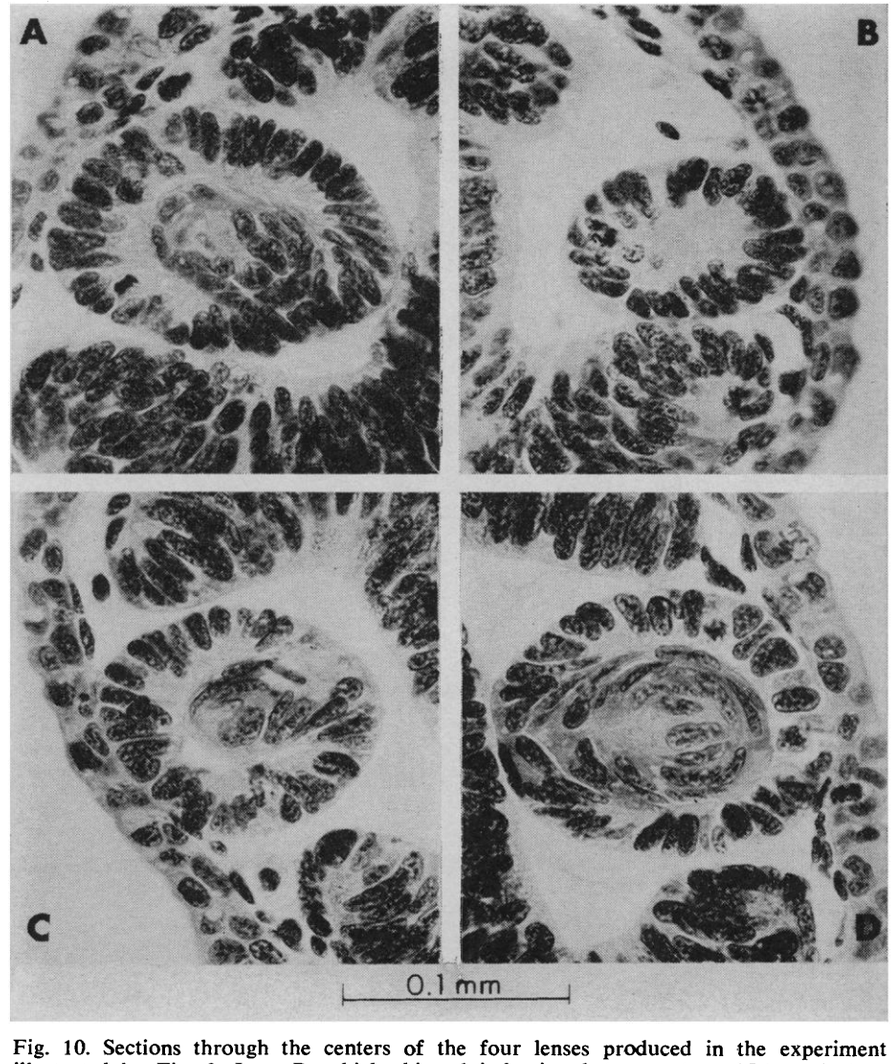

Fig. 10. Sections through the centers of the four lenses produced in the experiment illustrated by Fig. 9. Lens B, which skipped induction between stage 15+ and stage 20, is smaller and less differentiated than either control lens A or C. Lens D, which repeated the same period of induction, is larger and more differentiated than either control lens even though it is in the younger host.

is far less likely to respond with lens formation, and early endoderm not at all. These differences among various regions of the blastula and early gastrula trace back to conditions established in the egg cytoplasm during oögenesis and shortly after fertilization. Thus in the model of the normal course of lens determination (Fig. 1), the level of determination between stage 1 (zygote) and stage 9 (early gastrula), before ordinary lens induction begins, is placed somewhat above zero.

Predetermination for parts of the nervous system is much greater. For comparison with lens, nose, and ear, I have pictured the normal course of determination of a portion of the central nervous system (Fig. 13). The level of determination when the ordinary inductor begins to induce is already very high, and the time it takes for the inductor—the chordamesoderm—to elicit a neural plate is very short. It appears that the anterior parts of the central nervous system are the most predetermined, the most readily induced, and the earliest to lose their competence if subsequent induction does not occur. These matters have been extensively discussed by Saxén and Toivonen (*10*).

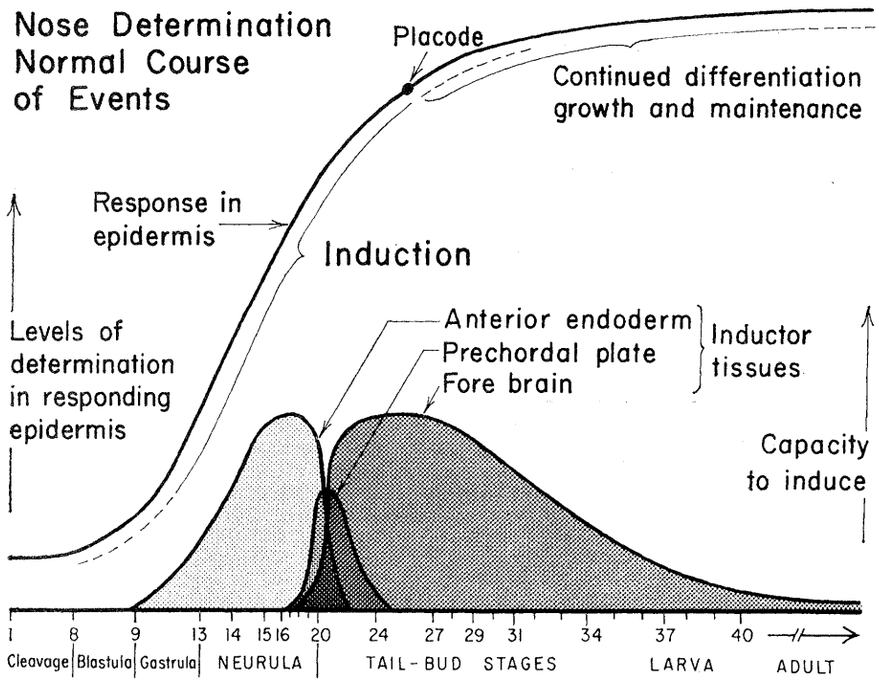

Fig. 11. Nose induction, like lens induction, involves a succession of diverse inductor tissues. The anterior endoderm ordinarily accounts for more than half of the total nose-induction process, and may by itself elicit nose formation in experiments that force continued association of endoderm and nose epidermis (*4*).

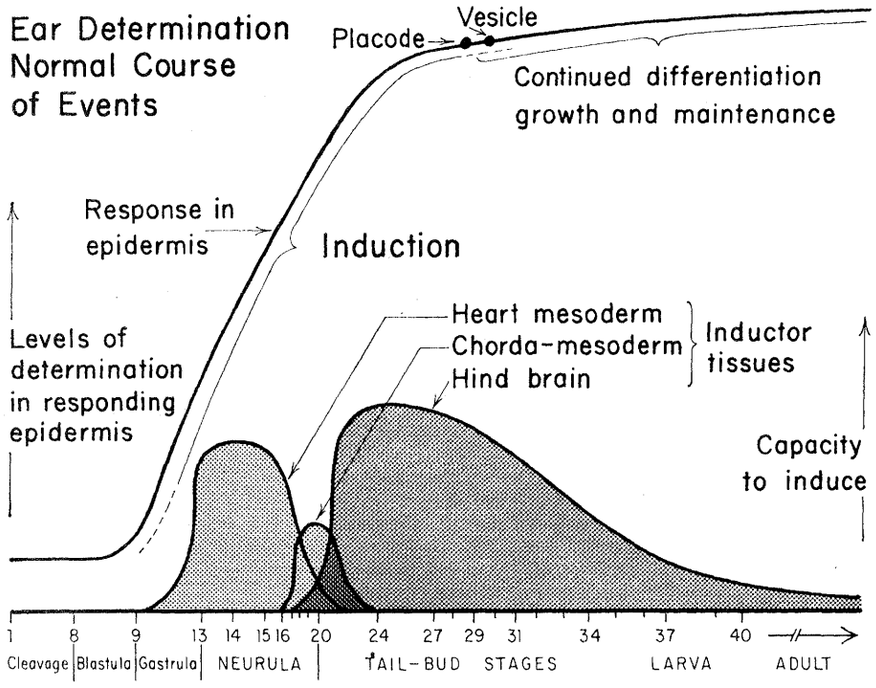

Fig. 12. Ear induction, like lens and nose induction, is a gradual process utilizing diverse inductor tissues, and continued induction after placode formation is essential for complete differentiation and growth.

What Fixes Organ Sites?

A lens has no significance to the organism unless it forms in proper relationship to the rest of the eye. Nose, ear, brain, leg, heart—all organs of the body—are strictly limited to a particular site if they are to have well-adapted functional integration with the rest of the organism. A major problem of embryology is to account for the normal positioning of organs.

Since organs arise as a result of predetermination and induction, and since the distribution of specific inductors ultimately traces back to predetermination, the solutions to the problems of what fixes organ sites must finally come from investigations of events that occur during oögenesis and at and shortly after fertilization—events that establish the patterns of predetermination. Fortunately, this area of study is beginning to get the attention it has long needed (*2*, *11*). Descriptive electron microscopy of developing ova and early embryos is rapidly progressing (*12*), and the monumental task of descriptive chemical embryology continues (see *13*).

The morphogenetic movements that bring inductor and reacting tissues together in quite precise fashion under normal conditions must be accounted for in any complete explanation of site determination. Steinberg (*14*) has presented good evidence that the mechanism underlying these movements may be a relatively simple hierarchy of cell adhesivities based on the relative num-

bers of randomly distributed adhesive sites on the cell surfaces.

In every case that I know of, the first visible hint that induction has occurred is a change in the behavior of the reacting cells. They may change their shape and clump into a placode, as in nose, lens, and ear induction. They may change their shapes and directions of movement in a very complicated way, as in the area induced to form neural plate (*15*). At the first appearance of the lens placode in the chick embryo, oriented microtubules have been found in the elongating cells (*16*).

The implication is that induction rather directly affects adhesivity and other surface properties of the reacting cells. The new associations and shapes that result from induction may lead to additional interactions that in turn may accelerate changes in the responding tissue mass. In most cases continued presence of the inductor tissues is necessary for maintaining and augmenting the new associations in developing organs.

Since inductive capacities are broadly distributed in gradient fashion throughout the several inductor tissues, there must be considerable overlap of inductive capacities for different organs. The prospective heart mesoderm, which underlies the prospective ear epidermis when the embryo is in the open-neural-plate stage, is not only an important ear inductor, it also participates in lens induction. In fact, lens-induction capacities extend into both nose and ear regions, nose-induction capacities extend posteriorly into the ear region, and ear-induction capacities extend as far forward as the nose region (*4*). During early development any region of the epidermis of the head is simultaneously being induced to become nose, lens, and ear. A level of determination for each of these organs is discernible in any region of the head epidermis in the neurula stage (*4, 17*). Nose, lens, and ear form from the strip of epidermis that is just lateral to the anterior neural folds. This strip can be removed and rotated 180 degrees to put prospective nose epidermis in the ear region and ear epidermis in the nose region (*4*). The lens area between is pivoted upon. When the experiment was done at an open-neural-plate stage, the ear epidermis in the nose region formed both an ear and a nose. Because of previous induction, ear determination was advanced enough so

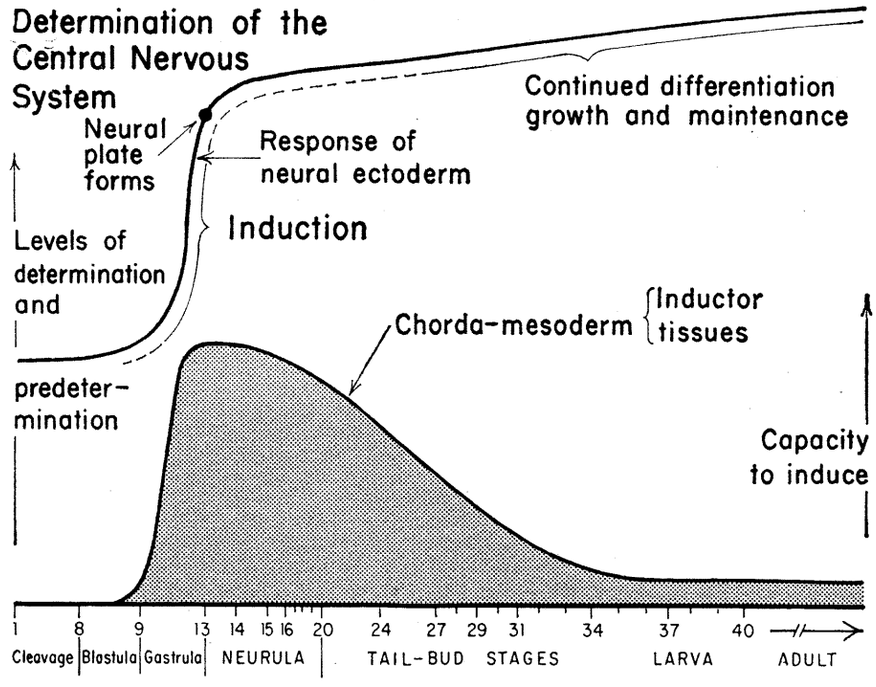

Fig. 13. The normal course of determination of a portion of the central nervous system is shown for comparison with nose, lens, and ear determination. Induction begins at a very high level of predetermination, is intense at early stages, and the course of induction is brief, the organ forming at a very early stage.

that the epidermis could respond to the lesser ear-induction capacities of the tissues in the nose region, and because of the broad distribution of nose-induction capacities, there was already a small base of nose determination from which the stronger nose-inductors of the nose region were able to elicit a nose. The same sort of operation done at closing-neural-plate stages resulted in formation of noses and ears both anteriorly and posteriorly. By this stage the nose had been sufficiently induced in its normal site to respond to the lesser nose induction of the ear region and form a nose. In other experiments, when the neural plate was reversed instead of the epidermis and the forebrain was thus put next to the ear epidermis and hindbrain next to the nose epidermis, noses and ears formed in the normal positions. The forebrain is thus not the principal or the only site-determining factor for the nose, and the hindbrain cannot be for the ear. The endodermal and mesodermal inductors of nose and ear fixed the sites in these cases.

The lens forms in its normal site even in the absence of the optic vesicle (*4*). The capacities of the endoderm and mesoderm to induce lens are so distributed that their greatest cumulative effect is in the area of the epidermis that normally forms lens. Contact of the optic vesicle with this area and the ensuing induction further ensures proper positioning in normal development.

Conclusions and Implications

An understanding of the spatial and temporal organization of an induction process is necessary for productive chemical investigations of induction and for the interpretation of ultrastructural findings. Many investigators have presumed that lens induction begins when the optic vesicle contacts the epidermis and essentially ends with the appearance of the lens placode. Considering the small part of the total course of lens induction that their studies encompassed, it is not surprising that no clear picture of the process has emerged from them. In most systems in which the chemical basis of induction has been or is being studied, the greater amount of determination has occurred before the study begins. In the cases of the central nervous system and of all mesodermal organs, most determination occurs before cleavage; that is, these organs are largely predetermined.

Induction may proceed over a long time and have cumulative effects in the responding tissues, or it may begin from

a high level of predetermination and have a shorter time course. Any group of cells may respond simultaneously to several specific inductors, the organ that emerges depending upon which sort of inductor first has sufficient cumulative effects. When artificially imposed conditions bring about a "tie," then two organs may emerge side by side, or even from the same cell mass (*4, 17*). Induction is clearly not a trigger event, and progress toward formation of one organ does not interfere with progress toward formation of a different organ from the same cells.

Specific inductors seem to be doing the same thing through the whole course of induction, but in the responding tissue there is finally a sequence of qualitatively different events in response to the cumulative effects of the constant inductive stimulus. Late in the sequence, the responding cells become more firmly committed to a particular course of differentiation. The initiation of cell-specific protein production must be one of the terminal events.

But a specific inductor always elicits many cell types with their diverse arrays of specific proteins. I know of no case at all in which induction elicits just one cell type. The lens is probably the simplest induced structure, and it consists of two, or perhaps three, cell types. Usually a whole organ is induced by a specific inductor, and the distribution of cell types in the organ is not immediately fixed by induction. Recently induced organ primordia have the characteristics of an embryonic field. At first more cells are involved than actually later form the organ, and any part of the early field can be made to form the whole organ. The axes of the organ become fixed in a specific order, and gradually the parts become delimited and eventually established fairly permanently.

The segregation of the parts of a developing organ occurs over a rather extensive period following the first appearance of the organ rudiment as a whole (*8*). The segregation of the parts of an embryonic field is not at all well understood. Probably it involves continued induction from surrounding tissues and even induction among emerging parts of the organ itself. The epithelio-mesenchymal interactions in developing mesodermal and endodermal organs that are being extensively investigated as induction systems (*18*) are examples of segregating embryonic fields.

The highly organized and regulated processes of development begin in oögenesis and end with the death of the animal. Embryonic induction is an integral part of these processes during the transition from a unicellular to a multicellular organism. Studies of induction systems in their organized states continue to provide new information about the role of induction in cell differentiation.

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Cubic Carbides

Solid-state physics explores materials having ionic structure, metallic conductivity, and covalent hardness.

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Transition metals are like modern music—relatively hard to understand. We would expect compounds of the transition metals to be even more puzzling to those seeking harmony between theory and experiment. However, one family of transition-metal compounds, the monocarbides, has the simple and familiar rock-salt crystal structure. The cubic symmetry of this structure simplifies the problems of obtaining good samples, determining their properties, and treating these properties theoretically.

Interest in the transition metal carbides has increased greatly in the last few years because industry and government need better high-temperature materials. The carbides have the highest melting points of any known compounds. In addition, they are chemically inert and extremely hard. In this article I will describe recent progress in interpreting these properties from the point of view of solid-state physics, emphasizing the nature of the binding as suggested by electrical, mechanical, and thermal properties and as inferred from theoretical considerations. Other reviews of the transition-metal carbides have been given by Schwartzkopf and Kieffer (*1*), Samsonov (*2*), Storms (*3*), Westbrook and Stover (*4*), and Costa and Conte (*5*).

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