

A Contribution to the Physiology of the Pineal Body.

By

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The problem concerning the function of the pineal body is not yet definitively decided. The importance of the pineal body in man is, however, clear from the fact that its tumor is often attended by pineal disorder, namely premature development of primary and secondary sexual characters.

A Historical Review of Experimental Results.

Howell was the first who tried the intravenous injection of pineal extract. He records that its effect upon the blood pressure is inconstant. Von Cyon states as a consequence of the intravenous injection of pineal extract and of electrical stimulations that the pineal body plays a role in preserving certain inorganic substances as organic compounds, moreover it regulates the flow of cerebrospinal fluid in the third ventricle.

In 1909 Dixon and Halliburton examined the effect of the pineal extract but their results were negative so far as the blood pressure, heart rate, respiration, the volume of the intestine and kidney and urine secretions are concerned.

Jordan and Eyster observed transitory diuresis and glycosuria after the injection of the pineal extract. Otto and Scott report similar results.

Horrax states that the intravenous injections of the pineal extract

would cause a constant but slight fall in blood pressure.

According to Dana and Berkley, as well as Mc. Cord, a prolonged administration of the pineal drug brings on a relatively rapid growth of the animals subjected to the experiments.

Although no serious effects were observed in the animals subjected to the administration of the pineal drug, the extirpation of the pineal body caused striking results.

Biedl and Dandy subjected dogs, and Exner and Boesse rabbits to pinealectomy, but they obtained no affirmative results.

On the other hand Sarteschi succeeded in getting positive results after pinealectomy. In 1913 he recorded that guinea-pigs and puppies subjected to the operation revealed an increase in body weight and in the size of the testes, but no change in the other endocrine glands. In papers by Foà we find that pinealectomized cocks showed a hastened maturity and crowed earlier than controls. Besides he observed a marked hypertrophy of the comb and testes in the cocks that were operated on, there was no change in the case of hens. The fact that pinealectomized rats showed an increase in weight of the testes was also recorded by him. These observations were on the whole affirmed by Zoia.

Recently Horrax has obtained remarkable results after pinealectomy in many guinea-pigs and rats. His conclusions are as follows:

“Pinealectomized male guinea-pigs showed a hastened development of the sexual organs, manifested before maturity by a relative increase in size and weight, both of testes and seminal vesicles, over control pigs of the same litter. Histologically the testes and seminal vesicles of these animals, if taken before the age of sexual maturity, showed a more advanced physiological state than controls.

Pinealectomized females appear to show a tendency to breed earlier than controls of the same age and weight.”

Therefore appears to be quite certain that in pinealectomized young males the body weight and the size of the testes (in the case of cocks, the combs, and in the case of guinea-pigs, the seminal vesicles also) grow

much more rapidly than in control animals. On the contrary no considerable change has been reported as yet in the case of females.

In order to ascertain the function of the pineal body, both in young males and young females, I have undertaken the extirpation of the pineal bodies in many chickens, males as well as females.

In all, I performed the operation of pinealectomy on thirty-six chickens ranging from 4 to 5 weeks of age. Besides these chickens eleven others of the same age and weight as those operated on were used for comparison.

Method of Operation.

The operation was conducted after taking careful aseptic precautions, so that no infectious suppuration should occur. Without using any anæsthetic, the animal was wrapped with steril gauze, and after shaving and making an application of iodine tincture, the skin on the posterior end of the skull was cut along the median line. Then the bone was so far removed as to allow the exposure of the posterior portion of the superior longitudinal sinus, where two lateral sinuses join. After a transverse section of this portion of the sinus had been made by means of small scissors, without ligating it, the under stump of the sinus wall was drawn out, which manipulation permitted an exposure being made of the pineal body.

This was grasped firmly with a small pair of forceps and gently pulled out, sufficient caution being taken so as not to snap it in two but to remove it whole.

After the extraction of the organ, which was accompanied by a somewhat serious hæmorrhage from the sinus, the wound was closed by suture of the skin. In the control animals also, the skull was opened in like manner, but the wound was immediately closed without opening up the dura mater.

Observations after the Operations.

Most of the pinealectomized chickens died shortly after the operation owing to intracranial haemorrhage. Only 4 (3 males and one female) survived the operation for any length of time. These were fed under the same conditions as the control animals and the effects observed.

Compared with the control chickens the pinealectomized animals showed a retarded growth for a few weeks following the operation, but about a month later they began to grow more rapidly than the controls (with the exception of one male chicken in which the pineal body had not been entirely removed, as was revealed by the autopsy that was made later) their body weight becoming greater and their hind legs longer than in the case of the controls (figg. 1 and 2). In the two males whose pineal bodies were completely removed, the rapid development of the comb and the premature crow deserve special attention and they gave evidence of sexual instinct from 31—50 days before their controls. (See Table I)

Autoptic Findings and Histological Examinations.

Among the animals that survived the pineal body was completely removed in three chickens, two males and a female, as the autopsy testified.

One of the males lived 182 days, the second 220 days, and the third 130 days after the operation, whereupon all each of them were killed, together with the controls. After weighing or measuring, the endocrine organs were fixed with formalin and sections of them stained with eosin-haematoxylin.

As seen in Table I, the development of the sexual organs (testes, ovary, and fallopian tube) was most remarkable, as compared with the controls (figg. 3—5). In the long fallopian tube the voluminous ampullary part was sharply contrasted with the slender upper portion, while

Table I.

		Case 1 (♂)		Case 2 (♂)		Case 3 (♀)	
		Pineal-ectomized chicken	Control	Pineal-ectomized chicken	Control	Pineal-ectomized chicken	Control
Age of animal on the day of operation in days		28	28	31	31	35	35
On the day of killing the animal	Age in days	210	210	251	251	165	165
	Body weight in G.	1820	1200	1950	1600	1400	1050
	Weight of testes in G.	14.3	1.49	18.0	7.0		
	Relative weight of testes in G. to a Kg. of body weight	7.85	1.24	9.7	4.3		
	Weight of ovary in G.					1.12	0.5
	Length of fallopian tube in Cm.					16.0	9.0
	Weight of comb in G.	5.0	0.7	16.0	2.5		
	Weight of hypophysis in G.	0.012	0.015	0.012	0.013	0.01	0.0085
	Its relative weight in G. to a Kg. of body weight	0.006	0.0125	0.0061	0.0081	0.0071	0.0080
	Weight of parathyroidea in G.	0.0078	0.007	0.009	0.011	0.02	0.015
	Its relative weight in G. to a Kg. of body weight	0.0042	0.0058	0.0046	0.0058	0.0142	0.0141
	Weight of thyroidea in G.	0.09	0.065	0.1	0.085	0.12	0.05
	Its relative weight in G. to a Kg. of body weight	0.049	0.054	0.051	0.053	0.085	0.047
	Weight of suprarenal capsule in G.	0.16	0.182	0.15	0.135	0.135	0.085
	Its relative weight in G. to a Kg. of body weight	0.081	0.151	0.077	0.084	0.096	0.081
	Weight of thymus in G.	2.75	1.7	3.1	2.7	1.85	1.9
	Its relative weight in G. to a Kg. of body weight	1.51	1.41	1.58	1.7	1.32	1.9
	Weight of pancreas in G.	3.1	3.25	4.0	3.8	2.8	2.82
	Its relative weight in G. to a Kg. of body weight	1.7	2.7	2.0	2.3	2.0	2.08
	Weight of bursa fabricii	2.1	2.0	1.8	1.9	1.5	1.7
Length of left femur in Cm.	10	9	11	9	8	8	
Length of left tibiotarsus in Cm.	13	10.5	14	11	9.0	8.5	
Length of left tarsometatarsus in Cm.	11	9	12	10	8.5	7.9	
Age of animal on the day when it crowed the first time in days		185	*	205	240		

* It did not crow until sacrificed.

the same tube in the control is not only short but uniformly slender through its whole length (fig. 5).

Microscopically the seminiferous tubules were markedly dilated and contained several layers of epithelium cells showing all stages of spermatogenesis (fig. 6 A). On the other hand those of the controls remained small and were almost filled with a few layers of not yet differentiated epithelium cells (fig. 6 B).

With regard to the interstitial cells of the testes, they seemed somewhat increased in number in the pinealectomized animals.

In the ovarian section of the animal subjected to the experiment well developed follicles measuring more than $390\ \mu$ were often met with, some of them projecting over the surface of the ovary, while the same organ of the control contained no such follicle, the largest being less than $100\ \mu$ (compare fig. 5).

As to the other endocrine organs, it may be said that the difference between the pinealectomized and control animals was not as great as it was in the case of the sex organs. Some of them showed no difference at all, while others showed only a slight difference.

The pituitary bodies of the pinealectomized chickens retained quite normal conditions so far as their weight, size and structure were concerned, with the exception of case 1, where the animal subjected to the experiment seemed to contain more numerous eosinophil cells in the anterior lobe of the organ, than in the control animals.

On the other hand the thyroidea of the pinealectomized chickens were generally a little heavier than those of the controls. Histologically the vesicles were lined with cubical or columnar epithelium cells and were distended and contained much colloid substance, while those of the controls were lined with flattened cells and retained small.

With regard to the suprarenal capsule, in which the medullary and cortical elements were intermixed and formed columnal groups of cells, there was no clear distinction to be observed between the pinealectomized and the control animals, although the former seemed to possess

slightly enlarged cell columns. Other endocrine organs, such as the parathyroidea, thymus, and pancreas, revealed no peculiar condition either macroscopically or microscopically, in the animals upon which the experiments were made. The same thing can be said regarding the bursa fabricii.

Discussion.

With respect to the male chickens my results coincide with those of Foà and Zoia exactly, but concerning the female chickens the two authors state no change is to be observed as a result of pinealectomy, and Sarteschi reports that the pinealectomized female animals dislike to copulate. On the contrary Horrax says in regard to guinea-pigs:

“Pinealectomized female appear to show a tendency to breed earlier than controls of the same age and weight.”

Under these circumstances I lay stress on the finding in the case of the pinealectomized female chicken premature development of the sexual organs. Although the case is only a single one, the finding is so remarkable (see fig. 5), that there remains no doubt of the fact that the pineal body acts as an inhibitory organ upon the sexual apparatus in young female animals as well as in the males.

Concerning the tumor of the human pineal body there are about 90 cases reported, so far as I know, but only 29 of them are cases occurring before puberty, and again only 14 of these cases showed the pineal disorder, (Oestreich-Slawyk, Frankl-Hochwart, Ógle, Nagayo, Hijmans, Boehm, Gutzeit, Odermatt, Raymond-Claude, Beiley-Jelliffe, Horrax, Goldzieher, Takeya, Holzhauser), the others revealing no symptom of sexual prematurity (Schearer, Williamson, Rydinger, Load, Marburg, Weigert, Falkson, Coats, Gauderer, Zenner, Hoesslin, Laurence, Newmann, Pappenheimer, Garrod, Gieble).

The existence of these negative cases, however, does not prove the uninhibitory function of the pineal body in sexual development, for the

pineal disorder would appear only when the other endocrine organs could not make compensation for the loss of the pineal body.

In this connection it is interesting to refer a case of hyperpinealism which Prof. Kōsaka* kindly permits me to quote.

It concerns a man aged $21\frac{1}{3}$ years, who died of tubercle of lungs and ribs. In spite of his age he seemed like a boy of only about 13 years.

There were no pubic hairs, the penis remained very small, the testes being only 1.5 Cm. in length, 1.0 Cm. in breadth and 0.9 Cm. in thickness.

The development of the bones was very much retarded, so that a part of the skull still retained a membranous state. As regards the pituitary body, thyroid gland, parathyroidea, suprarenal capsule and pancreas, nothing particular was observed, only the pineal body showing a relatively strong development, its transversal diameter being 9 Mm. and sagittal length 8 Mm. Histologically it had a structure resembling that of a baby's pineal body, the poorly cellulated lymphsinus-like portion remaining remarkably, and the trabecule of the connective tissue scanty. This case indeed affords another proof of the above mentioned statement concerning the function of the pineal body. Nevertheless it appears somewhat strange that the above quoted 12 positive cases, and the case of Kōsaka should all belong to the male sex, while no similar cases are known in women, with the exception of one reported by Askanazy and Brock.

According to these authors an idiotic woman, who died of an epileptiform fit at the age of 23 years, had shown a premature development of secondary sexual character. When she was only 10 years old the mammae became considerably enlarged, at the age of 11 the pubic hair appeared, and two years later she experienced menstruation. In the autopsy the pineal body was found as a very rudimentary organ, its

* The report of this case will appear in the festive publication dedicated to Prof. S. Kure.

weight being only 0.04 G., its length 3 Mm. and its breadth 2 Mm. The other endocrine organs revealed nothing uncommon except the thyroid gland which suffered from the change seen in Basedow's disease. Although Askanazy himself is of another opinion I think this case offers sufficient ground for the theory that the pineal body inhibits the premature development of the sexual organs in the female as well as in the male, and I believe firmly that the theory is valid, for my experimental results in the case of the female chicken prove it quite conclusively.

Summary.

1. Pinealectomized young cocks grow more rapidly than the controls, begin to crow prematurely, and show an earlier development of the combs and testes.
2. Pinealectomized young hens reveal likewise a premature development of the ovary and fallopian tube.
3. In the pinealectomized chickens the endocrine organs, except for the sexual glands, show nothing abnormal, or only a slight difference, as compared with those of the controls.
4. Therefore it is certain that the pineal body acts chiefly so as to repress the premature development of the sexual organs in the female as well as in the male.

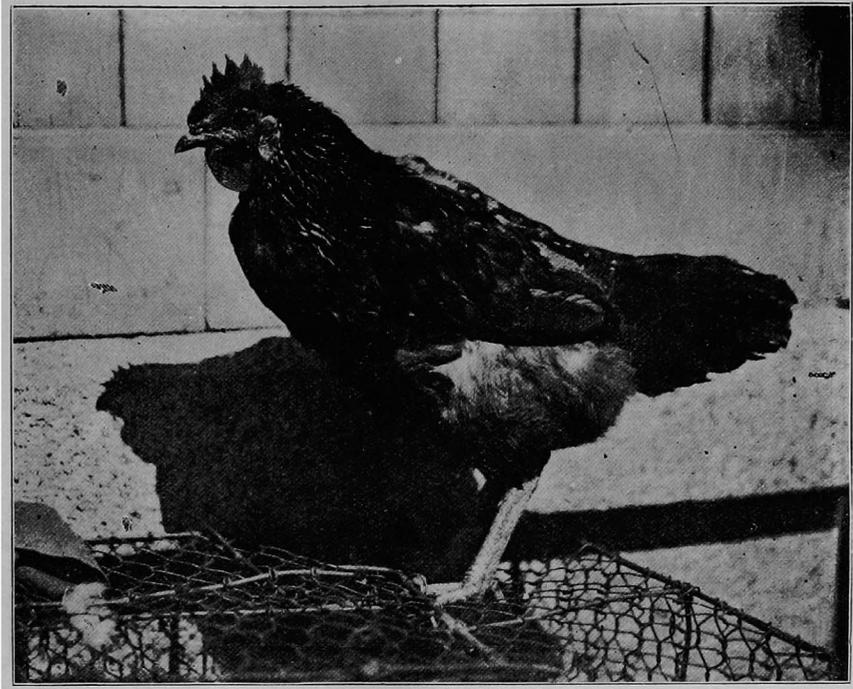
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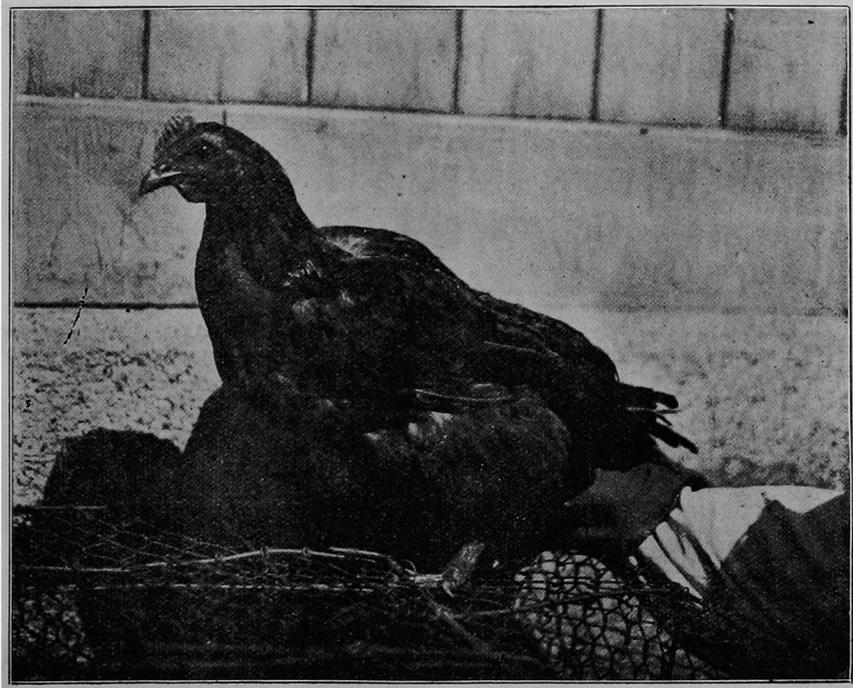
Explanation of Figures.

- Fig. 1. Cocks (case 1) aged 30 weeks, 182 days after operation.
A: Pinealectomized cock.
B: Control.
- Fig. 2. Cocks (case 2) 251 days old, 220 days after operation.
A: Pinealectomized cock.
B: Control.
- Fig. 3. Testes of the cocks belonging to case 1.
The upper: Those of the pinealectomized animal.
The lower: Those of the control.
- Fig. 4. Testes of the cocks belonging to case 2.
The upper: Those of the pinealectomized cock.
The lower: Those of the control.
- Fig. 5. Sexual organs of hens aged $23\frac{1}{4}$ weeks, 150 days after operation. (case 3)
Right: Those of the pinealectomized hen.
Left: Those of the control.
a: Ovary.
b: Fallopian tube.
c: Bursa Fabricii.
- Fig. 6. Sections through the testes of the cocks belonging to case 1.
A: From the pinealectomized cock.
B: From the control.

Fig. 1.

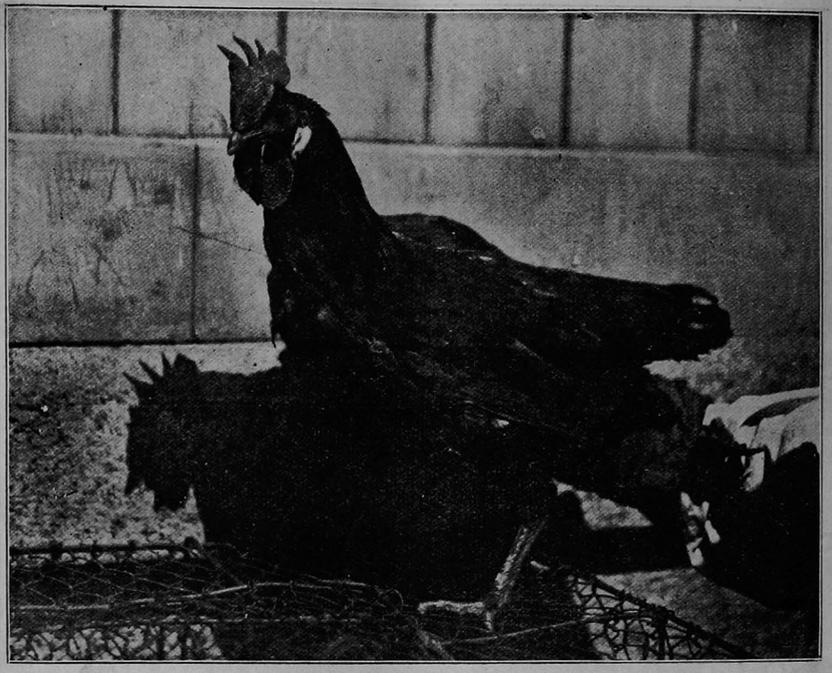


A.



B.

Fig. 2.



A.



B.

Fig. 3.



Fig. 4.

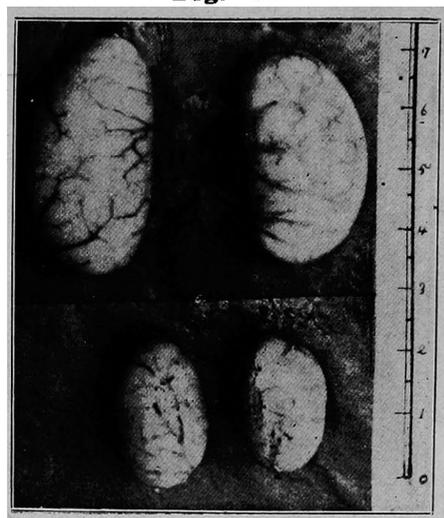


Fig. 5.

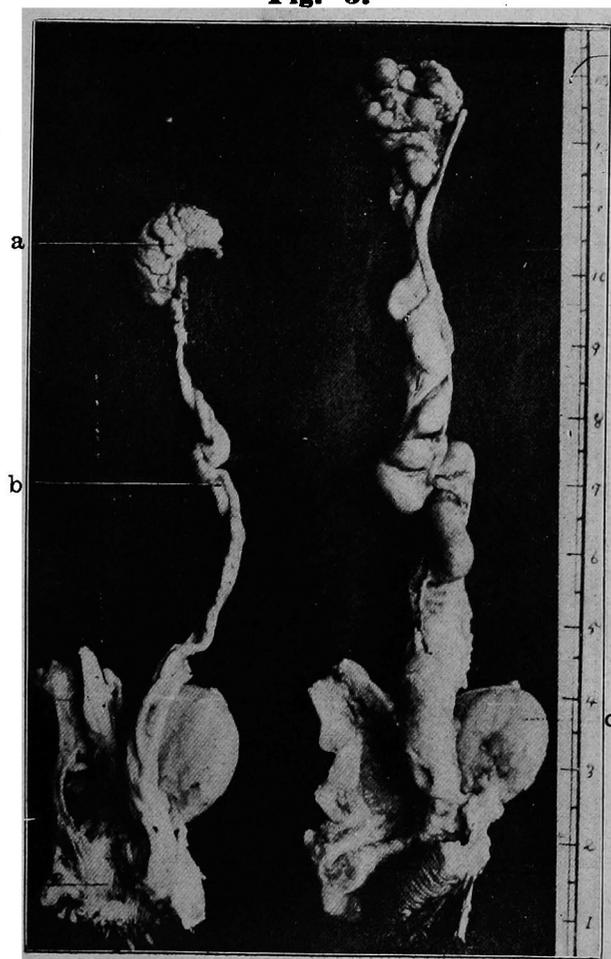
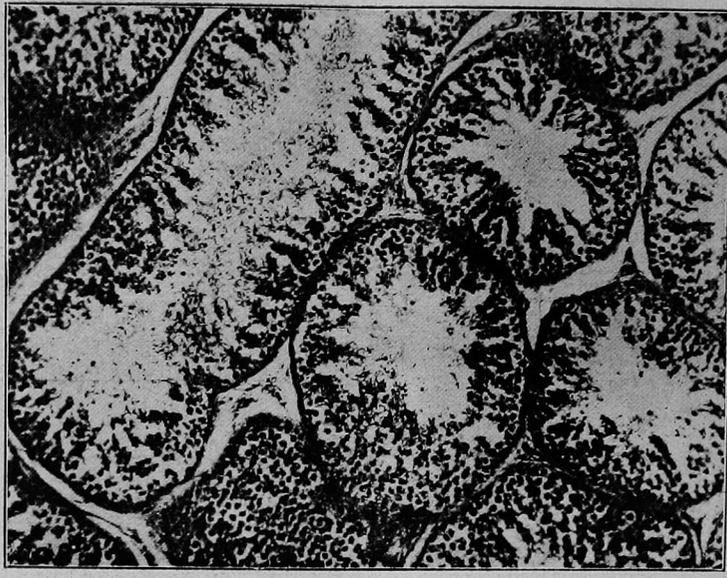
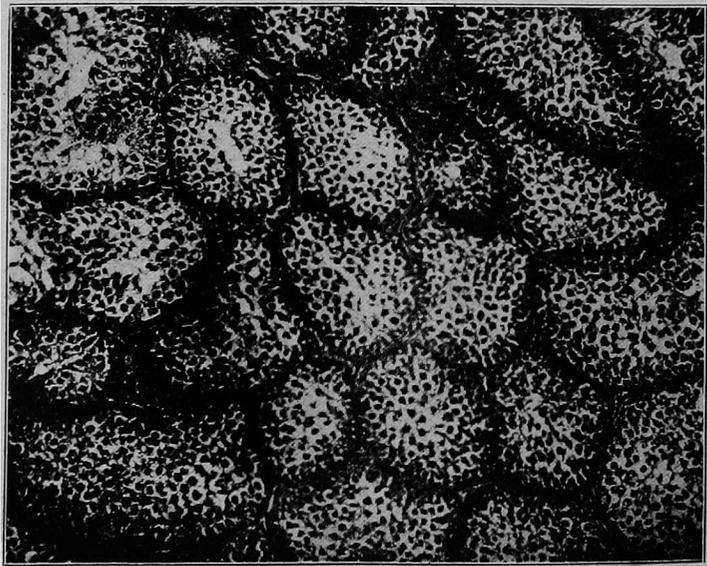


Fig. 6.



A.



B.

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