(From the Strangeways Research Laboratory, and the Laboratory of Experimental Zoology, Cambridge, England.)

INDUCTION BY HETEROPLASTIC GRAFTS OF THE PRIMITIVE STREAK IN BIRDS [1].

By

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With 26 figures in the text.

(Eingegangen am 15. November 1932.)

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Introduction.

The main object of this paper is to describe certain experiments in which it has been shown that inductions can be obtained by grafting pieces of duck primitive streak into chick blastoderms, or pieces of chick primitive streak into duck blastoderms. This inductive capacity is retained by the head process and sinus rhomboidalis, which are derivatives of the primitive streak (WADDINGTON 1933a), and some heteroplastic grafts of these structures are described here. Induction by heteroplastic grafts of isolated neural plate has not yet been obtained, but

[1] The experiments described in this communication were done partly by WADDINGTON and partly by SCHMIDT. But the writing of the paper and the preparation of the material for press are due to WADDINGTON, who takes sole responsibility for the opinions expressed.

[2] This work was done while I was in receipt of a part-time grant from the Medical Research Council, for which I should like to express my thanks.

only rather few experiments have been made with this end in view: doubtless such inductions are possible.

Certain considerations as to the mutual interaction of the host, the graft and the induced neural plate arise out of the experiments with heteroplastic grafts, and in order to provide a larger basis for discussion, a few relevant homoplastic grafts have been described.

Technique.

The technique employed for the operations was identical with that described previously (WADDINGTON 1932). The duck embryo, owing to the toughness of its endoderm, is particularly easily manipulated.

A few cinematograph films of developing operated embryos have been made by Dr. R. G. CANTI of St. Bartholomews Hospital, London, from cultures prepared by WADDINGTON. As yet only one satisfactory series of photographs of an embryo which developed in an interesting manner has been obtained. We wish to thank Dr. CANTI for permission to use some pictures taken from this film (Fig. 11).

The embryos were fixed in BOUIN's fluid and stained as whole mounts in DELAFIELD's haematoxylin Sections of WADDINGTON's material were cut at 15 μ, of SCHMIDTS at 10 μ. Sections were stained in DELAFIELD's haematoxylin or haemalum.

Description of Experiments.

1. Grafts of the head process and sinus rhomboidalis[1].

a) Grafts from chick into duck.

32—69 CD. *Host.* Duck. $21^1/_2$ hours. S pr. s. *Donor.* Chick. $30^1/_2$ hours, head fold. *Graft.* Posterior half of head process, not including HENSEN's node, in right anterior region. *Cultivated* 43 hours.

[1] In the description of the specimens the protocol number of the operation is given first. Embryos operated on by WADDINGTON have the year-number 32 (e. g. 32—69 CD) while those of SCHMIDT have no year number (e. g. 17 CD). The letters CD in the protocol number mean that the operation consisted of a graft from a chick into a duck, and the letters DC mean that the graft was from a duck into a chick. Similarly homoplastic grafts are numbered CC or DD. In the descriptions of the conditions of the experiment, the contraction *pr.s.* is used for „primitive streak", and the stage of development of the blastoderm is indicated by a classification of the length of the primitive streak into S short, M medium and L long, with intermediate SM and LM classes (see WADDINGTON 1932). The contraction *dv.* (dorsoventral) means that the grafted tissue lay upside down, with its ectodermal side against the host's endoderm. The contraction *ap.* (anterio-posterior) means that the longitudinal axis of the graft lay in the opposite direction to that of the host. The contraction *aa.* (anterio-anterior) is the opposite to *ap.* The contraction *no end.* means that the endoderm had been removed from the grafted fragment.

In the sections, the anterior part of the induction consists of a closed induced neural tube, which is underlain by the graft neural tube and a large mass of grafted notochord (Fig. 1*a*). There is no sign of the induced neural tube forming a head, although it lies near the head of the host. Further posteriorly, the induced neural tube opens out on the surface, and then bends slightly so that it is no longer parallel to the host axis but diverges more widely from it as it is traced towards the posterior (Fig. 1*b*). The graft neural plate disapears before the induced plate, but there is another large mass of graft notochord which extends further posteriorly than the induced plate. In the middle region, there is a small strand of notochord which appears to belong to the induced tube rather than to the graft.

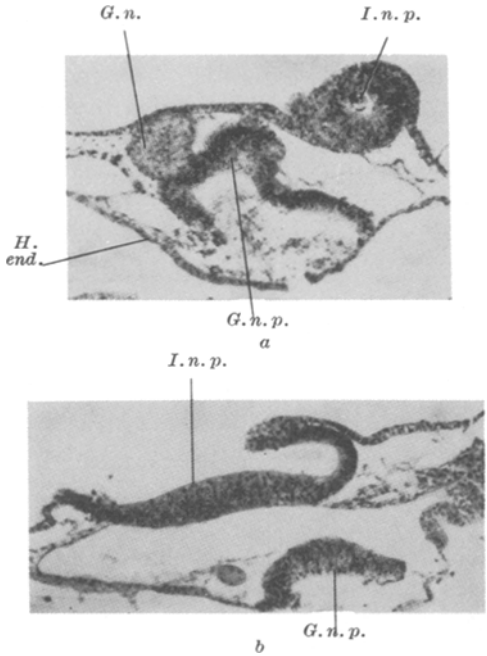


Fig. 1*a*–*b*[1]. No. 32–69 CD. 1*a*, section through anterior end of graft structures (× 110); 1*b*, section through more posterior region (× 110).

17 CD. *Host.* Duck. LM pr. s. *Donor.* Chick. Young head process. *Graft.* Head process and HENSEN's node, all three layers, dv. ap. in left anterior region. *Cultivated.* 27 hours.

At fixation, the implant was visible as a confused mass in the left anterior region of the host blastoderm. The sections show a large tubular mass of neural tissue derived from the graft. The ectoderm above this is thickened and rather folded. Most of the thickened ectoderm is probably not neural in character, but over the middle of the graft a small neural plate is developed (Fig. 2). The association of the thickened ectoderm with an induced neural plate suggests that the thickening of the ectoderm, which is frequently seen in specimens where no induction of neural plate has occurred, can be interpreted as a first stage of, or an unsuccessful attempt at, such an induction.

[1] The words anterior, posterior, right and left in the explanations of the figures are always to be interpreted with reference to the host embryo. Lettering is as follows: *ect.* ectoderm, *emb.* embryonic axis, *end.* endoderm, *fgt.* foregut, *hd.* head, *h. f.* head-fold, *ht.* heart, *mes.* mesoderm, *n.* notochord, *n. p.* neural plate, *s.* somite. Host, graft and induced structures are distinguished by the prefixed letters *H*, *G* and *I*.

8 CD. *Host.* Duck LM pr. s. *Donor.* Chick. Young head process. *Graft.* Head process and HENSEN's node, all three layers, dv. ap. in right anterior region. *Cultivated.* About 20 hours.

After 20 hours' cultivation the host embryo had not developed, but was still in the primitive streak stage. The sections show that the tissue is very unhealthy and is beginning to disintegrate. Most of the grafted tissue lies anterior to the region of necrosis, which only affects the most posterior part of it and that only slightly: this part has differentiated into a head, with a large tubular mass of neural tissue. Further towards the anterior of the host blastoderm, the tissues are fairly healthy, and the graft here consists of a small neural groove, lying with its dorsal surface against the clot and united to the host's endoderm; associated with it is a notochord and somitic mesoderm. The host ectoderm lying above the middle part of the graft has formed a rather small but normal neural plate (Fig. 3), which is, however, absent in the two end regions of the graft.

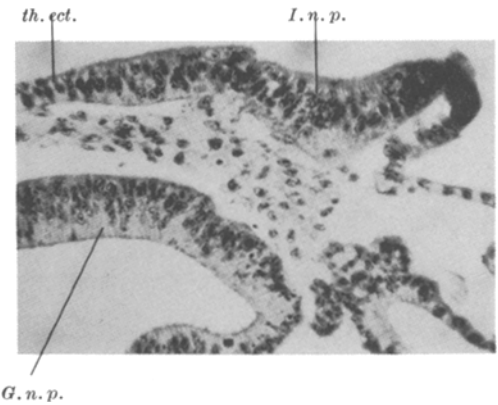


Fig. 2. No. 17 CD. Section, *th. ect.* thickened ectoderm (× 240).

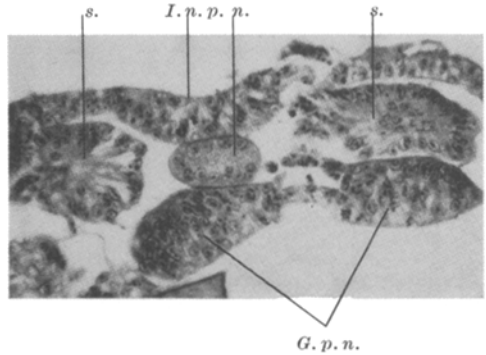


Fig. 3. No. 8 CD. Section. The section has been injured by the razor in the cutting (× 240).

This specimen demonstrates the interesting fact that a neural plate can be induced in a blastoderm, most of which is so unhealthy that the development of the normal embryo cannot go on.

20 CD. *Host.* Duck. M pr. s. *Donor.* Chick. Early head fold. *Graft.* Region of HENSEN's node, with posterior part of head process, all three tissue layers, dv. ap. in right anterior. *Cultivated* 26 hours.

In the fixed specimen, a large structure derived from the graft could be seen. It consisted of a neural tube, with somites. The anterior part of the neural tube lay opposite to the head of the host, and the rest of the graft was in the form of a rather bent, but not very distorted, embryo

stretching towards the anterior edge of the area pellucida. That is to say, the graft embryo lay in the ap. direction, coerrsponding to the orientation of the grafted fragment.

This large and complete self-differentiation has only succeeded in producing a very small induction. Above the most anterior end of the graft neural plate (i. e. the part opposite the head of the host, and thus as regards the host the most *posterior* part) is a small flat induced neural plate (Fig. 4) extending through about 35 sections, while the graft neural plate can be traced for another 100 sections in which there is no sign of an induced neural plate. This comparative failure of induction, although the graft has self-differentiated quite normally and is in contact with the host's extoderm, is rather surprising. It seems to occur much more frequently in the bird embryo than in the Amphibia. It has been particularly common in the experiments carried out by SCHMIDT and may be due to some special feature in his technique. It raises several interesting possibilities, which are now being investigated: possibly complete self-differentiation of the graft is to some extent antagonistic to the performance of an induction, and the frequency of such specimens among those operated on by SCHMIDT may be due to the fact that he grafted rather large fragments which were able to self-differentiate more harmoniously than the smaller fragments usually employed. Or again, it is noticeable that in many such specimens the grafted tissue lies at the extreme anterior edge of the *area pellucida*, and it is possible that the host ectoderm in this region is not so sensitive to the inducing stimulus.

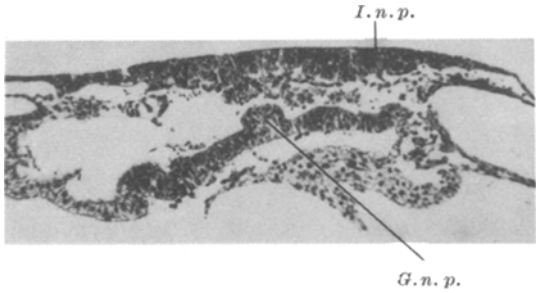


Fig. 4. No. 20 CD. Section (× 110).

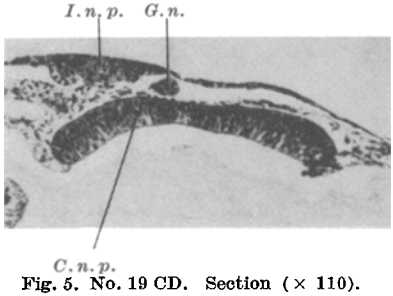


Fig. 5. No. 19 CD. Section (× 110).

19 CD. *Host.* Duck. M pr.s. *Donor.* Chick. Early head fold. *Graft.* Region of HENSEN's node, with posterior part of head process, all three tissue layers, dv. ap. in right anterior region. *Cultivated.* 26 hours.

In this specimen, as in 20 CD, the graft has differentiated into a fairly well-formed embryo with neural plate and six or seven pairs of somites. It is difficult to find any definite criterion to enable one to decide if the most

anterior part of the head is present in the tissue derived from the graft in this specimen or in 20 CD, but the appearances suggest that it is absent.

The induced neural plate (Fig. 5) is still smaller in this case than in 20 CD. It is very narrow, and only extends through 10 sections out of the 160 in which the graft is in contact with the host's ectoderm.

b) Grafts from duck into chick.

32—76 DC. *Host.* Chick. 22 hours. L pr. s. *Donor.* Duck. 8 somite pairs. *Graft.* Neural plate, notochord, etc. from region posterior to the somites, dv. in right anterior region. *Cultivated* about 24 hours.

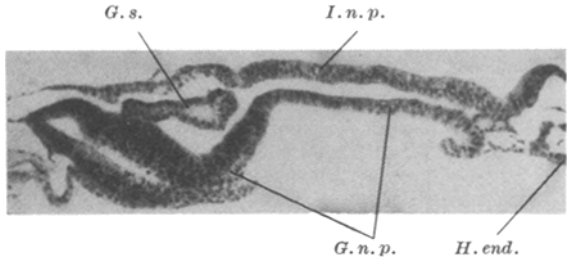


Fig. 6. No. 32—76 DC. Section, which cuts the induced plate longitudinally (× 110).

The graft mass consists of neural plate, notochord and somites. Its long axis lies almost exactly at right angles to the host axis. Above it is an induced neural plate, which is flat and not so broad as the graft plate. The sections are transverse to the host axis, and therefore cut the graft and induced plates longitudinally (Fig. 6).

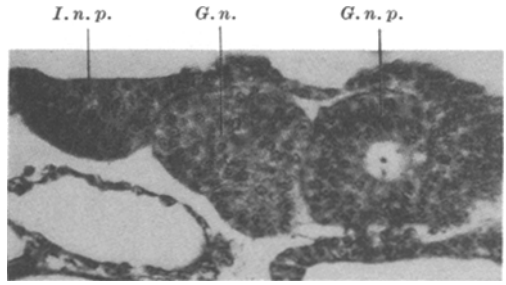


Fig. 7. No. 32—194 DC. Section (× 190).

32—194 DC. *Host.* Chick. 18 hours. SM pr. s. *Donor.* Duck. Early head fold. *Graft.* Posterior half of head process in right anterior region. *Cultivated* $43^1/_2$ hours.

After 43 hours' cultivation, there was a large blister in the right anterior region, at the edge of the area opaca, and between this and the host the graft and induced structures could be seen, running at right angles to the host's axis.

The sections show that the blister is a large, nearly hollow, bag of ectoderm, containing a thin strand of graft mesoderm. The induced neural plate begins close up against the blister, and perhaps passes up on to its upper surface. The graft has given rise to neural tube and notochord, and there may be a little induced notochord present (Fig. 7). There is no trace of the formation of a head.

32—214 DC. *Host.* Chick, 17 hours, M pr. s. *Donor.* Duck, 44 hours, early head fold. *Graft.* Posterior half of head process, not including HENSEN's node, all three tissue layers, dv. ap. in left anterior. *Cultivated* $21^1/_2$ hours.

The graft mass lies close up against the left side of the host neural plate, extending forwards from the anterior somite region. The most posterior (with reference to the host) part of the graft consists of a large lump of notochord, above which is a flat neural plate induced in the host's

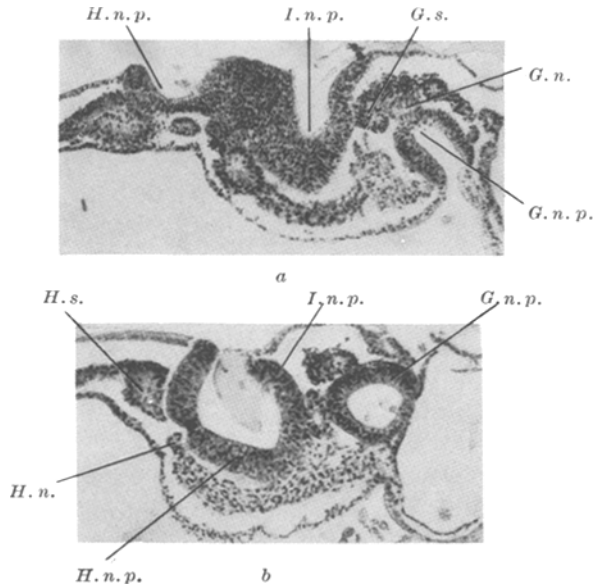


Fig. 8*a*—*b*. No. 32—214 DC. 8*a*, section through posterior region of graft (× 110); 8*b*, section through more anterior region (× 110).

ectoderm. Very slightly further towards the anterior, this induced neural plate is deeply folded, and graft neural plate and somites have appeared (Fig. 8*a*.) After a few sections, the ridge separating the induced neural groove from the host neural groove disappears, and the two fuse together to form a single well-shaped tube, the composite nature of which is shown by the asymmetrical position of the host notochord (Fig. 8*b*). This configuration can be traced for some distance towards the anterior, but after the disappearance of the host notochord the neural tube becomes very contorted and it is not possible to determine which part is host and which is induced. The graft notochord does not extend so far anteriorly as the graft neural tube; it is probable that this part of the graft where the neural plate is present but the notochord absent represents the more posterior part of the graft-structure, since it is only in the development of the posterior part, which normally involves considerable movements

of tissue, that there could be an opportunity for such a separation to occur. This argument suggests that the graft has retained its reversed (ap.) orientation. The graft mass is probably shorter than might be expected, and it is therefore possible that the performance of tissue movements within it has been affected by its proximity to the host.

2. Grafts of the anterior part of the primitive streak.

a) Grafts from chick into duck.

32—133 CD. *Host.* Duck $25^1/_4$ hours. M pr. s. *Donor.* Chick $24^1/_4$ hours. M pr. s. *Graft.* Anterior third of pr. s. including HENSEN's node, no end. dv. ap. in right middle region. *Cultivated* 27 hours.

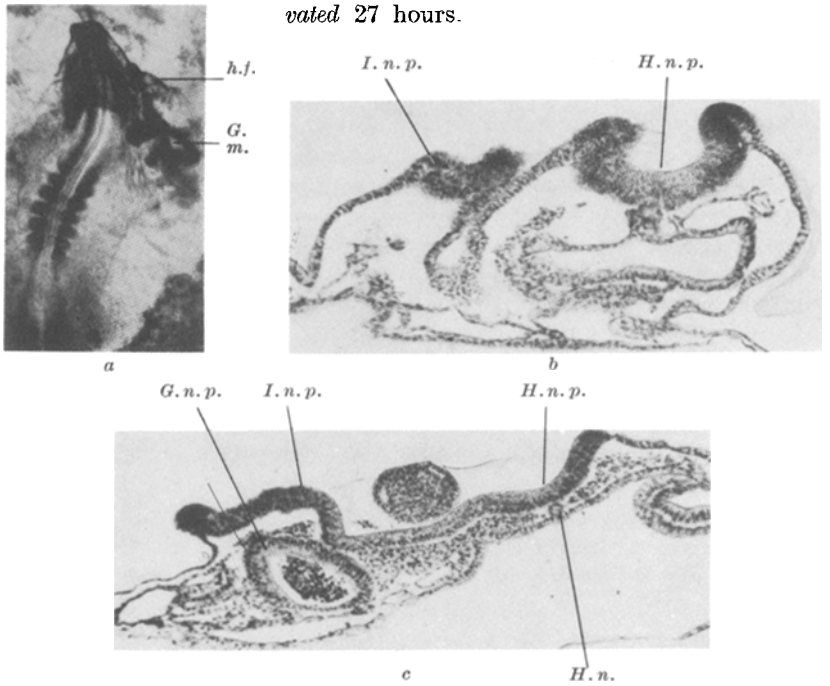


Fig. 9*a*—*c*. No. 32—133 CD. 9*a*, whole mount, *G. m.* graft mass (× 30); 9*b*, section through anterior region of graft (× 110, sides reversed); 9*c*, section through more posterior region (× 90, sides reversed).

The graft and induced structures lie to the right of the host's head (Fig. 9*a*).

In the sections, the most anterior part of the induced plate is found to lie on the top of a fold in the blastoderm, and thus bears some resemblance to a head (Fig. 9*b*). This fold soon flattens out, and the induced plate unites laterally with the host neural plate. In the region of this union there is a tubular mass of graft neural tissue lying beneath the

induced plate, but slightly further posteriorly this mass becomes confluent with the induced neural plate (Fig. 9*c*) and soon afterwards both plates disappear.

The presence of what appears to be a head-fold in the anterior part of the induced structures, indicates that the induced embryo is probably orientated similarly to the host, although the graft was made with the reversed orientation (ap.).

32—135 CD. *Host.* Duck 26 hours. M pr.s. *Donor.* Chick. 15 hours. M pr.s. *Graft.* Anterior half of pr.s. including HENSEN's node. dv. in right middle region. *Cultivated* $31^1/_2$ hours.

After $26^1/_2$ hours a very beautiful induced head was visible in the culture. It seems to be in exactly the same stage of development as the host's head (Fig. 10*a*). Fixation destroyed to some extent the shape of the head (Fig. 10*b*). In the sections the most anterior part of the induced neural tube is not underlain by any graft material, but a short distance towards the posterior a piece of neural tissue and a little mesoderm appear below the induced tube and these are presumably derived from the graft (Fig. 10*c* und 10*d*). In two sections, the floor of the induced groove breaks through and the lumina of the induced and graft tubes are continuous; but even so the two tubes retain their individuality and the boundary between them can be roughly made out. Posteriorly from these two sections, the tubes round up again and are entirely separate (Fig. 10*e*). In the most posterior part, somitic mesoderm appears associated with the graft neural tube, which then disappears, leaving the induced tube underlain by mesoderm only. This tube finally disappears quite suddenly.

In spite of the beautiful and unmistakeable head seen in the living specimen, the head fold associated with the induced tube is not very perfect, particularly on the side nearest the host, where the surface of the blastoderm is already elevated by the formation of the host's head. Neither is any proper foregut ever found under the induced head, probably because the graft material lying under the induced tube was in the way and prevented the necessary foldings.

32—171 CD. *Host.* Duck 41 hours, L pr.s. *Donor.* Chick 17 hours, LM pr.s. *Graft.* Anterior half, not including HENSEN's node or primitive pit, dv. aa. no end. in left anterior region. *Cultivated* 19 hours.

A cinema film of the development of this embryo was taken by Dr. R. G. CANTI to whom I am indebted for permission to reproduce Figs. 11*a—e*.

The grafted tissue can be seen to lengthen by posteriorly directed growth, so that its shape changes from a short triangle to a long narrow strand. At the same time the backwardly directed movements along the primitive streak of the host is very clear in the projected film. There seems to be no longitudinal movement of host tissue at the sides of the

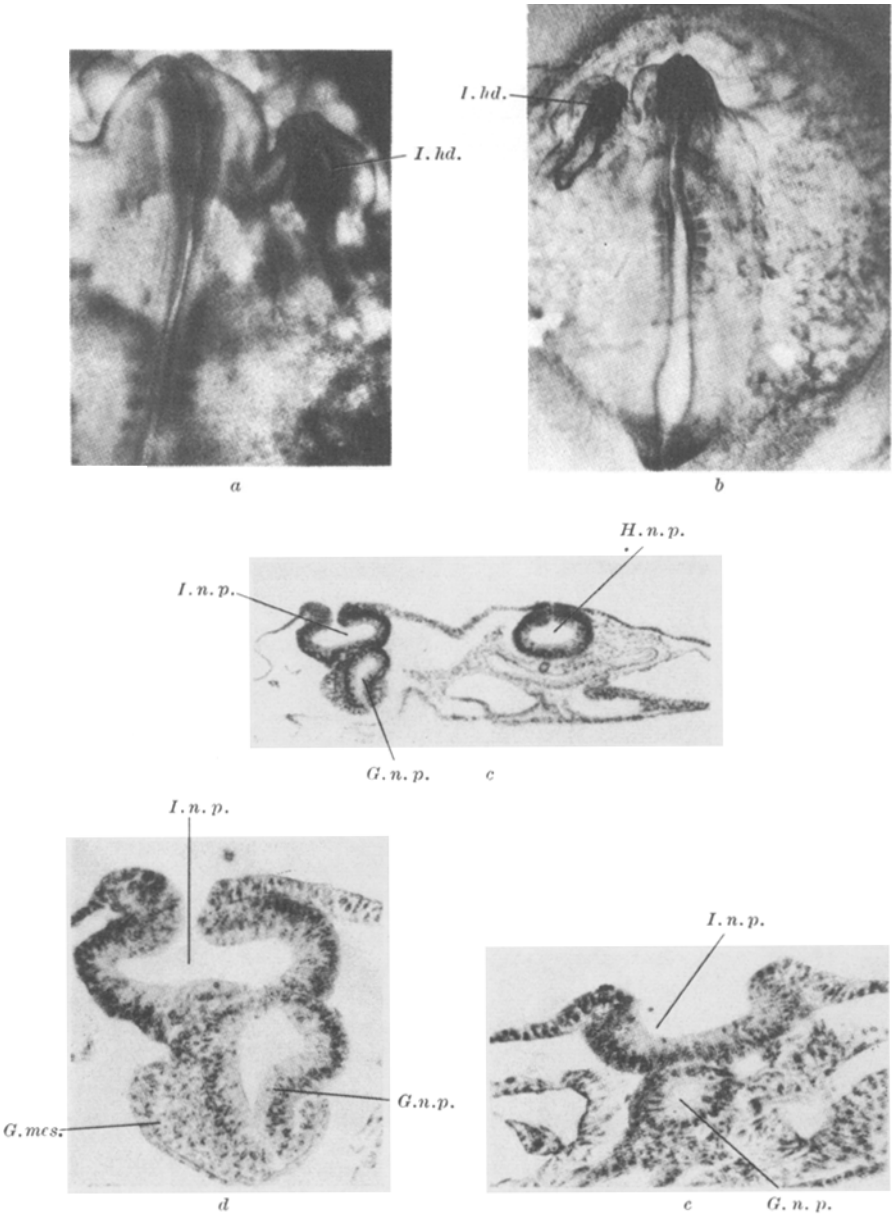


Fig. 10*a–e*. No. 32–135 CD. 10*a*, Living specimen, cultivated 26½ hours, *I. hd.* induced head (× 70); 10*b*, whole mount, fixed after 31½ hours (sides reversed, × 30); 10*c*, Section through anterior region (× 70, sides reversed); 10*d*, same section as last, induced and graft masses enlarged (× 315, sides reversed); 10*e*, Section through more posterior region (× 315, sides reversed).

area pellucida. There is also a movement of material from the sides inwards towards the primitive streak, which is partly the movement

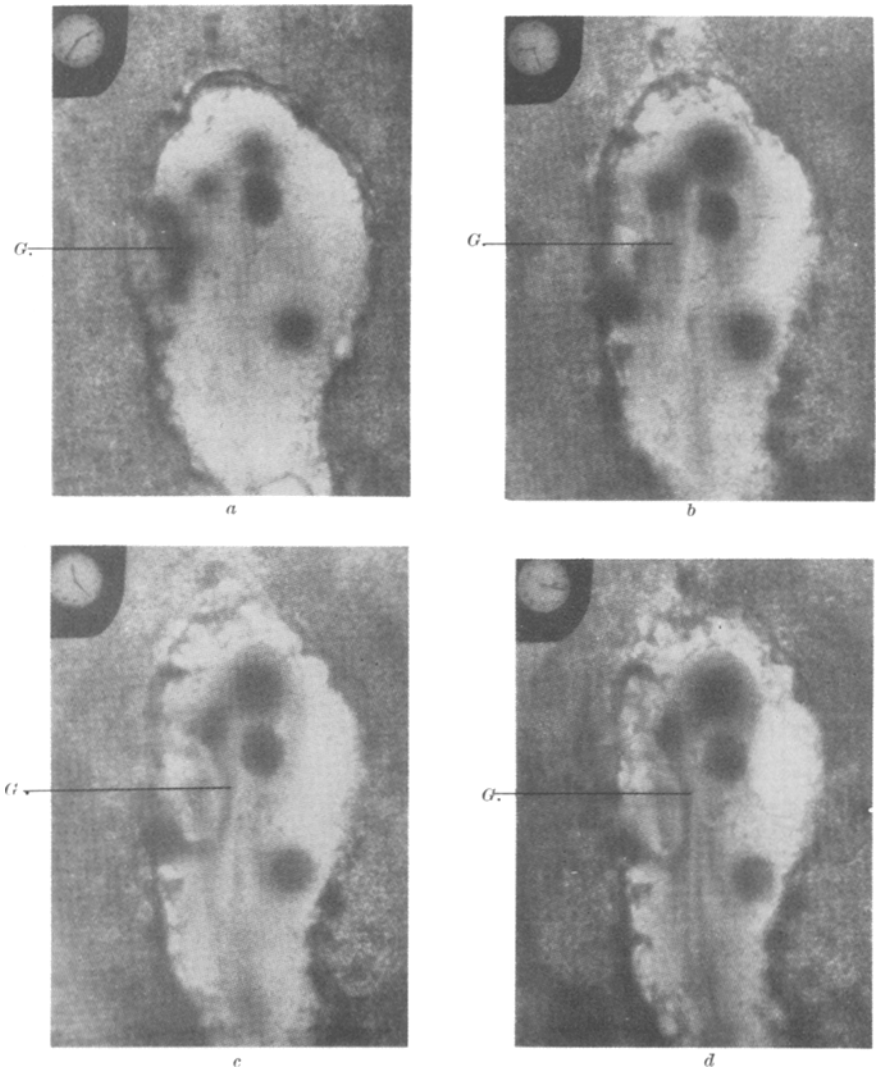
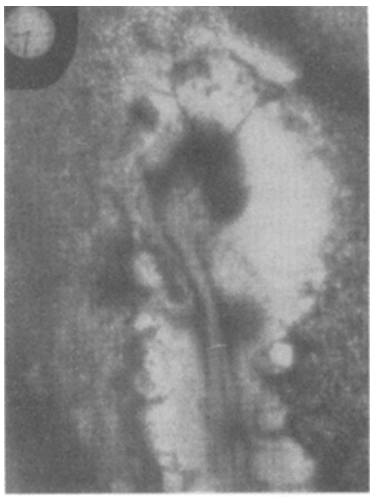


Fig. 11*a*–*d*. No. 32–171 CD. 11*a*, *b*, *c*, *d*, *e*, from a cinema film taken by Dr. R. G. Canti; a, shortly after operation; 11*b*, after 6 hrs. 50 mins.; 11*c*, after 9 hrs. 50 mins.; 11*d*, after 12 hrs. 40 mins.

responsible for the formation of the mesoderm, and is partly associated with the condensation and folding of the neural plate. The grafted mass is strongly affected by this lateral movement and moves in towards the

mid-line of the blastoderm, until it appears to lose its identity in that of the host, the only sign of its presence being a slight bending of the host's axis from the straight line towards the left side in the middle of the head region. It is impossible from the film to see whether the graft had induced a neural plate before it united with the host, but that is perhaps unlikely.

In the sections, very little sign of the graft can be seen. The anterior part of the neural plate is folded into a double trough, with one more or less centrally placed notochord: the foregut however lies asymmetrically under the right side of the plate (Fig. 11*f*). Further posteriorly, the left side of the neural groove is not so much folded as the right side, and passes over gradually instead of sharply, into non-neural ectoderm (Fig. 11*g*). In the region of the anterior somites, the left side of the groove has acquired a sharp boundary, but is now slightly larger than the right side. All these slight disturbances of the normal anatomy are probably due to the presence of the graft.



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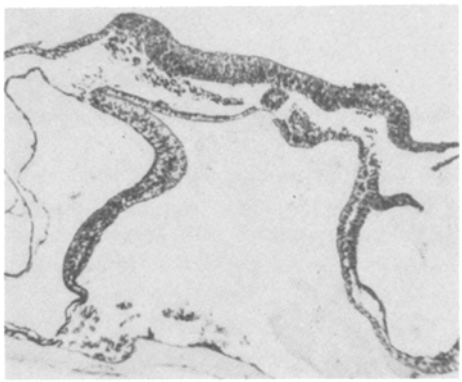


g

Fig. 11*e*–*g*. No. 32—171 CD. 11*e*, after 19 hours. The round dark masses are lumps of golk. 11*f*, section through anterior end (× 90, sides reversed); 11*g*, section through more posterior region (× 90, sides reversed).

b) Grafts from duck into chick.

32—130 DC. *Host*. Chick $20^1/_2$ hours, M pr. s. *Donor*. Duck $44^1/_2$ hours, L pr. s. *Graft*. Anterior third including HENSEN's node dv. in left anterior region. *Cultivated* $20^1/_2$ hours.

At the time of fixation, the host embryo was in the stage of the first appearance of the neural folds in the head region. On the left side of the host, was a second induced embryonic axis, running alongside of and quite near the host's axis and orientated in the same direction. The culture was, in fact, in a similar stage to 32—136 CD (see p. 542) when the first photograph of it was taken. The specimen thus shows an early stage in the process of induction.

The graft can be seen in the sections as a strand of mesoderm on the left of the host's axis. Above the anterior part of this mesoderm, a young neural plate is in process of formation (Fig. 12). The notochord and the foregut are not yet visible. No neural tube has developed in the graft. The induced neural plate can only be recognised as such in the anterior region: posteriorly it becomes very thin and cannot be distinguished from the rest of the host ectoderm. In this posterior region, the host's neural plate is very thin, but can be recognised by being underlain by the notochord: the region is in fact in the head process slage of development. In the most posterior part of the induction, there is a large accumulation of graft mesoderm, which forms a projection from the surface of the blastoderm. Within this projection, the mesoderm is united with the host ectoderm in a manner which recalls a primitive streak.

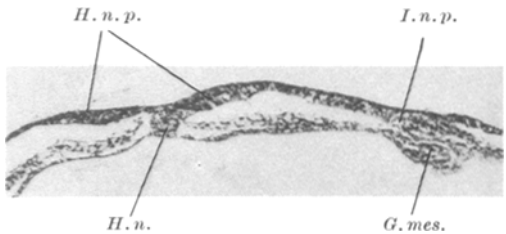


Fig. 12. No. 32—130 DC. Section (× 90 sides reversed).

32—170 DC. *Host.* Chick 17 hours, L pr. s. *Donor.* Duck 41 hours, early head process. *Graft.* Anterior half without HENSEN's node, dv. aa. in left side. *Cultivated* 24 hours.

In the entire specimen, an induced neural plate can be seen attached to the host neural plate in the hind-brain region and running leftwards and forwards from this position. It terminates in a process projecting above the surface of the blastoderm (Fig. 13*a*).

The sections are parallel to the host axis and therefore cut this process longitudinally. It consists of a bag of ectoderm filled with mesoderm. The induced neural plate is thin and runs along the upper surface of the process, dying out before it reaches the tip. The plate is better seen nearer the host's axis where it is cut transversely: it is in this region underlain by a compact and rather widely spreading layer of mesoderm, presumably derived from the graft (Fig. 13*b*). In some places the mesoderm is arranged in somites; it is possible that a little graft neural tissue is also present. The induced plate becomes larger and better developed as it is traced towards the host embryo, with which it eventually unites,

and its more advanced development in the region near the host shows that this is its most anterior end. It will be noticed that the induced neural plate is in this specimen orientated almost in the reversed (ap.) direction, although the graft was orientated similarly to the host (aa.).

32—188 DC. *Host.* Chick 15 hours, M pr.s. *Donor.* Duck L pr.s. *Graft.* Anterior quarter including primitive pit, aa. in right anterior region. *Cultivated* $46^1/_2$ hours.

After 27 hours' cultivation the host embryo was in the stage when the neural folds are just closing in the head region (Fig. 14*a*). The graft and associated structures could be seen as an elongated mass on the right side of the host: the anterior end of these structures appeared to include a neural plate on the surface

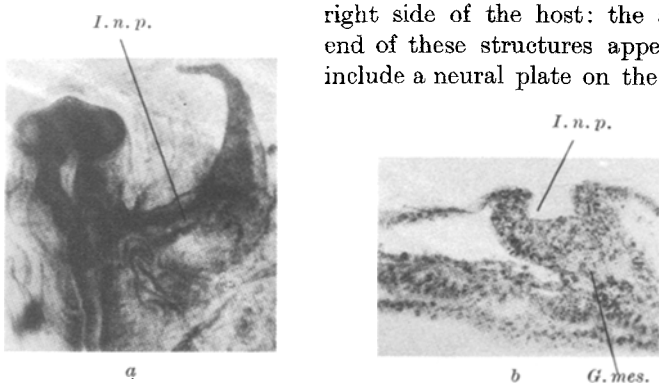


Fig. 13*a*–*b*. No. 32 –170 DC. 13*a*, whole mount (× 35, sides reversed); 13*b*, section (× 190).

of the host blastoderm, which would therefore be an induced plate, while the posterior end consisted of a finger-like process projecting from the surface of the blastoderm. In the fixed and stained specimen the gross anatomy is not very different (Fig. 14*b*). The host is slightly further developed and the graft structures have moved in rather nearer to the host's axis.

In the sections, the anterior part of the induced embryo is separated from the host by a deep fold in the ectoderm (Fig. 14*c*). The induced neural plate in this region is in the form of a tube, and is quite separate from the ectoderm. It is associated with a notochord, which is probably also induced; a notochord derived from the graft appears in the more posterior part of the embryo. The induced neural tube fairly soon opens out on the surface of the host ectoderm, forming a neural groove, and this becomes united laterally with the host neural groove (Fig. 14*d*). Further posteriorly, the graft structures are separated off from the host blastoderm in the finger-like process mentioned above. This consists of a bag of ectoderm containing graft neural tube, graft notochord and graft mesoderm and a very small induced neural plate, which does not seem to be continuous with the main induced plate.

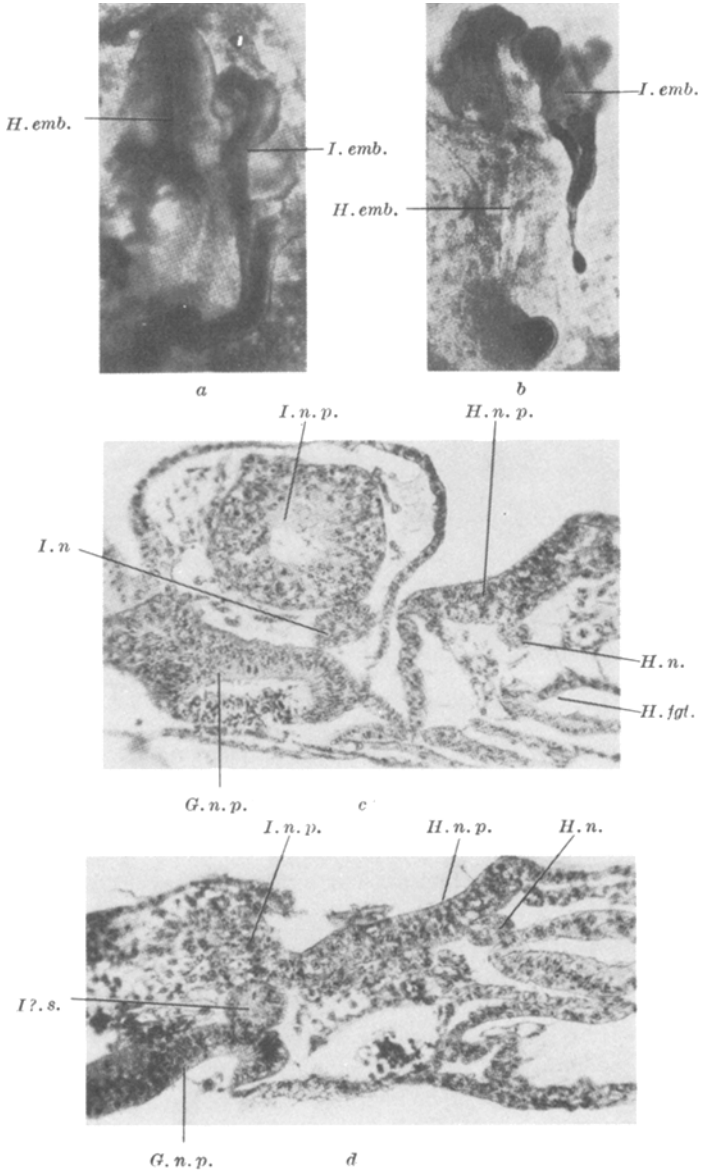


Fig. 14*a*–*d*. No. 32–188 DC. 14*a*, living specimen, cultivated 27 hours (× 35); 14*b*, whole mount, fixed after 46½ hours (× 30); 14*c*, section through anterior (× 190, sides reversed); 14*d*, section through central region (× 190, sides reversed).

32—190 DC. *Host*. Chick 15½ hours, M pr.s. *Donor*. Duck L pr.s. *Graft*. Anterior quarter including primitive pit, aa. dv. in left anterior region. *Cultivated* 22 hours.

In the entire, stained and cleared specimen, the graft and induced structures could be seen lying near the left side of the head of the host, just anterior to the first somite. There was an induced neural plate, united with that of the host and running at right angles to the host's neural tube away towards the left edge of the blastoderm. There were three pairs of somites associated with this neural plate. A short distance from the host's neural tube, the graft and induced structures formed a finger-like process projecting from the surface of the blastoderm: this process was curved backwards over the rest of the structures which it more or less hid from view. The fact that the induced plate is at right angles to the host plate, although the graft was made in the aa. orientation, is to be

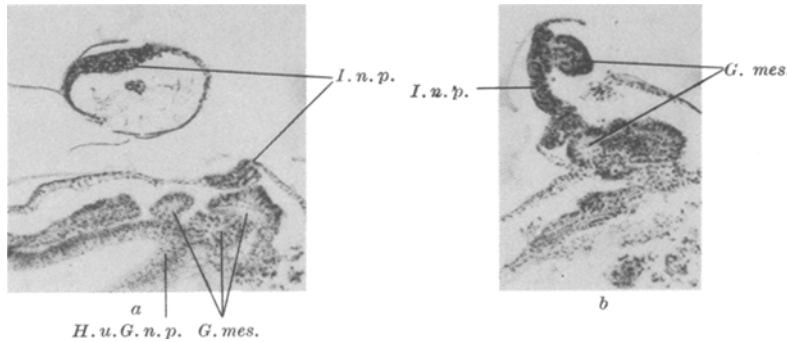


Fig. 15*a*–*b*. No. 32–190 DC. 15*a*, section through right end of graft and induced structures (× 90); 15*b*, section through left end of graft and induced structures (× 90).

explained by the shifting of the graft during the form-building movements of the host. The section plane was tranverse to the graft structures, and therefore cuts the host embryo longitudinally. The graft has given rise to neural plate, notochord and somites, and the neural plate has united with the host neural plate, which makes the sections very complicated in the immediate neighbourhood of the host. The section shown in Fig. 15*a* passes somewhat to the left of the host neural plate. It shows the main part of the induced neural plate associated with notochord and somatic mesoderm. It also shows above, the thin neural plate which runs along the upper surface of the finger-like process, which is hollow except for a thin strand of mesoderm. Fig. 15*b* shows the junction of the process with the main part of the blastoderm, and the origin of this mesoderm can be clearly seen.

32—222. DC *Host*. Chick $15^1/_2$ hours. LM pr. s. *Donor*. Duck. $39^1/_2$ hours. SM pr. s. *Graft*. Anterior two-thirds of primitive streak, including HENSEN's node, dv. ap. no end. in right anterior region. *Cultivated* 22 hours.

The entire specimen appeared nearly normal, except that the right neural fold in the posterior part of the region was spread out flat. The

sections show a large accumulation of loose mesenchymatous tissue in the right side of the embryonic axis opposite the most anterior somites. The right neural fold spreads out above the mass of tissue. As the sections are traced towards the anterior part of the embryo, the mesenchymatous tissue is found to occupy a wider and wider area on the right side, and at the same time there is a greater and greater amount of thickened ectoderm above it: this thickened ectoderm is continuous with the right

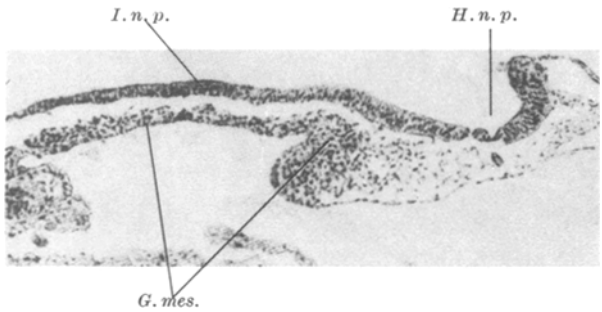


Fig. 16. No. 32—333 DC. Section (× 90, sides reversed).

neural fold and appears to be neural in nature (Fig. 16). This extensive thickening dies out rather rapidly further anteriorly and the host's head is normally formed.

11. DC. *Host*. Chick. LM pr. s. *Donor*. Duck. M pr. s. *Graft*. Anterior half of primitive streak, with endoderm, dv. in right anterior region. *Cultivated* 21 hours.

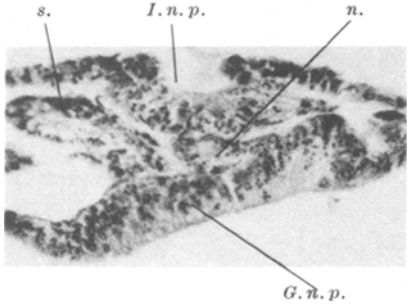


Fig. 17. No. 11 DC. Section (× 240).

The graft lies parallel to, and to the right of, the host embryo, in the heart region. The implanted tissue has differentiated into neural plate, notochord and somites, with a small foregut derived from the grafted endoderm at the anterior end. The induced neural plate is thin in the posterior region, and is best developed in the middle region, where the grafted somites are small (Fig. 17). In the most anterior part, the induced plate dies out altogether, and the grafted plate, accompanied by the foregut derived from the implanted endoderm, is folded downwards away from the host ectoderm, and forms quite a typical head.

c) Homoplastic grafts.

32—165 DD. *Host*. Duck 43 hours. LM pr. s. *Donor*. Duck. 43 hours. LM pr. s. *Graft*. Right lateral half of anterior half including HENSEN's node, dv. ap. no end. in right anterior region. *Cultivated* 46½ hours.

After 23 hours cultivation, the host had about six pairs of somites, and a large projecting structure was visible on the right opposite the head of the host. When the culture was fixed, two hearts were beating, one in the left side of the host, and the other on the right, posterior to the induction mass. These hearts, as can be seen in the sections, are derived from the two heart-rudiments of the host, and are not connected with the induction.

The sections show that the most anterior part of the induction consists of a large induced neural tube, which is cut off from the surface of the blastoderm by a head fold (Fig. 18*a*). Slightly posteriorly, the head fold disappears and the induced tube opens out on the surface, lying on the upper side of a swelling of the host's ectoderm: this swelling is filled with mesoderm, in the lower part of which the graft neural tube appears. Still further posteriorly the mesoderm becomes thinner and the graft neural tube disappears; shortly after this the endoderm pushes up into the swelling and forms a foregut (Fig. 18*b*) which extends as a pocket towards the more *posterior* part of the induction (Fig. 18*c*). After the disappearance of the foregut, the most posterior end of the induced neural tube becomes separated from the host blastoderm by the appearance of another fold, similar to a head fold.

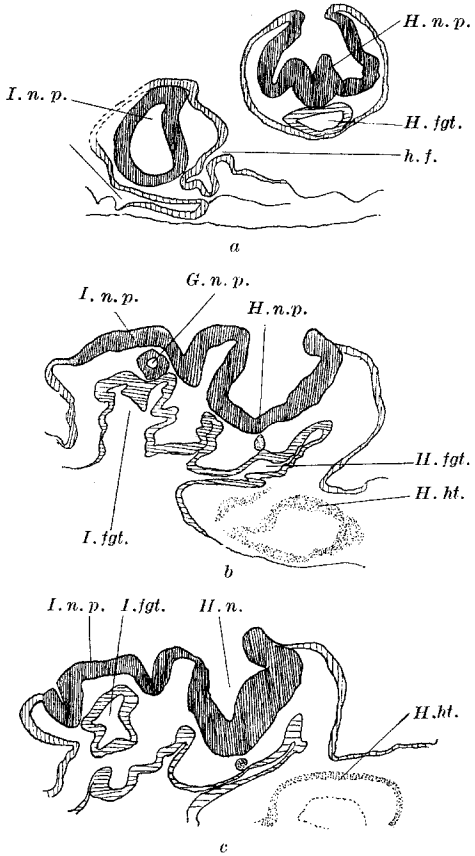


Fig. 18*a*–*c*. No. 32–165 DD. 18*a*, section through anterior (× 50); 18*b*, section through more posterior region (× 50); 18*c*, section trough still further posterior region (× 50). Camera lucida drawings, all with sides reversed.

It will be seen that this induced neural plate appears to have two anterior ends. The end which is most anterior as regards the host presents considerable similarity to a head, and the neural plate is most higly developed in this region: but the foregut extends from its opening backwards (as regards the host) towards the other end. These facts are interpreted as the result of a struggle between the polarities of the host and of the graft.

It should be noticed that the induction is laterally symmetrical, although the graft consisted of a right lateral half of the primitive streak.

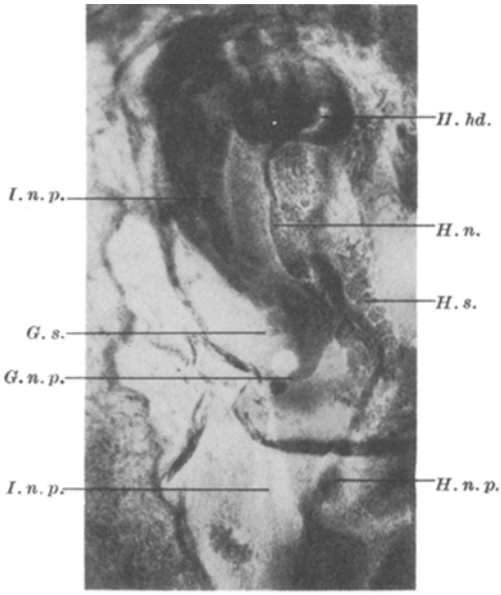


Fig. 19*a*. No. 32 – 217 CC. Whole mount (× 70).

32—217 CC. *Host*. Chick, aged 14 hours, LM pr. s. *Donor*. Chick aged 14 hours, M pr. s. *Graft*. Anterior half of primitive streak, including HENSEN's node, dv. ap. no end. in left anterior. *Cultivated* about 24 hours.

Fig. 19*a* shows a photograph of the whole mount fixed after 24 hours cultivation. At the left side of the host axis, the induced structures are seen. There appears to be a neural plate extending some distance to the anterior of the host neural plate. Somites appear associated with the middle part of this plate, on the same level as the somites associated with the host plate.

In the most anterior part of the specimen, the sections show two flat neural plates, of which that on the left side, i. e. the induced neural plate,

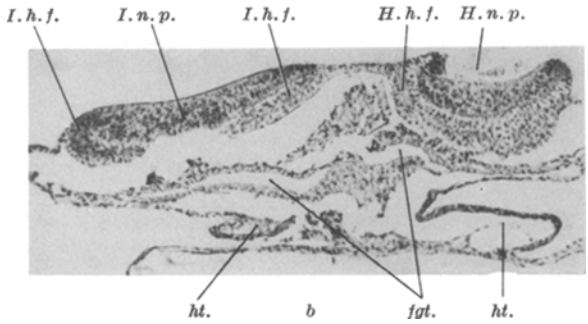


Fig. 19*b*. No. 32–217 CC. Section through anterior (× 90).

extends further anteriorly than the other. Both neural plates are cut off from the surface of the blastoderm by head-folds; the head fold of the host neural plate is deeper and more complete than that of the induced plate. The right heart-rudiment extends very far forward under

the most anterior part of the host head. Above it is a wide foregut which extends under both neural plates (Fig. 19*b*). Slightly posteriorly, the host neural plate becomes deeply folded into a tube, and the induced plate, which remains flat and unfolded, unites laterally with it. A notochord appeares under the host neural plate, and a little further posteriorly another mass of notochordal tissue appears under the induced plate (Fig. 19*c*), accompanied by a small separate lump of graft neural tissue: the host neural groove has also become flat in this region. The graft neural tissue unites with the induced plate, forming a small swelling on its lower surface and then disappears. The notochord beneath the induced neural plate, which is probably to be interpreted as graft notochord, also disappears as the sections are followed towards the posterior. The induced and host neural plates are very closely united in this region, the only sign of the composite nature of the neural plate being its asymmetry. Somites appear first under the right side of the neural plate, and shortly towards the posterior the composite neural plate becomes folded into a tube, with a somite on its right side, and one slightly to the left of the mid-ventral line: this latter somite would therefore be on the left side of the host part of the tube. Very slightly posteriorly, the neural tube splits into two: the host neural plate is completely folded into a tube, and has a somite on each side of it, while the induced neural plate is a rather shallow groove (Fig. 19*d*). Below the induced plate there is a mass of neural tissue derived from the graft; possibly this is really continuous with the small piece of graft neural tissue which can be seen further anteriorly, and in this case, the neural plate of the mid-region of the embryo must be supposed to be a triple structure, composed of host, induced and graft neural material. The graft neural plate forms a small process projecting from the lower surface of the blastoderm and then disappears. The induced neural plate can be traced for some distance

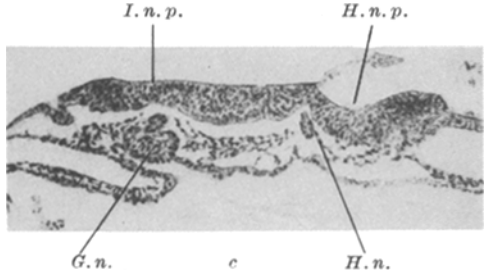


Fig. 19*c*. Section through central region (×90).

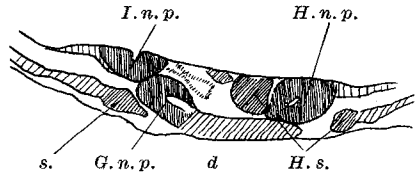


Fig. 19*d*. Section through region of the most anterior somites (Camera lucida, × 75).

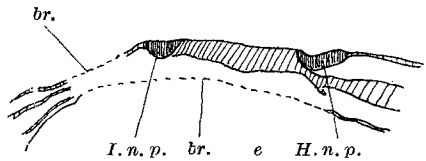


Fig. 19*e*. Section through posterior region *br.* material broken off and lost from the section (Camera lucida, × 75).

further (Fig. 19*e*): it is small and flat. The most posterior part of the specimen was damaged.

3. Grafts of middle and posterior parts of primitive streak.

a) Grafts from chick into duck.

32—126 CD. *Host.* Duck $37^1/_4$ hours. M pr. s. *Donor.* Chick 19 hours. LM pr. s. *Graft.* Middle third, no end. dv. to left opposite the anterior end of the primitive streak. *Cultivated* 23 hours.

The graft has given rise to mesoderm only. This is united with the host ectoderm which is thickened and grooved, forming anteriorly a very early neural plate and posteriorly a typical primitive streak (Fig. 20).

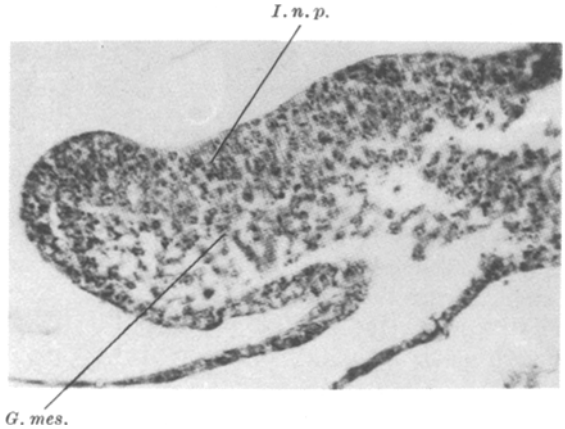


Fig. 20. No. 32—126 CD. Section (× 240).

The anterior part of the induced structure lies on the surface of the host blastoderm, but the posterior part is on a finger-like process projecting from the surface. The structure is nearly parallel to the host's axis, diverging slightly posteriorly: it lies at a considerable distance from the host's axis, near the edge of the area pellucida. The host had about 12 somite-pairs when fixed, so that the induced plate has lagged considerably behind the host in development.

32—136 CD. *Host.* Duck 28 hours. M pr. s. *Donor.* Chick 15 hours. M pr. s. *Graft.* Posterior half of donor to 32—135, dv. in left anterior region. *Cultivated* 45 hours.

After $26^1/_2$ hours cultivation the host embryo was still in the head-fold stage (Fig. 21*a*). Lying to the left of the host embryo was another embryonic axis. Anteriorly this ended in a small fold, which may have been a head-fold: posteriorly it curved away to the left and ended in a process projecting from the surface of the blastoderm. On the following day the living specimen could not be understood, but in the cleared and stained whole mount (Fig. 21*b*) it became clear that the two embryonic

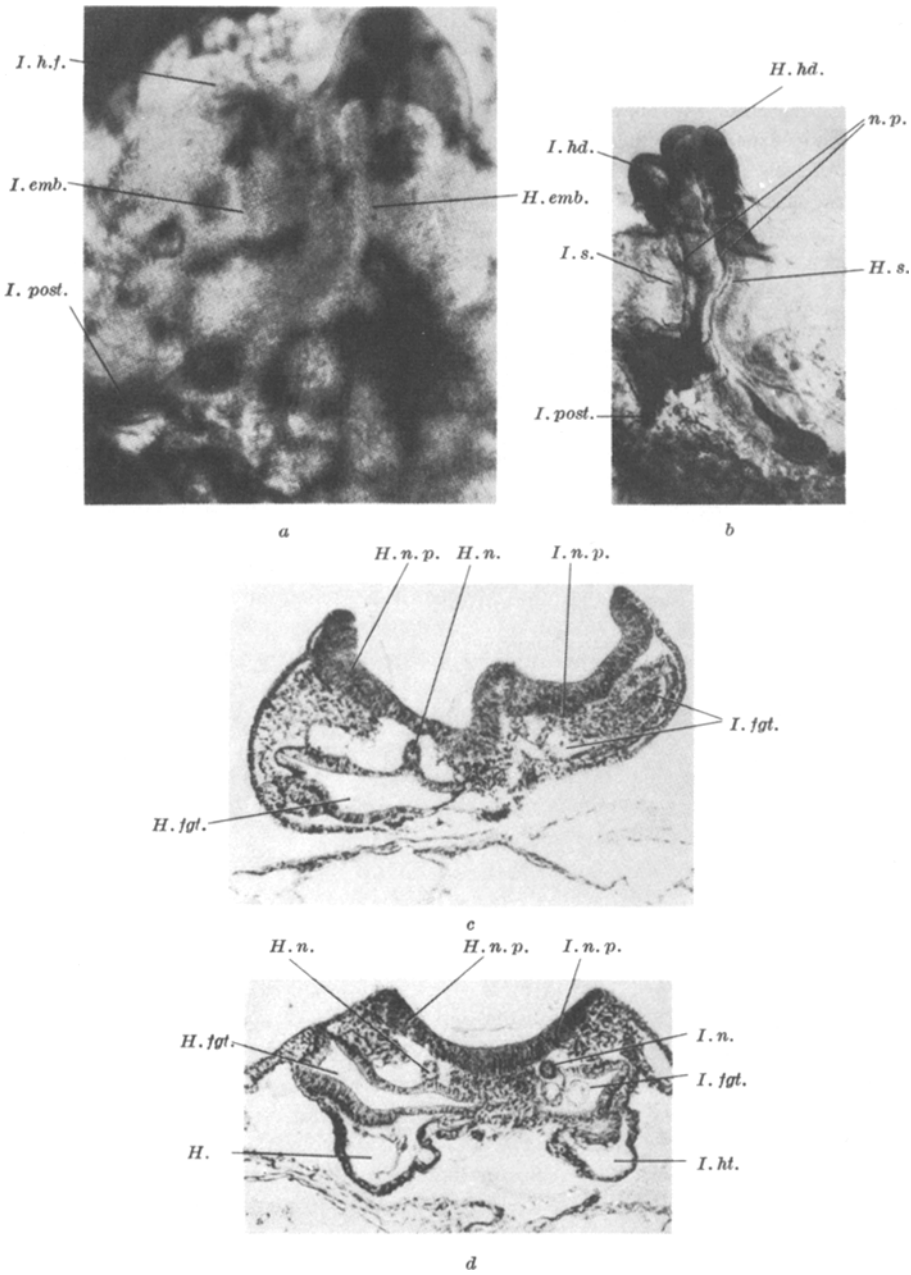


Fig. 21*a*–*d*. No. 32 – 136 CD. 21*a*, living specimen, cultivated 26½ hours, *I. post.* posterior end of induced axis (× 70); 21*b*, whole mount fixed after 45 hours (× 30); 21*c*, section through anterior region (× 90); 21*d*, section through heart region (× 90). All sections with sides reversed.

axes had united laterally for nearly their whole length, only the posterior ends being separate. Such lateral movement of the axes is very common (cf. 32—171 CD). Both axes have a head at the anterior end and in the middle region there is only one very wide neural plate present.

The sections (Figs. 21*c*, *d*, *e*) show that each embryo is surprisingly complete. Thus there are two well-defined heads, two foreguts, two hearts, two notochords and two rows of somite-pairs. As SPEMANN (1931) has noticed in similar inductions in Triton, the somites of one embryo correspond to those of the other, that is the somites of one are opposite somites of the other, and the intersomitic grooves of one opposite intersomitic grooves of the other. The same correspondence is seen in all the other structures, the foreguts, hearts, etc of the two embryos. In the most posterior part, the two median lines of somites fuse and later the induced embryo separates off and is bent sharply to the left.

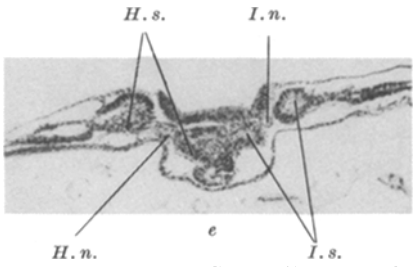


Fig. 21*e*. No. 21—136 CD. Section through central region (× 70, sides reversed).

In this specimen there is no neural tissue which appears to be derived from the graft, and the graft mesoderm is so harmoniously incorporated in the body of the induced embryo that it is impossible to distinguish it from mesoderm formed from the induced embryonic axis.

It should be noticed that the induced embryo includes structures from all levels of the body whereas the graft contained only material which would normally lie fairly far posteriorly. No presumptive notochord was included in the graft.

b) Grafts from duck into chick.

32—197 DC. *Host.* Chick, M pr. s. *Donor.* Duck, head fold, with two intersomitic grooves. *Graft.* Middle region of primitive streak, not including HENSEN's node, all three layers, dv. in right middle region. *Cultivated.* 28 hours.

The graft-mass lies at the edge of the *area pellucida*. The graft has given rise to a mass of tissue which is closely united with the host's ectoderm lying above it. The whole formation suggests that the graft tissue and the host's ectoderm have united to form a primitive streak (Fig. 22).

32—221 DC. *Host.* Chick, aged 15 hours, LM pr. s. *Donor.* Duck, aged 39 hours, M pr. s. *Graft.* Posterior half of primitive streak, dv. ap. in left anterior region. *Cultivated* 22 hours.

In the fixed and stained specimen, no trace of the graft could be seen. In the sections, however, it is found that the neural tube opens out on the surface into a groove in the region just anterior to the somites,

although further posteriorly it is a closed tube. The left side of the open groove is larger than the right, and beneath it is a piece of tissue which is probably derived from the graft. Anteriorly this forms a flattened vesicle (Fig. 23) but posteriorly it merges with the somatopleure and splanchnopleure of the host. The most anterior part of the neural tube is very contorted, but there is no evidence that any induction has taken place, unless the assymmetry of the folds can be interpreted in this way.

32—154 DC. *Host.* Chick, 17 hours, M pr. s. *Donor.* Duck, 21 hours, LM pr. s. *Graft,* right lateral half of pr. s., not including anterior third, in left anterior region. *Cultivated* $19^1/_2$ hours.

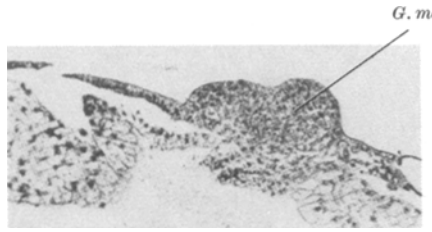


Fig. 22. No. 197 DC. Section (× 110, sides reversed).

In the fixed specimen the induced structures can be seenlying anteriorly to, and to the left of, the host embryo, which is badly developed. The most leftward part of the induced structure consists of a long projection from the surface of the blastoderm, this projection being bent into a semicircle. To the right of this, immediately anteriorly to the head of the host, lies a structure which bears a superficial resemblance to a head, which indeed it probably is (Fig. 24*a*).

The specimen was obviously unhealthy when fixed, and the sections show large numbers of disintegrating cells. The left part of the semicircular projection is quite free from the surface of the blastoderm, and consists of a bag of thin ectoderm filled with necrotic mesenchyme; there is no sign of an induced plate. The projection is united with the blastoderm only at the end which is most anterior as regards the host; the ectoderm here is thin and non-neural, and is underlain by similar mesenchymatous tissue. Further to the right, a large hollow vesicle appears in the sections, and only a few sections further to the right an induced neural plate can be seen. Beneath the induced plate is a tubular mass of tissue which can be seen to arise from the endoderm a few sections to the left of the appearance of the vesicle; it probably represents a foregut. There is also a little necrotic mesoderm, probably derived from the graft. Still further to the right, the vesicle and the neural plate are cut off from the surface of the blastoderm by a fold which may be interpreted as a

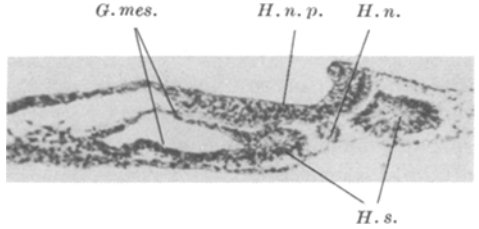


Fig. 23. No. 32 – 221 DC. Section (× 110).

head fold (Fig. 24*b*). The whole appearance suggests that the right end of the induced structures is a head, and that if the specimen had not been so unhealthy, the semicircular projection would have developed into the posterior part of an embryo.

The induced plate itself is nearly bilaterally symmetrical, although only one lateral half of the primitive streak was grafted; but the structure

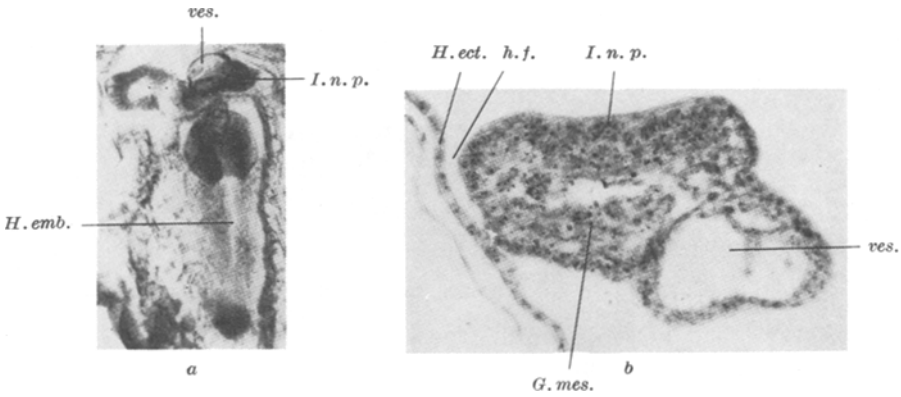


Fig. 24*a*–*b*. No. 32–154 DC. 24*a*, whole mount (× 30); 24*b*, section through the right of the graft and induced structures (× 240).

as a whole is made asymmetrical by the greater development of the vesicle on the anterior side, where it is not interfered with by the host embryo.

Discussion.

1. The Organising Function of the Primitive Streak.

The experiments described in this paper give conclusive evidence that in birds, as in Amphibia, the organising potentiality is not narrowly specific, but is capable of obtaining its effects on tissue belonging to different species or genera. This is true, in birds, for grafts of the primitive streak or of the head-process or *sinus rhomboidalis*; very few heteroplastic grafts of pure neural tissue have been made, and no satisfactory inductions have as yet been obtained, although there is little reason to suppose that such inductions are not possible.

At the stage of development at which the operated embryos were killed, duck tissue cannot be distinguished histologically from chick tissue, so that the distinction between host and graft tissues has to be made on morphological grounds. The general basis on which the distinction can be made has been discussed previously (Waddington, 1932). An examination of the photographs reproduced here will give some idea of the weight of the morphological evidence, though that evidence is more convincing when the whole series of sections can be worked through.

In general, it is found that one can usually decide whether masses of neural tissue are derived from the host or the graft, but it is often impossible to make this decision in regard to the mesoderm.

In the present experiments, as in those reported previously, inductions have been performed by pieces of the primitive streak which do not include HENSEN's node, as well as by those which do. 32—170 DC, 32—126 CD, 32—136 CD, 32—154 CD and probably 32—197 DC are examples of the former type. These specimens, in conjunction with various previously described embryos, make it impossible to suppose, with WETZEL (1929 and previous papers), that HENSEN's node is the organisation centre. Undoubtedly the node is part of the organisation centre, but the organising capacity is present over a much wider area, including at least the anterior two-thirds of the primitive streak. This might have ben expected by analogy with the Amphibia, where BAUTZMANN (1926) has shown that the organising capacity is not narrowly localised, but is possessed by a whole quadrant of the egg.

With the possible exception of 32—170 DC, none of the transplanted fragments which lacked HENSEN's node have formed neural tissue although certain of them have given rise to somitic mesoderm. However, examples of the development of neural tissue in the absence of the node have been described previously (WADDINGTON 1932). It was on a failure to obtain differentiation of the posterior parts of the embryo in the absence of the node that WETZEL based his idea that the node was the organisation centre, but with the positive proof that the posterior parts of the streak can perform inductions, WETZEL's negative evidence must be held to be inconclusive. Probably, as HOADLEY suggested (1927), mechanical factors played an important part in preventing the presumptive areas from differentiating normally. HUNT (1929, 1931) also failed to obtain differentiation of posterior pieces of the blastoderm transplanted to the chorioallantoic membrane in the absence of the node. He concluded that the node is "a centre of development essential to the formation of the embryo" (1931, p. 425). WILLIER and RAWLES (1931) came to essentially the same conclusion. A re-reading of the papers of these two authors has however convinced me that I[1] was guilty of misrepresenting them in my former paper (1932) when I stated that they regarded the node as an organisation centre. HUNT, indeed, stated in 1929 that this was so, but later (1931) he took a more cautious view, as quoted above. However, the results which I have obtained invalidate even the more guarded conclusion that the node is essential for the formation of the embryo. The node, I would suggest, is to be regarded merely as the most active part of the definitive primitive streak, differing in its developmental functions from the rest of the streak only in a quantitative and not in a qualitative manner.

[1] C. H. W.

The induction performed by the primitive streak gives rise to the same end-product as that performed by the endoderm, namely a neural plate, with in some cases the associated mesodermal and endodermal structures. It is important to discover the relations between these two processes of induction. It would be possible to suppose *a priori* that the endoderm induced a primitive streak which developes into an embryonic axis, but that the streak induces simply a neural plate. This seems to be contradicted by those cases in which mesodermal structures appear to have been induced by the streak. It is difficult to prove such cases with certainty, since host mesoderm is often indistinguishable from mesoderm derived from the graft. But in a specimen such as 32—136 CD it seems probable that some of the mesodermal material in the induced embryo is host material; another case which suggested the same conclusion has been described previously (1932, 350). In specimens such as 32—126C and 32—197 DC, we apparently see the mesoderm actually being proliferated from the epiblast, in a way which is typical of a primitive streak. The intimate association of the mesoderm, part of which is admittedly graft mesoderm, with the epiblast, suggests that we are dealing with a true primitive streak and not with a mere thickening of the epiblast preparatory to the formation of a neural plate. It is then probable that in some cases at least the axis induced by a fragment of the streak, itself passes through a primitive streak stage, but it is not possible to prove that this is always so.

In some of the cases described here, particulary in 32—136 CD, and in 32—43 (described WADDINGTON 1933a), the induced embryo is very complete, containing notochord, foregut and heart as well as neural plate. The development of a gut in connection with an induced neural plate is also known in Amphibia. The phenomenon has been interpreted (e. g. by MARX 1931) as an indication that the fundamental activity of the organiser is an attempt to build up a complete embryonic individual. The usual induction of neural plate would then be regarded as only one of the part-reactions by which this total effect is brought about. But the process of induction can be at best only partially under the control of the postulated unitbuilding forces, since even when the organiser (i. e. the mesoderm) is left in contact with the appropriate quantity of graft ectoderm, as in the grafts of head-process or *sinus rhomboidalis* or the experiment with opposed epiblasts (WADDINGTON 1932), it still succeeds in inducing the formation of a neural plate in the overlying host ectoderm: and this involves the production, under the influence of the organiser, of more neural plate than is required to build up one complete embryo (see Fig. 25). Moreover it is difficult to see how the fact of homoigenetic induction is to be accommodated in such a scheme. On the other hand, support for the idea might be drawn from the behaviour of many of the head-process grafts performed by SCHMIDT, which gave beautiful

differentiation of the graft unaccompanied by any trace of induction, although the graft appears to be in immediate contact with the host's ectoderm. 20 DC and 19 DC, which are described here, are border-line cases, in which there is a very small induction, much smaller than might

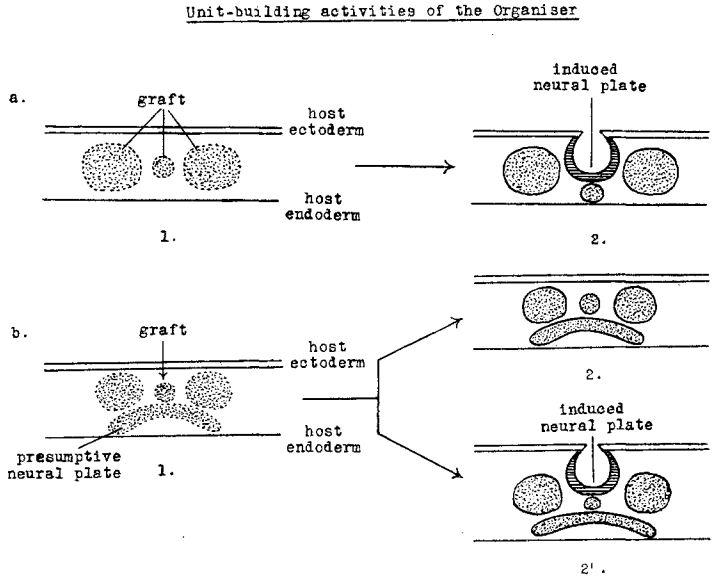


Fig. 25. An organiser (presumptive somites and notochord) is grafted between the ectoderm and endoderm of a host embryo (a. 1).

It might be supposed that the organiser has a tendency to form round it the kinds of tissue by which it is normally surrounded, i. e. in this instance to induce the host to form a neural plate (a. 2).

On this assumption, if the graft contains pressumptive neural plate (b. 1), there should be no such tendency to call into existence still more neural plate (b. 2).

But actually it is found that neural plate is induced under such circumstances (b. 2').

Conclusion. The induction of neural plate by the mesoderm cannot be due to a tendency of the organiser to surround itself with the tissues by which it is normally surrounded.

have been expected from the perfection of the graft structures, but in many other cases there was an equally good differentiation of the graft without any trace of induction. Now it is probable that SCHMIDT grafted somewhat larger pieces of tissue than I have been accustomed to employ, and it is possible, but perhaps not very likely, that the failure of induction in so many of his experiments is to be explained by the supposition that the unit-building forces of the graft were satisfied, as regards neural tissue, by the quantity of this tissue which was included in the graft.

One frequently meets with cases of the induction of neural plate without an accompanying foregut; 32—135 CD is a case in point: but I know of no example in birds of the induction of a foregut without an accompanying neural plate, although certainly in 32—43 the neural plate

is very small in the anterior region. Foregut induction is most successful in the experiments in which the epiblast and endoderm have been rotated relatively to one another (WADDINGTON 1932, 1933*b*). In some of these experiments a foregut has been induced in non-presumptive endoderm, the mesodermal and ectodermal parts of the embryonic axis being present with their mutual relations undisturbed, so that it is not possible to say which of these two parts has actually exerted the organising influence, although it is perhaps more natural to suppose that the mesoderm is the more important of the two. It is not yet certain whether it is possible to bring the foregut induction out of the control of the suggested unit-building activity; that is to say, whether a foregut can be induced by an epiblast which is already associated with a sufficient quantity of endoderm. Experiments will shortly be made to test this by placing two endoderms under one epiblast.

A unit-building activity of the organisation centre makes itself apparent in another respect. An isolated organiser tends to rearrange its regional structure so as to include all regions of the embryo. That is, an organiser whose prospective fate was to become the mesodermal part of the middle region of an embryo may rearrange itself so as to become the mesodermal part of a whole embryo (Fig. 26*a*). This regional rearrangement is one aspect of the action of the "individuation field" discussed below, where it is suggested that an organiser tends to rearrange the regional structure both of itself and of any tissue lying near it in such a way as to make that tissue part of a complete embryo (Fig. 26*b*, *c*). This is then a true unitbuilding activity of the organiser, which works, not by controlling the process of induction, but by modifying the products of that process.

It may then be possible to make, as a working hypothesis, a provisional classification of the activities of the organisation centre, which can be categorically stated as follows. There are on the one hand more or less autonomous processes of induction of neural plate, of foregut etc., by which the organisation centre can prepare from its surroundings all the types of tissue necessary for the formation of a complete embryo. These processes are not under the direct control of a unit-building force, as can be seen by the occurrence of homoiogenetic induction. But in point of fact the amounts of the various sorts of tissues which are normally formed by these processes just suffices for the production of one embryo. Meanwhile, a process of a different type, which is expressed in the individuation field, is in control of the regional character of these tissues, and attempts to build them into one complete unit.

2. The Mutual Interaction of the Host, the Graft and the Induced Neural Plate.

SPEMANN (1931) has discussed the influence of various factors on the regional character of the neural plates induced in Triton by grafts of

the organisation centre. He showed that, firstly, there is a regional structure within the centre itself, since if the presumptively anterior mesoderm is used as a graft in such a way that it performs an induction in the posterior part of the host's body, it induces an embryo which includes a head, whereas the presumptively posterior mesoderm in the same situation only succeeds in inducing an embryo which does not extend so far forwards as the head. There is the complication that grafts of both types complete themselves, as was mentioned above, and induce more than their prospective fate would lead one to expect; but the important fact in the present connection is that the same region of the host reacts to the two different grafts in different ways.

This experiment has not been performed often enough in birds for any conclusions to have been reached. As yet, no good case of the induction of a head in the posterior part of the host is known. As will become clear later, grafts of pieces of primitive streak in the anterior part of the host would not be expected to yield definite information, and in fact they do not do so. But there are several other grounds for suggesting that a regional structure of the inductive capacity of the primitive streak probably exists. (1) The prospective fate of the primitive streak is very different in its different parts, the anterior end containing a considerable amount of material destined to become neural tissue, as well as the prospective notochord, while the more posterior parts contain only prospective axial and side-plate mesoderm. (2) The inductive capacity of the anterior end seems to be stronger, i. e. to be able to perform an induction in a greater proportion of cases, than that of the posterior end. It is still uncertain whether the most posterior part of the streak has any inductive capacity at all. (3) The data which are at present available suggest that neural plates induced by the middle or posterior parts of the streak develop more slowly than those induced by the anterior end; that is, that by the time an anterior third of the streak has induced an neural plate, a middle third may have only induced a primitive streak. But it is still unknown how these differences depend on the position of the induction in the body of the host. (4) Pieces of primitive streak undoubtedly possess an anterior-posterior polarity in inductive capacity, since the orientation of the grafted piece of primitive streak is capable of determining the orientation of the induced embryo. Embryo 32—43 (described WADDINGTON 1933*a*) is a particularly good example; the induced embryo lies at the edge of the *area pellucida* and is oriented in the opposite direction to the host. Cases are known in which the orientation of the induced embryo is not determined by that of the graft (e. g. 32—217 CC) but in such cases the induced axes always lie near the host's axis, and they are interpreted as evidence that the host's organisation centre can influence the development of embryonic axes in its neighbourhood (see later). (5) In the Amphibia

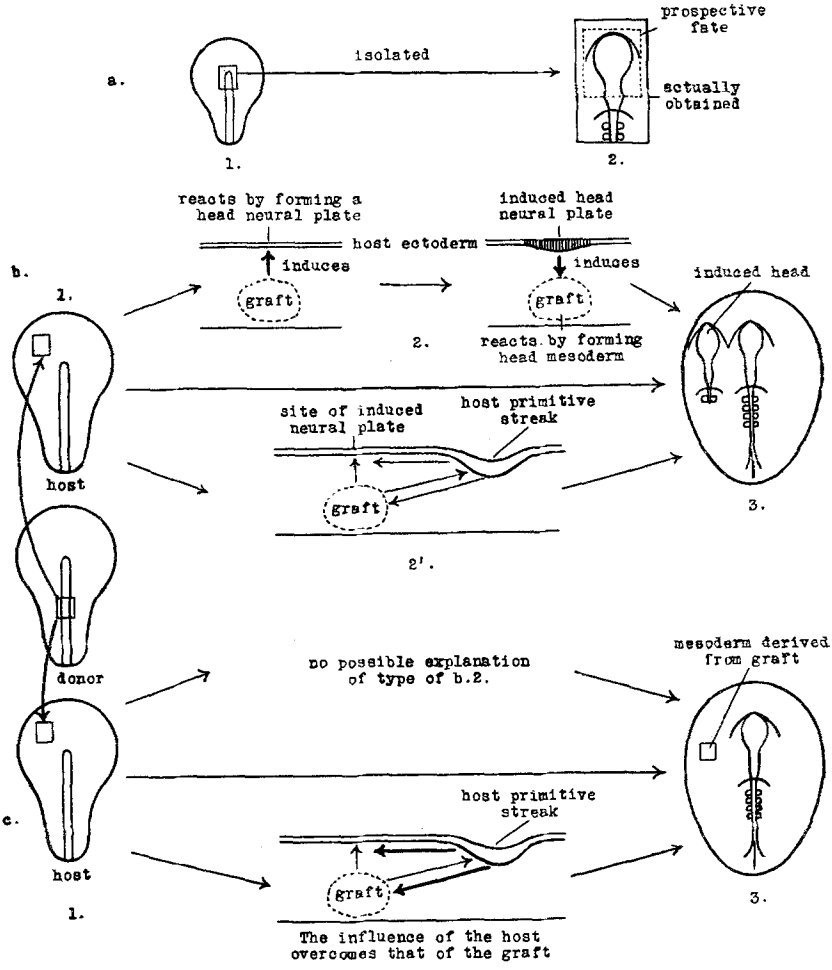
the regional character becomes more and more rigidly determined as development proceeds (SPEMANN 1931). Now in birds, heads have been, induced in the anterior part of the host by primitive streak grafts which did not include the presumptive head (e. g. 32—135 CD, 32—154 DC) but it is noticeable that when more highly developed tissue is used as a graft a head is only induced by grafts which themselves include the presumptive head material. This suggests that in the head process stage a regional structure is present, which again suggests that the structure is also present, in a more labile form, in earlier stages. All these various lines of argument, taken together, seem to me to justify one in adopting the working hypothesis that the different parts of the primitive streak have a tendency to induce different parts of the neural plate.

SPEMANN then proceeded to show that the host also played a part in determining the regional character of the induced neural plate. He showed that in the anterior part of the host's body, a trunk organiser, i. e. an organiser whose prospective fate was to become part of the trunk, induced a head (Fig. 26), although in the posterior part of the host, it could only induce an embryo which did not extend so far forwards as the head. SPEMANN seems to have been inclined to regard this regional structure of the host as being expressed in a regionally different reaction of the host's ectoderm to the stimulus of the trunk organiser. But the attribution of this difference solely to the different reactions of the host's ectoderm obviously depends on the assumption that the grafted trunk organiser remains trunk organiser. But it is clear that at any rate by the time the regional character is morphologically recognisable, this is not the case. When a trunk organiser, grafted into the anterior region of the host, induces a head, the graft mesoderm appears as head mesoderm conformable with the induction. Thus it is a pure assumption that the grafted prospective trunk mesoderm was trunk mesoderm when it performed the induction. This assumption may of course be true. It is quite possible that the labilely determined trunk mesoderm retains this determination while it performs the induction, that the host ectoderm reacts to the inducing stimulus by the formation of a neural plate which includes a head, and that this neural plate then has a second interaction with the grafted mesoderm in which the latter is caused to lose its labile determination and become head mesoderm (Fig. 26, b 2): but this hypothesis appears somewhat artificial and unnecessarily complicated.

SPEMANN did not perform his experiments in a manner which made it possible to determine how much of the mesoderm was derived from

Conclusions. 1. The host has an influence on the regional character of the tissue derived from the graft, as well as on that of the induced neural plate.

2. According to the argument represented in b. 2′ and c. 2′, this influence is due to a direct interaction of the host's organisation centre with the graft. The region over which the host's influence extends is called its "individuation field".



Regional structure of an isolated part of an organisation centre. a. A part of an organisation centre is isolated. Suppose that its prospective fate is to form the mesodermal part of the head. Then actually it is found to form the mesodermal part not only of the head, but also of some of the parts of the embryo lying near the head. It may even form the mesodermal part of a whole body.

Fig. 26. *Regional structure of the graft and the induced neural plate.* b. A part of the organisation centre, whose presumptive fate is to become mesoderm of the trunk region, is grafted into the presumptive head region of a host embryo (b. 1).

The final result (b. 3) is an induced head, containing induced neural plate, induced foregut and head mesoderm.

Two possibilities are presented. In one (b. 2) the grafted trunk mesoderm first induces a neural plate in the host ectoderm, which reacts in such a way that this neural plate has the regional character of head: and then the induced neural plate induces the grafted mesoderm to become head mesoderm.

In the second possibility (b. 2'), the organisation centre of the host and that of the graft interact directly with one another and with the induced plate, each organisation centre attempting to rearrange the whole complex of tissues so as to form a single complete individual.

c. An experiment is made exactly similar to that represented in b. 1 (c. 1). In some cases the result is a single complete embryo, part of the mesoderm in the area pellucida near the head region being derived from the graft (c. 3). Since no induced neural plate is formed, it is not possible to explain the conversion of the trunk mesoderm into head mesoderm on the lines represented in b. 2. But an explanation of the type of b. 2' can easily be found, it being only necessary to suppose that the host's influence has dominated over that of the graft.

the graft and how much from the host. Part of the head mesoderm accompanying an induced head may therefore have been host mesoderm. But this does not invalidate the important point, which is that if a regional structure of the reaction capacity of the host's ectoderm determines the regional character of the induced neural plate, it must also be responsible for the determination of the underlying mesoderm in those cases where the mesoderm has the same regional character as the induced plate.

Although SPEMANN did not discuss the conversion of trunk mesoderm into head mesoderm, he drew attention to another similar phenomenon which is probably suggestive in this connection. If the induced embryo lies parallel to, and close alongside of, the primary, the two inner rows of somites may lie exactly opposite one another and may even fuse to form one single well-formed row. From this fact SPEMANN developed the alternative possibility that even the mesodermal parts of the secondary embryo may differentiate under the direct influence of the host organisation centre. I wish to suggest that SPEMANN, owing to his failure to realise the difficulty about the conversion of trunk mesoderm, tended to underestimate the weight of evidence which favours this second suggestion. In fact he regarded the hypothesis that the host organisation centre influenced the development of an induced plate as somewhat bizzarre (etwas Befremdendes).

In the Amphibia, the two embryos, the primary and the induced, lie on the surface of a sphere, and since they are usually more or less on opposite sides of it, they are mirror-images of one another in the ventral plane. SPEMANN seems to suggest that this relation may be causally effective. But in the birds the two lie in the same plane, and if they are mirror-images at all, they will be images in the sagital plane. The fact that the mirror-plane is different in the two cases shows that the phenomenon is fortuitous. It will be shown later that the primary can influence the secondary without any mirror imaging (e. g. in 32—170 DC, 32—190 DC, 32—154 DC). Probably there would be a second mirroring at a later stage, when the two embryos have acquired their primary asymmetry, and differ on their right and left sides: then if they were parallel to one another, they would probably always be mirror images, mirrored in the sagital plane in both cases, and this mirroring might be an important relationship. A possible case in the present material is 32—135 CD, where the two hearts probably show a relationship of this kind.

SPEMANN also suggested a comparison with the phenomenon of the development of bilateral symmetry from a lateral half of an egg. That is to say, he brought the faculty of an organisation centre to influence the development of a secondary embryo in its neighbourhood into relation with its tendency to rearrange itself so as to form a whole. This tendency has been mentioned above and I believe that the comparison is a

valuable one. In the present connection, I wish to suggest the idea that an organisation centre is surrounded by a field, which may be called the individuation field, within which its unifying action makes itself felt. The individuation field is imagined as acting on any tissue, whether ectodermal, mesodermal or endodermal, lying within it, mpressing on that tissue the regional character appropriate to the part of the field in which the tissue lies (Fig. 26, b 2′ and c 2′). If then oneimagines a piece of neural plate in process of being induced in some ectoderm lying within an individuation field, there are three possible results which may eventuate from the action of the field. (1) The process of induction may be suppressed, and the "induced plate" caused to become normal body ectoderm of the host: this probably does not happen very often, but has probably occurred in some of the cases in which grafted fragments of the primitive streak have disappeared into the body of the host. (2) The induced plate may develop as a separate structure, sharing the regional character of the contiguous parts of the host. (3) The induced plate may become fused with the host, and the two may be built up into a composite neural plate. All intermediate stages between alternatives (2) and (3) occur, although at first sight one seems to be rather a contradiction of the other.

In order to obtain an idea of the properties of the individuation field (referred to in the descriptions as I.F.) it will be advisable to discuss some of the specimens which have been described in this and former papers.

Grafts of Head-process and Sinus Rhomboidalis.

None of the grafts of this type described in this paper included the most anterior part of the head process, and in no case did the induced plate develop any of the structures characteristic of the most anterior part of the embryonic axis. In the inductions described in a former communication (WADDINGTON 1933a) the induced neural plate formed a head only when the graft included the most anterior part of the head-process. The tendency of the graft to complete itself, and to induce a complete embryo, appears therefore to be small or absent.

There is little evidence that the I. F. of the host has any effect on the regional character of the structures developed from grafts of this advanced stage. Thus in specimens 17 CD, 8 CD, 20 CD, 19 CD, and 32—214 CD, in which the graft was in the reversed (*ap.*) direction, the embryo developed from the graft is also oriented in the *ap.* direction. In 32—214 DC the longitudinal tissue movements which should have gone on in the graft have perhaps been interfered with by the host.

32—214 DC is a good example of the effect of the host's I.F. on the induced neural plate, which is united with the host neural tube, the whole combination forming a single unified tube. It is difficult not to suppose that the induced plate shares the regional character of the host plate, if indeed they are not to be regarded as one organ. It is to be noted that the graft was made in the *ap.* direction, so that the host I. F. seems to have determined the polarity of the induced plate. In 32—76 DC on the other hand, the orientation of the induced plate (perpendicular to the host plate) was clearly determined by the graft.

Grafts of the Anterior parts of the Streak.

32—133 CD. The greater part of the induced plate is continuous laterally with the host plate, but the most anterior part is separate, and lies at the top of a fold

resembling a head-fold. There is therefore some evidence the induced plate is oriented similarly to the host, although the graft was *ap.* If this is true, the orientation of the induced plate must have been determined by the host I.F. There is no evidence that the host I.F. has affected the differentiation of the graft.

32—135 CD. The induced plate has formed a very perfect head. It lies at some distance from the host axis, and it is probable that the formation of the head was due to the I.F. of the graft rather than to that of the host.

32—171 CD. The graft is almost entirely built into the host's anatomy. It is possible that the fact that the left wall of the host's neural plate is not sharply marked off from the non-neural ectoderm indicates that the graft had induced a neural plate and that this induced plate was also incorporated into the host. The host's I.F., has not only affected the morphological development of the graft, but has probably influenced its histological development, since the graft has not formed the neural tissue which its presumtive fate would lead one to expect.

32—170 DC. Although the graft was oriented *aa.*, the induced plate as a whole is *ap.* The end with the most anterior regional character is the end which is united with the host neural tube. The facts could be explained by the hypothesis that the intensity of the I.F. falls off as the distance from the host axis increases. The induced plate has therefore taken on the regional character of the host plate at their point of junction, and since the graft did not contain any material which was presumptively more anterior in character than this, this point of junction becomes the most anterior part of the induced plate.

32—188 DC. The induced plate lies close against the side of the host plate, and shares its regional character, so that one must suppose that the host I.F. has been of determining importance.

32—190 DC. This case is somewhat similar to 32—170 DC. That part of the induced plate which is joined to the host plate is more anterior in character than the other parts of the induced plate. In this specimen the same thing is true of the graft tissues, which have differentiated into neural plate and somites, but do not include anything characteristic of parts of the embryo anterior to the point of junction. Thus the regional character of the induced plate and of the graft structures appears to have been determined by the host I.F. of the place at which they approach the host axis most nearly. This again shows that the host I.F. is most intense near the host axis, and may also indicate that the gradient of intensity as one moves away from the axis is of the same nature as the qualitative gradient of "anteriorness" as one passes along the axis towards the posterior.

The orientation of the induced plate, perpendicular to the host axis is presumably due to the position which the graft mass had reached during the gastrulation movements of the host.

32—222 DC. The graft was made in the *ap.* direction, but the induced plate has united laterally with the host plate and probably shares its regional character, in which case it must be *aa.* The host I.F. may also have had some effect on the differentiation of the graft, which has developed no neural tissue, but merely mesenchyme; this mesenchyme is not, however, built into the host's anatomy. Suppression by the host I.F. of neural tissue formation by the graft does not seem to occur very often, but in this case the graft came from an embryo which was considerably younger than the host, and this may have made such a suppression possible.

32—217 CC. The host I.F. has had a considerable effect on the induced plate. The graft was made *ap.*, but the induced plate very clearly shares the orientation of the host plate, having a head near the host's head, and being much less highly differentiated in the region of the posterior part of the host's axis. Somites appear under the induced plate at the same level on the anterior-posterior axis as they

do under the host plate. In the middle region the host and induced plates are continuous, and one might almost say the host I.F. has succeeded in buildung the induced plate into the host's anatomy. It is possible that in this region neural tissue derived from the graft also takes part in the formation of the composite plate. If this is so, the host I.F. has clearly had some effect on the differentiation of the graft, but the facts are not certain. On the other hand, the largest piece of neural tissue which is certainly recognisable as graft in origin lies towards the posterior, and therefore suggests that the graft has developed with its original *ap.* orientation.

32—165 DD. The graft was *ap.*, but the induced neural plate appears to be *aa.* since it has a rudimentary head-fold at its anterior end. The host I.F. seems to have had less effect on some of the other structures in the induced embryo, since the foregut, which is continuous with the host endoderm and is an induced structure, is oriented *ap.*, in accordance with the orientation of the graft. The I.F. of the graft must also be responsible for the fact that the induced embryo is more or less symmetrical, although the graft contained only a lateral half of the primitive streak; probably the graft completed itself before it performed the induction.

Grafts of the Middle and Posterior parts of the Streak.

32—126 CD and 32—197 DC. The I.F. of the graft has determined the time of development, which is a function of the regional character, of the induced plates, which lie at some considerable distance from the host axis.

32—221 DC. The graft has been fairly successfully built into the host's anatomy under the influence of the host's I.F. A large number of cases are known in which the graft has entirely disappeared into the body of the host. These are mostly grafts of the middle and posterior parts of the streak, and are probably to be explained as cases in which the host's I.F. has been even more efficaceous than in 32—221 DC: but there is the possibility that in some cases the graft has disintegrated and been absorbed.

32—136 CD. The induced embryo contains a foregut and heart as well as an induced plate. It is a very harmonious structure, with no morphologically abnormal pieces of tissue which can be identified as derived from the graft. That is to say, the I.F. of the graft has built the whole of the induced structures, together with the graft structures, into a single unified embryo. But at the same time, this induced embryo (or, what comes to the same thing, the graft I.F.) was clearly under the influence of the host I.F. since it shares the regional character of the host. The two I.F.s. of the host and of the graft, appear to have coincided to a large extent, but not sufficiently for only a single embryo to have been formed.

32—154 DC. The induced neural plate lies near the head of the host, and appears itself to represent a head. Since the graft did not contain presumptive head material, this is evidence of the action of the host's I.F., which has acted more or less equally on both the induced neural plate and the indueed foregut.

32—43 (described WADDINGTON 1933a). The induced embryo lies at the edge of the area pellucida, and is therefore very little affected by the host I.F. Its orientation is quite accurately *ap.*, and is clearly determined by the I.F. of the graft (but the orientation of the graft was not noted at the time of operation, except that it was either *aa.* or *ap.*). The I.F. of the graft has also caused a strong tendency towards building a complete embryo. Although only the posterior two-thirds of the primitive streak was included in the graft, the induced embryo contains a rudimentary head-fold, a foregut, heart rudiments etc. The induced embryo is fairly harmoniously shaped, so that it is often difficult in some sections to distinguish which is graft material, but it is not so well formed as the induced embryo in specimen 32—136 CD.

518, (described WADDINGTON 1932). The graft, which was a middle third, has formed a strand of mesodermal tissue lying outside of and parallel to the host somites; it has a tendency to be arranged in masses corresponding to the somites.

428 (described WADDINGTON 1932). The graft, a middle third of the primitive streak, has formed a short row of somites lying outside of and parallel to the right row of host somites. The intersomitic grooves of the two rows of somites correspond. This appears to be a very similar phenomenon to the lateral union of an induced plate with the host plate, except that in this case it is the graft tissues which have been affected by the host I.F.

The main facts about the individuation field which can be deduced from this discussion appear to be as follows:

(1) The field is strongest near the embryonic axis and falls off in intensity towards the edge of the *area pellucida*.

(2) The field is regionally differentiated along the longitudinal axis of the embryo.

(3) A more anterior part of the field dominates over a more posterior part. That is, the effect of anterior parts of the field on tissue from the more posterior parts is to cause this tissue to acquire a more anterior regional character. In the Amphibia, posterior parts of the field appear to have no effect on tissue from more anterior parts, and the same thing is probably true, but is not proven, in birds.

It is not yet known how the apparently quantitative gradient mentioned in (1) is related to the apparently qualitative gradient mentioned in (3), although specimens such as 32—170 DC and 32—190 DC may be suggestive in this connection. However, if both gradients are regarded as quantitative gradients of the same substance, it is difficult to account for the lack of effect of posterior parts of the field on tissue from more anterior parts, although it may be possible to cover these facts by a special hypothesis, as for instance that, when two masses of tissue containing different concentrations of the gradient-substance are in contact with one another, the regional character of *both* masses is determined by the mass which possesses the greatest concentration.

If the usefulness of the concept of the individuation field be granted, it still remains to discuss how it obtains its effects. It is probably permissable, at least provisionally, to consider separately the morphogenetic and histogenetic aspects of the field, although possibly these two are ultimately related.

Among the morphogenetic effects we can distinguish a group which are due to the mechanical effects of the host's gastrulation movements. An example would be the shifting of the whole graft mass: in 32—171 CD the graft has moved in towards the mid-line of the blastoderm, and in a lesser degree this movement is very common (cf. the two stages development of 32—136 CD, Figs. 21*a*, 21*b*). Similarly the partial rotation of the graft in 32—170 CD is probably due to the tissue movements of the host. There is also sometimes an influence of the movements of the

host on the tissue movements going on within the graft mass, impeding the longitudinal movements in *ap.* grafts, such as 32—214 DC and 32—165 DD for example. This type of interaction between host and graft is much more striking in the Amphibia, where the gastrulation movements of *ap* grafts are often entirely reversed (SPEMANN 1931, LEHMANN 1931).

An individuation field must be able, not merely to impede the tissue movements within a foreign mass of tissue but actually to induce new types of tissue movement, as is demontrated by cases in which the graft has been built up into the anatomy of the host. An example of the simplest type of case falling under this heading is the formation of the combined neural tube in 32—214 DC: once the host and induced neural plates had come together, it might have been expected *a priori* that the forces, whatever they may be, responsible for forming a neural tube from a neural plate would be able to form a single tube from the combined plate, as indeed they actually have done. In this case, then, it is probable that the host's individuation field is expressed by the workings of a general law governing the conversion of a neural plate into a tube. But in most cases it will not be possible usefully to discuss the morphogenetic action of the individuation field until the mechanics of morphogenesis are better understood.

In considering the histogenetic action of the individuation field one must, as has been shown above, admit that the field can exert an influence on the regional differentiation of mesoderm, which is particularly evident in those cases in which the graft has been incorporated into the host. It is also clear that an individuation field may have a direct effect on the differentiation of neural tissue, since the regional character of an induced plate may be partly determined by the individuation field of the graft (32—43, and induction of a head in the posterior region of the host in Triton). The individuation field of the host may either influence the induced plate in a direct manner, or it may act through the intermediacy of a regional differentiation of the competence (Reaktionsfähigkeit) of the ectoderm, as SPEMANN suggested. In fact, if this regional structure of the competence of the host ectoderm only persists while the ectoderm is in contact with the host's organisation centre, it becomes merely another way of expressing what has been called above a direct influence of the host's individuation field on the induced plate. But it may be that, although the regional structure arises in dependance on the organisation centre, it is capable of persisting even when its connection with the centre has been severed. Finally, it is also possible to imagine that a regional structure might arise quite independently of the host's organisation centre, in which case it would not be an aspect of the individuation field at all, but something quite different. It is clear, however, that, even if such an independant regional structure can arise, it is

in the normal course of events dominated by the regional determination due to the host's individuation field.

HALL, in a short note published in the last number of this journal, states that if the presumptive head mesoderm is removed from a young *Triton* gastrula, and presumptive trunk mesoderm substituted for it, no head develops in the operated embryo, the anterior part of the neural plate having a trunk- or even tail-like character. This result clearly shows that any possible regional structure of the competence of the gastrula ectoderm arises in dependance on the organisation centre, and, at least in the young gastrula stage, is not sufficiently fixed to persist after the determining region of the organisation centre is removed.

If the most anterior part of the neural plate consists of a *backwardly-directed* tail, as seems to be the case, the whole configuration would be rather similar to that of 32—170 DC, if the host's head were removed from the latter: as in that specimen, there seems to have been a development of an *ap.* organ from an *aa.* graft of a more posterior region of the embryonic axis.

Summary.

1) By means of the technique of *in vitro* cultivation of the entire blastoderm, parts of duck and chick primitive streaks have been transplanted heteroplastically into the *area pellucida* of the other species.

2) The grafted tissue differentiates into part of an embryonic axis, including neural plate, notochord, somites, etc.

3) An induced embryonic axis is frequently formed from the host tissues in contact with the graft. This axis may include neural plate foregut, and probably mesodermal structures, but the origin of the latter, whether from the host or from the graft, cannot usually be determined with certainty.

4) Heteroplastic induction of this kind can be performed by parts of the primitive streak which do not include HENSEN's node. The inductive capacity is retained by the head-process and the sinus rhomboidalis; the few heteroplastic grafts of neural tissue which have been made have not as yet yielded any inductions.

5) Even if the grafted tissue gives rise to a large quantity of neural tissue, it may succeed in inducing the formation of a neural plate by the overlying host ectoderm, so that in the combined graft and induced structures there is an excess of neural tissue over mesoderm. This fact makes it impossible to regard the induction of neural plate as an expression of a tendency of the organisation centre to form a whole.

6) On the other hand, there is a tendency for a part of an organisation centre to rearrange its regional structure, and that of any tissue lying near it, so as to form a regionally complete embryo. This "individualising" action is exerted by the host's organisation centre on the tissue lying near it, including any graft or induced tissue which may be in the neighbourhood, and this tissue may then become incorporated into the body of the host. But unless the graft lies very near the host axis, it usually succeeds in retaining its independance, and in this case the graft also influences the regional character of the induced tissues, which thus develop under the combined influences of the graft and host individuation fields.

7) Specimens are described in which the regional character of the induced structures appears to be determined chiefly by the graft, e. g. 332—135 CD, 32—43, or by the graft and thehost working together, e. g. 32—136 CD, or chiefly by the host, e. g. 2—217 CC.

8) The individualising action can be imagined as taking place in two phases, first the impressing on the tissue of the appropriate regional character, and secondly the building of the tissue into the host embryo. The second process is often very incompletely realised, so that, for example, an induced neural plate lying near the head of the host embryo may be modified into a head by the host's individuation field, but may not be incorporated into the host embryo.

Zusammenfassung.

1. Unter Anwendung der *in vitro*-Züchtung des gesamten Blastoderms wurden Teile von Enten- und Hühnerprimitivstreifen heteroplastisch in die *Area pellucida* der andern Art verpflanzt.

2. Das übertragene Gewebe differenziert zu einem Teil einer Embryonalachse, einschließlich Neuralplatte, Chorda, Somiten usw.

3. Häufig wurde von dem das Implantat berührenden Wirtsgewebe eine induzierte Embryonalachse gebildet. Eine solche Achse kann Neuralplatte, Vorderarm und wahrscheinlich auch mesodermale Strukturen enthalten; es kann aber gewöhnlich nicht mit Sicherheit entschieden werden, ob die Mesodermteile vom Wirtsgewebe oder vom Implantat ihren Ausgang nehmen.

4. Teile des Primitivstreifens können solche heteroplastische Induktionen veranlassen, gleichgültig ob sie den HENSENschen Knoten enthalten oder nicht. Die Induktionspotenz bleibt bis zur Ausbildung des Kopffortsatzes und Sinus rhomboidalis erhalten. Nur vereinzelte heteroplastische Transplantationen von Neuralgewebe wurden bis jetzt ausgeführt; sie haben keinerlei Induktion veranlaßt.

5. Auch wenn das Implantat eine große Menge von Neuralgewebe liefert, kann es zuweilen die Bildung einer Neuralplatte durch das darüberliegende Wirtsektoderm induzieren, so daß dann in den gesamten Implantat- und Wirtsstrukturen das Neuralgewebe das Mesoderm überwiegt. Deshalb ist es unmöglich, die Induktion der Neuralplatte als Ausdruck einer Ganzheitsgerichtetheit des Organisationszentrums zu deuten.

6. Andererseits besteht für einen Teil eines Organisationszentrums die Tendenz, seine regionale Struktur und die der nahe liegenden Gewebe umzubauen, wie um einen vollständigen Embryo zu bilden. Dieser ganzheitsformende Einfluß wird vom Wirtsorganisationszentrum auf jedes in der Nähe liegende Gewebe ausgeübt. Handelt es sich um überschüssiges implantiertes oder induziertes Gewebe, so kann es wohl auf diese Weise in den Wirtskörper eingebaut werden. Doch behauptet das Implantat gewöhnlich erfolgreich seine Individualität (außer wenn es sehr nahe der Wirtsachse liegt) und beeinflußt dann den regionalen Charakter des induzierten Gewebes, das sich infolgedessen unter dem Zusammenwirken von Implantat- und Wirts-„Ganzheitsfeldern" entwickelt.

7. Es werden Beispiele beschrieben, in denen die regionale Struktur des induzierten Gewebes hauptsächlich durch das Implantat bestimmt und das Implantat sehr wenig durch den Wirt beeinflußt erscheint, z. B. 32—135 CD, 32—43; andere, wo Implantat und Wirt zusammengewirkt haben, z. B. 32—136 CD; weitere, wo der Wirt einen großen Einfluß auf den regionalen Charakter der induzierten Neuralplatte (z. B. 32—217 CC) oder des Implantats (z. B. 32—171 CD) ausgeübt hat.

8. Den ganzheitsbildenden Einfluß kann man sich in zwei Phasen wirkend vorstellen. Zuerst wird dem Gewebe der nötige regionale Charakter mitgeteilt, dann wird das Gewebe in den Embryo eingebaut. Der zweite Vorgang ist oft nur unvollständig verwirklicht, so daß z. B. eine induzierte Neuralplatte nahe dem Kopf des Wirtsembryos durch das Ganzheitsfeld des Wirtes zwar in einen Kopf verwandelt, aber dem Wirtsembryo nicht einverleibt wird.

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