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COMMUNICATIONS

EXPERIMENTAL STUDY OF HISTOGENESIS OF
EYE ABNORMALITIES IN THE CHICK EMBRYO

BY

S. OCHI, M.D.

ASSISTANT PROFESSOR OF OPHTHALMOLOGY, DEPARTMENT OF MEDICINE,
IMPERIAL UNIVERSITY OF KYUSHU, JAPAN

THE eyes of all embryos are at the beginning of their development very large in comparison with the other organs of the body. No matter to what cause it may be due, this disproportionate growth seems to make the eye especially subject to malformations. I have recently obtained some eye abnormalities from experiments on chick embryos, and these I wish to record very briefly in this paper.

By eye abnormalities I mean here chiefly anophthalmia and microphthalmia. In regard to cyclopia I did not obtain a single perfect specimen in all my experiments with chick embryos, although Stockard¹ claims to have obtained a few typical cyclopean monsters. He found, however, that in most instances cyclopia did not develop. On the other hand, in the fish there have been many successful experiments in producing cyclopia since those of Stockard. It may

be possible that cyclopia is more easily produced in the fish than in the bird.

In a wide review of literature Weber² presents two theories regarding the production of monsters: (I) the amniotic theory, i.e., mechanical theory; (II) the chemical theory. He supports the latter with many interesting experiments.

Hess³ concluded, on the basis of his studies on several kinds of embryos, that inflammation processes do not play the chief rôle in causation of abnormalities of the eye, as was formerly thought to be the case, though even now some authors take the view that it does.

Bach⁴ announces an hypothesis, that microphthalmia, as well as many other abnormalities, is to be explained from a primary, abnormal character and size of the lens.

There are many other papers dealing with abnormalities of the eye, but they need not be summarized here.

Numerous methods of producing abnormalities have been tried in my experiments with chick eggs, but I describe here only 52 of the cases, which were obtained by 4 methods:

(1) Salt solution (0.85 per cent.) injected into the albumen near the blastoderm.

(2) Distilled water "

(3) Air "

(4) The albumen near the blastoderm is very slightly stirred with a needle.

As the first manipulation we disinfect each egg with alcohol or tincture of iodine at a place on the upper surface somewhat nearer the small than the large end of the shell. Here we make a small hole in the shell, and then keeping the eggs in the same position we inject some material with a sterilized syringe in the albumen or stir this near the blastoderm, because the blastoderm lies always on the upper surface of the yolk.

After these manipulations we close the hole in the shell with a piece of disinfected paper and paraffin, and then put the eggs away in the incubator, keeping always the same side up. Some time afterwards we break the shell carefully and examine the embryo in detail with the help of a lens or binocular microscope. Then, if we find an abnormally developing embryo, we fix it, imbed it in paraffin and cut it into serial sections. We diagnosed "anophthalmia," when there was no eye at all or a trace of an eye. As controls 54 eggs were used, but no abnormalities were found.

I. Sterile salt solution (0.85 per cent.) was injected into the albumen near the blastoderm.* In all 190 eggs were treated in this

*34 injected with 0.75 cc. solution; 124 with 1.0 cc. solution; 22 with 1.5 cc. solution; and 10 with 2.0 cc. solution.

way. After 3—8 days the shell was broken and the embryo was examined. The results were as follow :

Injected quantity.	0.75 cc.		1.0 cc.		1.5 cc.		2.0 cc.	
	Eggs.	Per cent.	Eggs.	Per cent.	Eggs.	Per cent.	Eggs.	Per cent.
Developed abnormally	2	5.88	31	25.0	1	4.55	2	20.0
Developed normally	5	14.7	25	20.16	3	13.64	1	10.0
Failed to develop or found dead	27	79.41	68	54.84	18	81.81	7	70.0

We obtained 36 abnormal embryos in all, or 18.95 per cent. We find the following abnormalities, when classified in detail.

Microphthalmia 18 $\left\{ \begin{array}{l} 10 \dots \text{one side} \\ 8 \dots \text{both sides} \end{array} \right.$

Anophthalmia 11 $\left\{ \begin{array}{l} 8 \dots \text{both sides} \\ 3 \dots \text{one side} \end{array} \right.$

Acephalous 6

Anomalia cerebri 18

The individual cases are as follows :

1. Embryo of five days; anomalia cerebri; microphthalmia (both sides). 1.0 cc. injected. The brain seems folded and covers the eyes. The prosencephalon is not closed dorsally. The eyes on both sides are somewhat smaller than normal, but their structure is not so far from the normal.

2. Embryo of six days; anomalia cerebri; microphthalmia (one side). 1.0 cc. injected. In the brain there are many dilated blood-vessels, especially on the left side, so that the brain-tissue of this side is pressed somewhat towards the right and therefore the right eyeball is smaller than the other, which seems normal.

3. Embryo of seven days; anophthalmia (one side). 1.0 cc. injected. On the right side there is no trace of the eye, while the other eye is normal.

4. Embryo of six days; anomalia cerebri; microphthalmia (both sides). 1.0 cc. injected. The eyes on both sides are smaller than normal, nothing else notable.

5. Embryo of six days; microphthalmia (one side). 1.0 cc. injected. One eye is smaller than normal and it has a luxatio lentis.

6. Embryo of seven days; anomalia cerebri; anophthalmia (one

side). 1.0 cc. injected. The head is very much deformed, and while one eye is almost normal in size the other is represented only by an accumulation of pigment cells (Figs. 1 and 2).

FIG. 1.

FIG. 2.

- 1.—Anophthalmia
(Trace of an eye.)
- 2.—Normal eye.

7. Embryo of seven days; anomalia cerebri. 1.0 cc. injected. The brain has many abnormal folds on its surface and the pro-sencephalon is not closed. The eyes are situated nearer each other than normal, but they seem to be of normal size.

8. Embryo of eight days; acephalous. 0.75 cc. injected. The heart is actively beating, but there is no development of the head or extremities. Even the notochord cannot be found.

9. Embryo of six days; microphthalmia (both sides). 1.0 cc. injected. The eyes on the both sides are a little smaller than normal and their lenses are dislocated.

10. Embryo of five days; anomalia cerebri; microphthalmia (both sides). 1.0 cc. injected. The head is somewhat flattened dorsally. One eye is much smaller and the other a bit smaller than normal.

11. Embryo of six days; anomalia cerebri; anophthalmia (one side); microphthalmia (one side). 1.0 cc. injected. The surface of the brain is irregularly folded. On the one side there is a trace of the eye, which exists only as a linear colony of pigment cells. On the other we find a smaller eye which consists of an imperfect optic cup and a lens.

12. Embryo of seven days; microphthalmia (one side). 1.0 cc. injected. One eye is smaller than the other, which seems to be of the normal size. Nothing else is notable.

13. Embryo of six days; anomalia cerebri; microphthalmia (both sides). 2.0 cc. injected. In the brain we see an enormous development of blood-vessels, especially on the left side. Therefore the brain looks deformed and the eyes are compressed and a little smaller than normal.

14. Embryo of five days; anomalia cerebri; anophthalmia (both sides). 1.0 cc. injected. The embryo being amorphous we cannot differentiate sharply the headpart from the rest, but in the serial sections we find on one side a colony of pigment cells, which, perhaps, may be a trace of an eye.

15. Embryo of five days; acephalous. 1.0 cc. injected. The neural tube and the notochord are developed imperfectly, and the head is not yet differentiated, therefore no eye is to be found.

16. Embryo of five days; microphthalmia (one side). 1.0 cc. injected. One eye is smaller than normal; nothing else notable.

17. Embryo of five days; microphthalmia (one side). 1.0 cc. injected. Just the same as No. 16.

18. Embryo of four days; microphthalmia (one side). 1.0 cc. injected. One eye is smaller than the normal size; nothing else notable.

19. Embryo of four days; anomalia cerebri; microphthalmia (both sides). 1.0 cc. injected. The head is sagittally flattened and the prosencephalon is not yet closed, so that both eyes are dislocated towards the front of the brain and approach each other. They are smaller than normal.

20. Embryo of four days; anomalia cerebri; anophthalmia (both sides). 1.0 cc. injected. The brain is abnormal, the prosencephalon is not yet closed and no trace of an eye is to be found.

21. Embryo of four days; acephalous. 1.0 cc. injected. The differentiation of the head was interrupted, so that there is not even a trace of an eye.

22. Embryo of six days; anomalia cerebri; anophthalmia (both sides). 1.0 cc. injected. The head is abnormally developed; the prosencephalon is not closed and no trace of an eye is to be found.

23. Embryo of five days; acephalous. 1.0 cc. injected. The differentiation of the neural tube is very irregular and there is no development of the head.

24. Embryo of six days; anomalia cerebri; anophthalmia (both sides). 1.0 cc. injected. The differentiation of the brain is abnormal and there is no trace of an eye, but the heart is nevertheless very large.

25. Embryo of six days; microphthalmia (both sides). 1.0 cc. injected. Both eyes are somewhat smaller than normal; nothing else notable.

26. Embryo of six days; anomalia cerebri. 1.0 cc. injected. In the brain there are greatly dilated blood-vessels, so that some brain tissues are compressed by them, but the eyes seem to keep the normal size.

27. Embryo of six days; anomalia cerebri; anophthalmia (both sides). 1.0 cc. injected. The head is sagittally flattened and the prosencephalon is not closed. On the one side some blood-vessels of the brain are dilated. One eye develops only as a small colony of pigment cells, while the other fails entirely.

28. Embryo of six days; anomalia cerebri; anophthalmia (both sides). 1.0 cc. injected. The differentiation of the brain is imperfect and there is no trace of an eye to be found.

29. Embryo of six days; microphthalmia (one side). 1.0 cc. injected. One eye is a bit smaller than normal; nothing else notable.

30. Embryo of four days; acephalous. 1.0 cc. injected. The development of the neural tube is imperfect and the differentiation of the head portion almost totally lacking, so that there is no trace of an eye to be found.

31. Embryo of six days; anomalia cerebri; anophthalmia (both sides). 1.5 cc. injected. The head is deformed and the prosencephalon is not closed. There is no trace of an eye.

32. Embryo of five days; acephalous. 0.75 cc. injected. The neural tube developed imperfectly and the head part not sharply differentiated from the other parts, so that no trace of an eye is to be found, but the heart is very large.

33. Embryo of four days; anomalia cerebri; anophthalmia (both sides). 1.0 cc. injected. The head is sagittally flattened and the prosencephalon is not closed. The eyes on both sides show themselves only as a vestige consisting of pigment cells.

34. Embryo of four days; microphthalmia (one side). 2.0 cc.

injected. One eye is smaller than normal; nothing else notable.

35. Embryo of three days; anomalia cerebri; microphthalmia (both sides). 1.0 cc. injected. Development of the brain is imperfect and its prosencephalon is not closed. The eyes on both sides are smaller than normal.

36. Embryo of three days; microphthalmia (one side). 1.0 cc. injected. One eye is a bit smaller than normal; nothing else notable.

II. Distilled water was injected into the albumen near the blastoderm. In all, 24 eggs were treated in this way. After four to seven days the shell was broken and the embryo examined. The results were as follow:

Injected quantity.	0.5 cc.		0.75 cc.		1.5 cc.	
	Eggs.	Per cent.	Eggs.	Per cent.	Eggs.	Per cent.
Developed abnormally ...	3	25.0	1	16.67	1	16.67
Developed normally...	1	8.33	0	—	0	—
Failed to develop or found dead ...	8	66.67	5	83.33	5	83.33

We obtained five abnormal embryos in all, or 20.83 per cent., and we can find on them the following abnormalities.

Microphthalmia 2 $\begin{cases} 1.....\text{one side} \\ 1.....\text{both sides} \end{cases}$

Anophthalmia 3 $\begin{cases} 1.....\text{one side} \\ 2.....\text{both sides} \end{cases}$

Acephalous 1

Anomalia cerebri 3

The individual cases are as follow:

37. Embryo of five days; acephalous. 0.7 cc. injected. The neural tube and notochord are poorly developed, and no part of the head can be identified, nor can any trace of an eye be found. The heart is well developed.

38. Embryo of seven days; microphthalmia (both sides). 0.5 cc. injected. One eye is especially small, and its lens is lying on the outside of the optic cup. The other eye is also a bit smaller than normal.

39. Embryo of four days; anomalia cerebri; anophthalmia (both sides). 1.5 cc. injected. The heart is dislocated over the

head and actively beating. The head is deformed and there is no trace of an eye.

40. Embryo of four days; anomalia cerebri; anophthalmia (both sides). 0.5 cc. injected. The neural tube and notochord are developed, but the differentiation of the head part is exceedingly imperfect, and there is no trace of an eye.

41. Embryo of six days; anomalia cerebri; anophthalmia (one side); microphthalmia (one side). 0.5 cc. injected. The head is deformed and the prosencephalon not closed. One eye is smaller than normal, while the other is lacking altogether.

III. Air was injected into the albumen near the blastoderm. In all 30 eggs were treated in this way. After four or five days the shell was broken and the embryo examined. The results were as follow:

Injected quantity.	1.0 cc.	
	Eggs.	Per cent.
Developed abnormally	5	16.67
Developed normally	2	6.67
Failed to develop or found dead	23	76.67

We obtained five abnormal embryos in all, or 16.75 per cent., and we can find on them the following abnormalities:

Microphthalmia	3	1.....one side
		2.....both sides
Acephalous	2	
Anomalia cerebri	1	

The individual cases are as follow:

42. Embryo of five days; acephalous. 1.0 cc. injected. There is no differentiation of the head beyond the stage of the medullary plate. In the area vasculosa we see here and there several aneurysm-like bodies beating. No trace of the eye is to be found in the serial sections.

43. Embryo of four days; microphthalmia (both sides). 1.0 cc. injected. The eyes on both sides are a little smaller than normal; nothing else notable.

44. Embryo of four days; acephalous. 1.0 cc. injected. There is an irregular development of the ectoderm and no differentiation of the head part.

45. Embryo of four days; microphthalmia (one side). 1.0 cc. injected. One eye is a bit smaller than normal; nothing else notable.

46. Embryo of four days; anomalia cerebri; microphthalmia (both sides). 1.0 cc. injected. The prosencephalon is not closed. The eyes on both sides are smaller than normal.

IV. Albumen near the blastoderm was stirred gently with a sterile needle. In all forty-eight eggs were treated in this way. After three to six days the shell was broken and the embryo examined. The results were as follows :

	Eggs.	Per cent.
Developed abnormally	6	12.5
Developed normally	7	14.58
Failed to develop or found dead...	35	72.92

We obtained six abnormal embryos in all, or 12.5 per cent., and we can find in them the following abnormalities.

Microphthalmia 3 $\left\{ \begin{array}{l} 2.....one\ side \\ 1.....both\ sides \end{array} \right.$

Anophthalmia 4 $\left\{ \begin{array}{l} 2.....one\ side \\ 2.....both\ sides \end{array} \right.$

Anomalia cerebri 4

The individual cases are as follows :

47. Embryo of six days ; anomalia cerebri ; microphthalmia (both sides). The head is deformed, and the prosencephalon is not closed. The eyes on both sides are very small and their lenses are not developed (Figs. 3 and 4).

FIG. 3.

48. Embryo of six days; anophthalmia (one side); microphthalmia (one side). Only one eye is developed, which is smaller than normal. No trace of the other eye is to be found.

49. Embryo of six days ; anomalia cerebri ; anophthalmia (both sides). The embryo was oval in shape. The differentiation of the head was exceedingly imperfect, and there was no trace of the eye.

50. Embryo of three days; microphthalmia (one side). One eye is smaller than normal; nothing else notable.

51. Embryo of four days; anomalia cerebri; anophthalmia (one side); microphthalmia (one side). The cavity of the brain is greatly enlarged. Only one eye is developed, which is smaller than normal. No trace of the other eye is to be found.

FIG. 4.
1.—Microphthalmia.

52. Embryo of three days; anomalia cerebri; anophthalmia (both sides). The differentiation of the brain is imperfect, and there is no trace of the eye to be found.

The abnormalities (52 chick embryos of three to eight days) may be summarized as follows :

Microphthalmia	...	...	...	...	27
One side	...	...	...	15	
Both sides	...	...	...	12	
Anophthalmia	...	...	...	...	18
One side	...	...	...	6	
Both sides	...	...	...	12	
One side microphthalmia and the other anophthalmia	...	...	...	...	4
Acephalous	...	...	...	...	9
Anomalia cerebri	...	...	...	...	27
(Anomalia cerebri without anomalia bulbi oculi, 2)					
Microphthalmia with anomalia cerebri (44·4 per cent. of all cases of microphthalmia)	...	...	...	...	12
Anophthalmia with anomalia cerebri (83·3 per cent. of all cases of anophthalmia)	...	...	...	...	15

That is to say, anophthalmia accompanies deformities of the brain oftener than microphthalmia. In short, anophthalmia and microphthalmia are due to the same cause, and anophthalmia is a more advanced stage of the deformity than microphthalmia.

In four cases (No. 2, 13, 26, and 27) we see great dilatation of blood-vessels in the brain. This phenomenon is, of course, a result of our manipulation of the eggs and it is accompanied by some deformity of the brain. Moreover, two of these cases have abnormalities of the eye (the one has microphthalmia and the other anophthalmia); but we cannot conclude from this dilatation of blood-vessels that all abnormalities of the eye are due to inflammatory processes of eye itself or of the tissues surrounding it, because in most of the cases there was no dilatation of blood-vessels in the brain.

By many authors various kinds of chemical substances have been used in their experiments on the origin of monsters. The present experiments on chick embryos demonstrate, however, that besides chemical substances we must recognize certain physical factors (stirring of the albumen or change of the pressure in the eggs, etc.) as causes of abnormal development of embryos. From these observations I draw the following conclusion:

At the beginning of the developing of the embryo, any factor, either chemical or physical, which can disturb the normal condition of the blastoderm itself or its circumference, may bring about an abnormal differentiation of the embryo. If such disturbance of the normal condition is too great, development of the embryo may be entirely arrested. But if development is still possible, some deformity of the embryo may result, especially terata of the head and abnormalities of the eye varying according to the degree of the disturbance.

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THE NOTATION OF AXES OF CYLINDERS

Systems in Vogue in the British Isles with Recommendation

BY

J. GRAY CLEGG,

MANCHESTER

It appears to me that now a suitable opportunity is presented of investigating the systems of designating the axes of cylinders at