In some parts of the world the snail has more or less of a reputation as a "cure" for consumption, concerning which it is only necessary to say that it may be considered a food of some value as affording a change of diet.

William Barnes.

THYMUS GLAND, DEVELOPMENT OF.—The first statements regarding the development of the thymus gland contradicted each other completely. Arnold[1] asserted that it arose in common with the thyroid from the entoderm of the pharynx, while Bischoff[2] in general denied this. Remak,[3] in his great work, confirmed Arnold and added that this gland arises from one of the branchial clefts; but he was placed in doubt after Ecker had described the large gland in the neck of the chick as the thymus. From now on, the prevalent view continued to be that the thymus was mesodermal in origin.

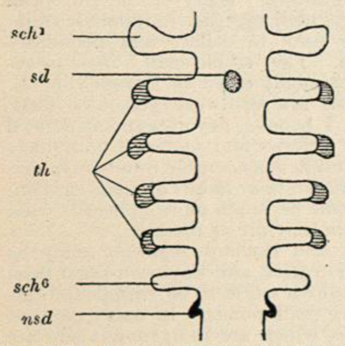

Fig. 5222.—Diagram showing the Branchial Clefts and the Glands arising from them in the Shark. (From Hertwig, after de Meuron.) *sch*¹, *sch*⁶, First and sixth branchial pockets; *sd*, thyroid; *th*, thymus; *nsd*, lateral thyroid.

We can well understand why these various views should be entertained when we consider that, for studies of this sort, the methods at that time were very crude; but in spite of all this we are under obligations to Remak for so much light regarding many problems in embryology, and it really seems a pity that his own view, which later on proved to be correct, should have been abandoned on account of his over-caution. By the more improved methods, both Kölliker[4] and His[5] observed that the thymus must be of epithelial origin, and therefore accepted the old view of Remak. It may be added that at this very same time two elaborate papers were published by Afanassiew[6] and Watney,[7] in which they attempted to demonstrate that the gland arises from the mesoderm. More accurate methods were now introduced, and it soon was demonstrated by Stieda[8] that in many animals the thymus arises from the third branchial pocket. This was also confirmed by Born[9] (and many others,[10, 19]), who in this study introduced his well-known method of reconstruction.

In the third part of his "Anatomie menschl. Embryonen," His[5] brought forth the view that the thymus arises from the sinus præcervicalis, and is therefore purely ectodermal in origin. This view he attempted to strengthen in a later publication,[20] and it was quite generally accepted. Later, however, in a response to a paper by the author,[14] His[21] retracts his older view and admits that the bulk of the thymus has its origin from the entodermal lining of the third branchial cleft. He therefore considers the origin of the thymus still an open question, and until more careful researches are made, accepts the view of Fischelis[22] and of Kastschenko,[23, 24] that is, that it arises from both ectoderm and entoderm.

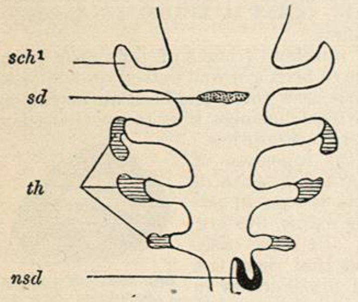

Fig. 5223.—Diagram showing the Branchial Clefts and the Glands arising from them in the Reptiles. (From Hertwig, after de Meuron.) *sch*¹, First branchial pocket; *sd*, thyroid; *th*, thymus; *nsd*, lateral thyroid.

Shortly after the branchial arches are formed there appears at the dorsal side of each cleft a thickening of the entodermal cells, which soon separate from the entoderm to form distinct groups of glands. This is the condition of things in low vertebrates, and as the scale is ascended certain groups become more and more prominent, until man is reached, when only the two groups from the third branchial pocket remain to form the thymus.

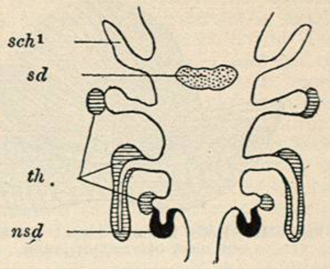

Fig. 5224.—Diagram showing the Branchial Pockets and the Glands arising from them in the Chick. (Modified from de Meuron.) *sd*, Thyroid; *sch*¹, first branchial pocket; *th*, thymus; *nsd*, lateral thyroid.

In the fishes the general relation of these glands to the branchial clefts is shown in Fig. 5222. These individual glands are soon united into one large gland on either side of the pharynx; in the bony fishes these groups unite into one gland before they have separated from the pharynx. In the reptiles the number of glands are reduced (Fig. 5223) to correspond with this number of branchial clefts. Van Bemmelen discovered in the elasmobranchs that the posterior cleft, or rudimentary cleft, produced a distinct body which did not unite with the thymus. This he has termed the suprapericardial body, and later its homology was found in many classes of vertebrates. In many reptiles it is unilateral, as shown in the figure. Considering their origin, they seem to be intimately related with the thymus, but in mammals it is probable that they are added to the thyroid, and will be discussed under that heading.

In birds the third branchial pocket gives the main origin of the thymus, as shown in Fig. 5224. Here we have a sharper line of demarcation between ectoderm and entoderm, as the branchial clefts do not break through as in fishes. We can now state with great certainty from what embryonic layer this gland arises, provided we have good serial sections to study. Very recently Kastschenko discovered a small gland in connection with the second branchial pocket, but as yet its fate has not been determined. It is no doubt a remnant of the portion of the thymus which arises from the same place in lower vertebrates. The third branchial pocket, however, becomes very prominent, grows toward the head, and is at no time blended with the ectoderm (Fig. 5225). To be sure, it comes in apposition with the ectodermal invaginations of the clefts, but recent work has shown that these have to do with the ganglia of the cranial nerves, and do not unite with the thymus as thought by His and others. Moreover, it is by no means probable that these sense organs of Froriep and Beard should suddenly leave the nerve ganglia in certain regions and unite with glands. Both observations and principles of development contradict this. The fourth branchial pocket, as well as a rudimentary fifth (fossa subbranchialis), gives rise to a few small bodies, the nature of which is not as yet truly known. That from the rudimentary fifth, no doubt, gives the gland which is homologous with Van Bemmelen's suprapericardial body.

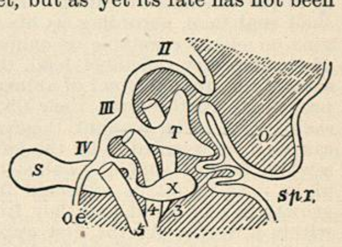

Fig. 5225.—Dorsal View of a Reconstruction of a Chick 110 hours old. × 35. *II, III,* and *IV*, Branchial pockets; *O*, operculum; *S*, thyroid; *spr*, sinus præcervicalis; *T*, thymus; *X*, body derived from the fourth branchial pocket; *oe*, œsophagus.

In mammals the condition of things is much simpler (Fig. 5226). The branchial grooves lie on the outside of the body, are shallow on their dorsal side, and deep on their ventral. As these arches fall over one another, the grooves as well as the third and fourth arches are buried in the side of the neck; while this is taking place a pit is first formed, the sinus præcervicalis of His.

From the dorsal side of the first groove an invagination unites with the ganglion of the fifth nerve; from the second, the invagination is to the ninth nerve; and from the third and fourth it is to the tenth nerve. A section through these organs in the region of the vagus and of the thymus is shown in Fig. 5227. The ectodermal invagination is absolutely blended with the vagus and is only in apposition with the thymus.

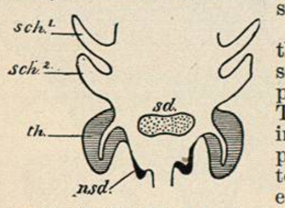

Fig. 5226.—Diagram showing Branchial Pockets, and the Glands arising from them in the Human Embryo. *sch*¹, *sch*⁴, First and second branchial pockets; *th*, thymus; *sd*, thyroid; *nsd*, lateral thyroid.

The pharynx side of the branchial clefts presents about the same appearance as the external. The entodermal lining is in the form of slit-like pockets, which are better called branchial pockets, to differentiate them from the ectodermal side, or branchial grooves. As the head flexes upon the body the pharynx widens near the mouth and becomes narrower where the trachea is formed. There is a peculiar kinking of this region due to the rotation of the head. The first branchial pocket is converted directly into the Eustachian tube; the second disappears completely; the third forms the thymus (Fig. 5228); and the fourth becomes rudimentary and gives rise to the auxiliary thyroid glands.

The general appearance in the human embryo is quite similar to that in other mammals, as Fig. 5229 shows. Already in this early stage of development, the third branchial pocket shows an ingrowth which indicates the origin of the thymus. The portion of the cleft represented by the fundus (*F*) is not continuous with the thymus tube, and no doubt never plays any part in its formation.

The general view of the branchial pockets in a human embryo is shown in Fig. 5230. The whole pharynx is represented as a cast and the branchial pockets are represented by the figures 1, 2, 3, and 4. It is the one marked 3 which is destined to become the thymus. It soon becomes separated from the pharynx and then grows into the thorax.

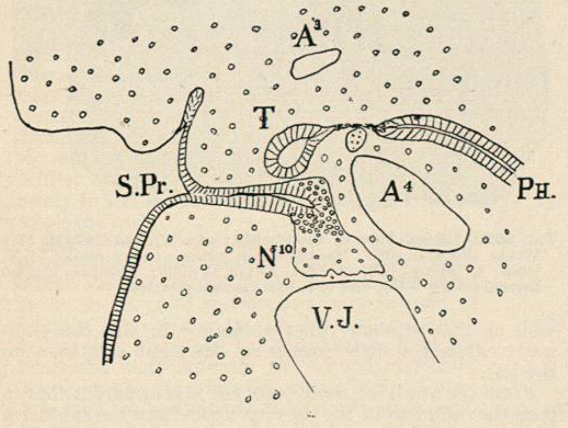

Fig. 5227.—Section through the Thymus and Fundus Præcervicalis of a Dog's Embryo, 10 mm. long. × 80. *Ph.*, Pharynx; *A*³, *A*⁴, aortic arches; *S.Pr.*, sinus præcervicalis; *V.J.*, jugular vein; *T.*, thymus still in connection with the pharynx.

Before the thymus is separated from the pharynx it contains a distinct lumen. This is soon lost in birds, where the thymus grows toward the head. In mammals, where the thymus grows into the thorax, the upper part contains a lumen, while the lower part grows by a mass of sprouts (Fig. 5231). This continues for quite a while until the whole organ is lobulated. New blood-vessels and lymph cells grow through the epithelial gland and change its nature. The entodermal cells become packed together into the Hassal's concentric bodies as shown by Maurer for the fishes, and by Ecker[25] and by His[26] for mammals. These bodies correspond with the "pearls" in carcinomata, which are present in cancers, that arise from the whole epidermis, as well as those from the œsophagus. The Hassal's bodies do not therefore indicate that the thymus arises from the ectoderm.

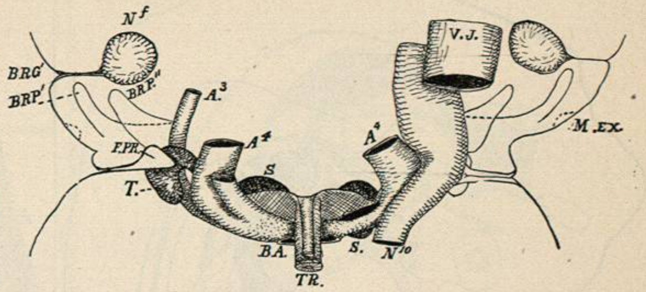

Fig. 5228.—Dorsal Reconstruction of the Branchial Region of a Dog's Embryo, 10 mm. long. × 25. *Nf*, *N*¹⁰, Ganglia of facial and vagus nerves; *BRP'*, *BRP"*, branchial pockets; *BRG*, branchial grooves; *A*³, *A*⁴, aortic arches; *B A*, aortic bulb; *Tr.*, trachea; *M.ex.*, external meatus of the ear; *S*, thyroid; *T*, thymus; *F.PR.*, fundus præcervicalis.

During the first two years of life the organ continues to grow and the two halves gradually approach each other more and more, until they seem as a single body. It now lies immediately in front of the heart, and often sends two horns which extend on either side of the neck to the thyroid, as is the case in the birds. From now on, the organ gradually atrophies.

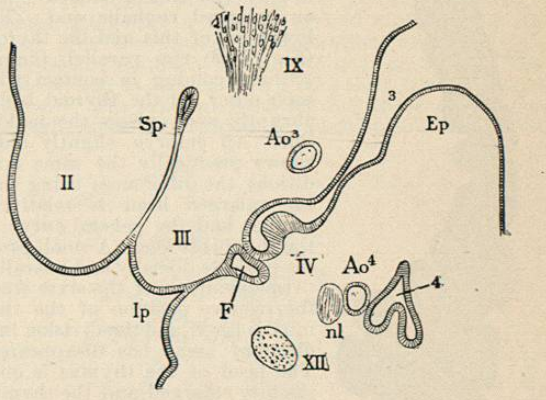

Fig. 5229.—Section through the Branchial Region of a Human Embryo, Five Weeks Old. (From Minot, after His.) *II, III, IV*, Branchial arches; *Sp*, second branchial grooves; *Ip*, infundibulum præcervicale; *F*, fundus of the infundibulum; 3, 4, third and fourth branchial pockets, with the thymus arising from the third; *Ao*³, *Ao*⁴, aortic arches; *Ep.*, epiglottis; *IX*, glosso-pharyngeal nerve ganglion; *XII*, hypoglossal nerve; *nl*, superior laryngeal nerve.

In the study of the human embryo Sudler[27] finds no indication of the thymus in a human embryo of the second week, but in one of the fourth week the third visceral pouch appears as a ridge with a ventral free end, with no differentiation of tissue to suggest a thymus. In an embryo four and one-half weeks old this ridge has disappeared and the third visceral pouch projects out

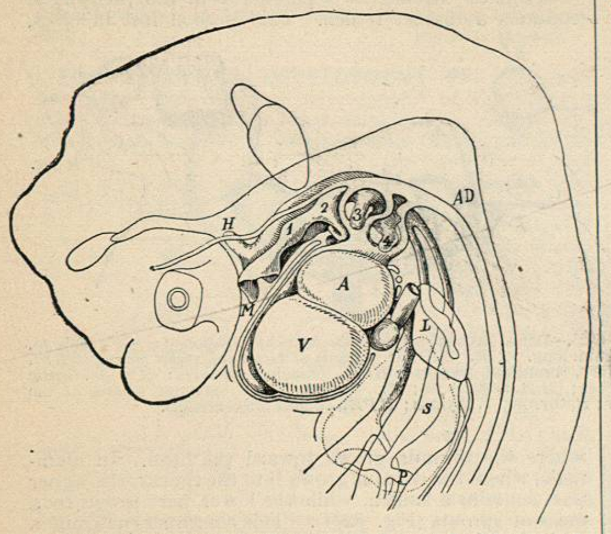

FIG. 5230.—Reconstruction of a Human Embryo Four Weeks old. (No. 2.) Enlarged sixteen times, and viewed from the left side. *H*, Hypophysis; 1, 2, 3, and 4, branchial pockets; *M*, mouth; *A*, auricle; *V*, ventricle; *AD*, descending aorta; *L*, lung; *S*, stomach; *P*, pancreas.

directly from the pharynx (Fig. 5232). In the next stage, of about five weeks, it is very similar to one described by Born, in which the thymus has become completely separated from the pharynx, and its original hollow is reduced to a crescent-shaped opening which is quite characteristic of the gland at this stage. The thymus now is a curved elongated body with an enlarged cephalic end. The lower end of this and the thyroid (Fig. 5233) run parallel, though without coming in contact with each other till the thyroid bends abruptly and crosses the middle line. An embryo slightly older shows practically the same conditions, the differences being that the enlarged head is relatively smaller and the general curve of the thymus is less. A small process projects dorsally and laterally.

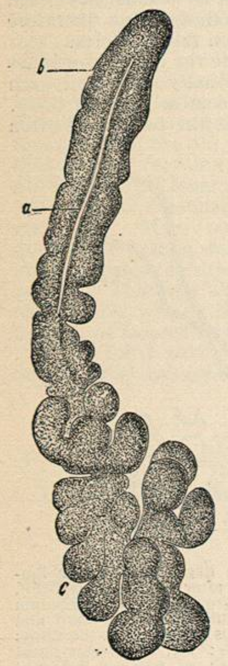

FIG. 5231.—Thymus of a Rabbit Embryo Sixteen Days Old. (After von Kölliker.) *a*, Duct of the thymus; *b*, head of the thymus; *c*, posterior enlargement of the gland.

In an embryo of the sixth week the relative position of the thymus is lower and the division into different areas has disappeared. The head of the thymus is only slightly enlarged and the thymus and thyroid have both approached the middle line at the aboral end though still without meeting. In an embryo slightly older the thymus is still lower, so that the thyroid is higher even than the head of the thymus. The whole of the thymus projects beyond the thyroid and is nearer the middle line.

The oldest embryo studied was one of the seventh week, which shows the thyroid rudiment as having sunken relatively still lower. It is in contact with the thyroid along half of its upper surface, the lower end being free. In this free half the thymus and the thyroid approach each other and meet in the middle line where the ends are slightly swollen and bend ventrally. This appears to be a beginning of the folding of the thymus found in the adult organ. In this embryo the thymus shows the same

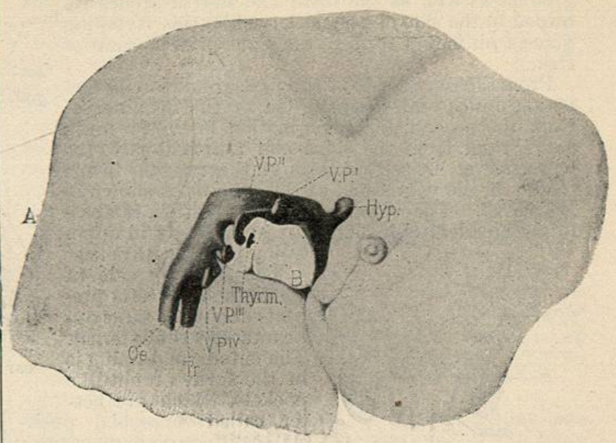

FIG. 5232.—Lateral View of a Human Embryo Four and One-half Weeks Old (No. 163). Enlarged ten times. (After Sudler.) *Hyp.*, Hypophysis; *Oe*, œsophagus; *Thyr.m.*, median thyroid rudiment; *Tr*, trachea; *V.P*^{i}–*V.P*^{iv}, first to fourth visceral pouches.

lack of bilateral symmetry which is apparent in the development of the pharynx in the human embryo as

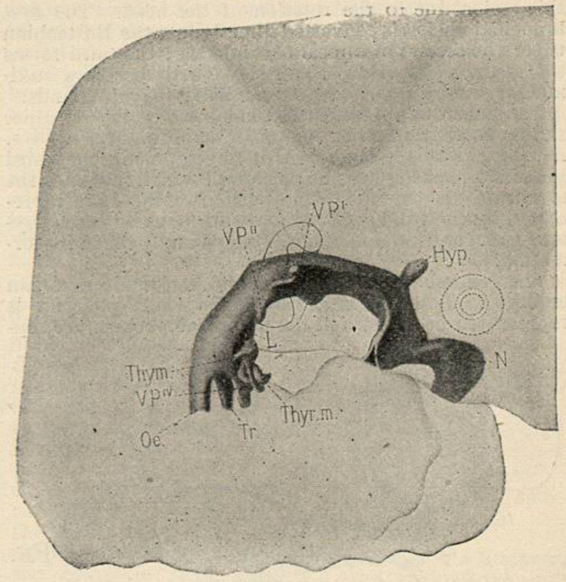

FIG. 5233.—Lateral View of the Pharynx of a Human Embryo Five Weeks Old (No. 109). Enlarged ten times. (After Sudler.) *N*, Nose; *L*, larynx; *Tr*, trachea; *Thym*, thymus; *Thyr.m.*, median thyroid; *V.P*^{i}–*VP*^{iv}, first to fourth visceral pouches.

well as that of some other animals. In this the rudiment extends a little higher on the right side than on the left.

From the study of these embryos it is apparent that in man the rudiment of the thymus arises from the entoderm of the third visceral pouch. *Franklin P. Mall.*

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THYROID GLAND, DEVELOPMENT OF.—Shortly after Rathke discovered the branchial arches in higher animals, Huschke[1] advanced the idea that the thyroid gland arises from the first arch. Later, however, he states that after the arches disappear the thyroid remains as their remnant.[2] A year later, Rathke[3] asserted that the thyroid arises as a bilateral organ from the posterior part of the trachea, immediately behind the larynx. This view was affirmed by Arnold.[4] Bischoff[5] accepted neither of these views, but added a third. According to him, the thyroid arises as a bilateral organ from the blood-vessels on either side of the neck.

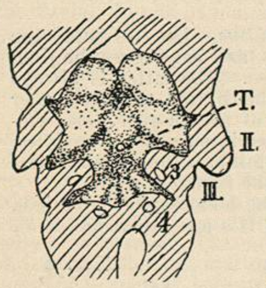

FIG. 5234.—Reconstruction of the Mouth of a Chick Eighty-eight Hours Old. The floor of the mouth is exposed by cutting off the back of the head. Dorsal view. × 20. *T.*, Tuberculum impar, back of which is the opening of the thyroid; *II*, *III*, branchial arches; 3, 4, third and fourth aortic arches.

The first careful investigations were made by Remak[6] upon the chick. In this subject, as well as in many others in embryology, he was the first to give accurate information. He found that the thyroid is entodermal in origin and arises from the ventral median line of the pharynx. At first it appears as a single vesicle, which soon divides into two parts, each half lying on either side of the trachea. Götte,[7] Müller,[8] and Seessel[9] confirmed Remak's views in general, differing only in minor points. They discussed whether or not the organ divided is a vesicle or is a solid body, although none of them found stages in which the thyroid was dividing. Remak placed the origin of the thyroid at seventy-nine hours in the chick; Müller in the third day; and Seessel very definitely in the second day before the head flexed upon the body.

His[10] revived the old view of Rathke by discovering that certain bodies arise from either side of the pharynx; he believed them to be the thyroid and the auxiliary thyroid of Remak. According to the illustrations which accompany his paper, the gland arises from the branchial cleft between the second and third aortic arches, therefore the second cleft. Later, however, he abandoned this view and accepted that of Seessel, who worked under his guidance. Later, Kölliker[11] accepted the old Remak-Seessel view for the rabbit, as His[12] did for man.

This group of excellent workers seemed to set the subject aside for a while, but, immediately following their work, two authors simultaneously described the thyroid as being bilateral in origin, arising from a branchial cleft on either side of the neck. Stieda[13] proved definitely that a glandular organ arises from the clefts on either side of the neck, but did not know from which cleft, although he was inclined to accept the fourth. Wölfler[14]

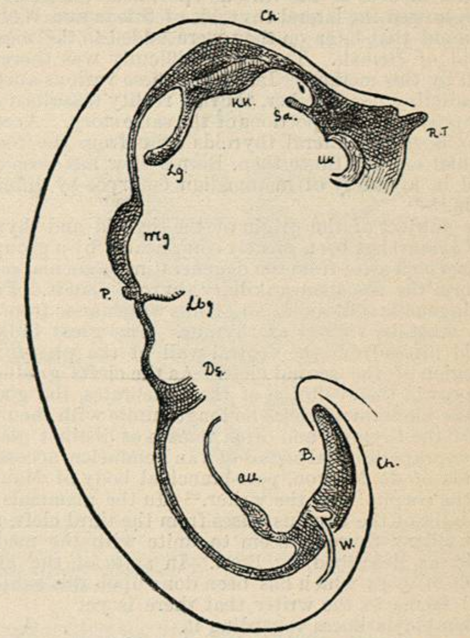

FIG. 5235.—Alimentary Canal of a Human Embryo. × 20. (After His.) *Uk*, Lower jaw; *Sd.*, thyroid; *Lg.*, lung; *Mg.*, stomach; *P.*, pancreas; *Lbg.*, bile duct; *W.*, Wolffian duct.

did not employ very accurate methods, and therefore got the location of the origin of the gland in the first branchial cleft—the one which later forms the Eustachian tube. He was so enthusiastic over his discovery that he denied altogether a median thyroid, although he had never seen the thyroid in connection with any cleft. Discussions naturally bring forth more accurate investigations, and in this case they bore their fruits in Born's paper.[15] The paper of Born not only threw a great deal of light upon the subject in question, but also added

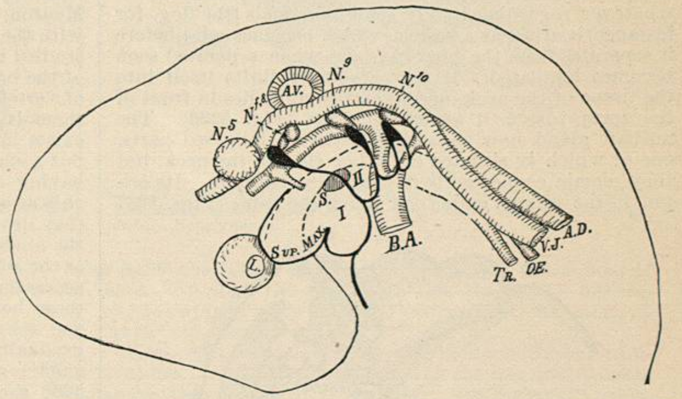

FIG. 5236.—Profile Reconstruction of a Dog's Embryo, 6 mm. long. × 25. N^{5}, Nf^{8}, N^{9}, N^{10}, ganglia or cranial nerves; *I*, *II*, branchial arches; *A.V.*, auditory vesicle; *Tr.*, trachea; *OE.*, œsophagus; *V.J.*, jugular vein; *A.D.*, descending aorta; *B.A.*, bulbus aortæ; *S.*, thyroid gland.

greatly to our methods of investigation. He introduced a method which to us now seems so logical that it is a surprise that it was not employed earlier. He began with embryos of the pig before the thyroid appeared, and followed them stage by stage until the organ was fully formed. In each stage the enlarged sections were drawn upon wax plates of the proper thickness, then cut out and the pieces piled upon one another, thus forming very accurate models of the various specimens studied. He then followed the lateral thyroids of Stieda and Wölfler, and found that later on they were added to the median thyroid of Remak. The great difficulty was therefore solved by this method. Instead of these various authors contradicting one another, they in reality described correctly only different portions of the same story. According to Born the lateral thyroids arise from the fourth branchial clefts. Since then, Born's view has been confirmed in a variety of mammalian embryos by different writers.[16–25]

The subject of the origin of the thyroid and thymus (see *Thymus*) has been greatly complicated by a group of glands which arise from the degenerating branchial clefts and form the so-called auxiliary thyroid glands. From a phylogenetic standpoint all glands which arise from the clefts must be viewed as thymus. The great bulk of thyroid arises from the ventral wall of the pharynx in the region of the second cleft. As the clefts gradually disappear in the evolution of the vertebrates, the glands from the hindermost clefts no longer unite with the main bulk of the thymus, and often remain as distinct glands—the suprapericardial bodies of van Bemmelen, accessory thyroids of de Meuron, post-branchial body of Maurer, or as the corpus Y of the writer.[26] In the mammals the main bulk of the thymus arises from the third cleft, and the auxiliary thyroids seem to unite with the median thyroid as described by Born. In spite of the great amount of work which has been done upon this subject, it still seems to the writer that there is yet considerable darkness regarding it.

The general view is that the thyroid has three distinct origins in nearly all vertebrates—a median and two lateral. The median arises from the ectoderm of the middle line in the neighborhood of the second branchial arch (Fig. 5234), and the lateral from the most posterior branchial clefts; in mammals, the fourth.

The median thyroid arises in all vertebrates from the entoderm of the pharynx shortly after the branchial arches are well formed (Fig. 5235). This has been known since the time of W. Müller, and, although contradicted many a time, has of late been verified by so many careful observers that there is no longer any doubt whatever regarding it. In some mammals (the dog, for instance) it arises as a vesicle, which becomes solid before it separates from the pharynx, and when separated soon becomes lobulated. It now gradually shifts itself into the tissue of the neck, and in early stages lies in front of the aorta just as it leaves the heart (Fig. 5236). The median gland now becomes constricted into two parts, one of which is situated on either side of the neck, but they remain connected by a band—the isthmus. Its origin in the human embryo is much the same (Figs. 5237

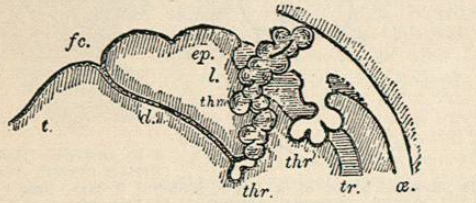

Fig. 5237.—Pharynx, Thyroid, and Thymus of a Human Embryo. × 25. (From Quain, after His.) *tr.*, Tongue; *fc.*, foramen cæcum; *ep.*, epiglottis; *thm.*, thymus; *thr.*, median thyroid; *thr'*, lateral thyroid; *d*, ductus thyreoglossus.

and 5238). According to His, it remains a vesicle for quite a long time, and the separation from the pharynx occurs quite late or may not take place at all. Later, however, the formation of the ligamentum hypothyroideum cuts the duct (*d. thyreoglossus*) into two, thus forming two ducts. The half communicating with the mouth has been termed by His *ductus lingualis*, and the one with

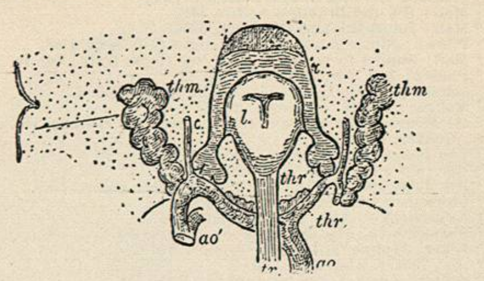

Fig. 5238.—Reconstruction of the Thyroid, Thymus, and Pharynx of a Human Embryo Five Weeks Old. (Slightly modified from His.) *thm*, Thymus; *thr*, thyroid; *c*, carotid; *ao'*, ascending aorta; *ao*, descending aorta; *tr.*, trachea.

the thyroid as the *ductus thyroideus*. His has found the ductus lingualis in five adults, and in all cases the ductus thyroideus was present also. The latter is always embedded in a median lobe of the thyroid, and the former opens into the foramen cæcum of the tongue. The ductus thyreoglossus may be broken into a series of vesicles, as first described by Verneuil, but as a rule it disappears fully, its only remnant being the foramen cæcum.*

The lateral thyroids were first demonstrated by Stieda and by Born, although Rathke, His, and others had in all

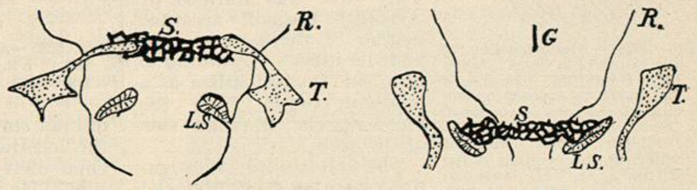

Fig. 5239. Fig. 5240.

Figs. 5239 and 5240.—Diagrams of Two Stages of the Development of the Lateral Thyroids. (Slightly modified from Born.) *R*, Border of the pharynx; *T.*, thymus; *G*, glottis; *L.S.*, lateral thyroids.

probability described them from time to time. The true meaning of them was fully made out by Born and by de Meuron, the former having discovered that they unite with the median thyroid in mammals, the latter having studied them from a comparative standpoint. Diagrams of the branchial pockets for some of the different classes of vertebrates are given in the article *Thymus*, and by them it is shown that a rudimentary branchial pocket exists in all of the classes. In certain reptiles there is but a single one on the left side, the one on the right not having developed. We can view this state of things only as an intermediate one between the reptiles (in which they develop on both sides) and the birds. In all classes the hindermost cleft gives rise to a distinct gland known as the suprapericardial body of van Bemmelen and as the accessory thyroid of de Meuron.[28–30] In the selacians these bodies remain far away from the median thyroid, and they never unite with it. In higher animals they gradually approach the median thyroid nearer and nearer, and in mammals they unite completely with it. Fig. 5238 shows the general relation of these glands in a human embryo before the lateral thyroid is fully separated from the pharynx. Figs. 5239 and 5240 show two stages in which the lateral thyroid is approaching and uniting with the median. This is brought about by a

* From the standpoint of evolution it is interesting to note that Dohrn[27] has advanced the hypothesis that the thyroid represents a lost branchial cleft. These speculations are, of course, the natural outcome when genetic relation is taken into consideration in the study of comparative embryology.

double shifting. The median thyroid sinks deeper and deeper into the tissue of the neck, and practically lies in contact with the lateral thyroids before they separate from the pharynx. When these in turn separate from the pharynx they are shoved into the tissue of the median thyroid instead of into the ordinary mesoderm tissue of the neck.

It will be noticed that the lateral thyroids do not always arise from the same branchial clefts: in selacians from the seventh; in reptiles from the fifth; in mammals from the fourth. It is only in mammals that they really unite with the median thyroid. Viewing the thing from the standpoint of homology, what is lateral thyroid in mammals is thymus in lower animals; in both selacians and reptiles the fourth cleft gives rise to a portion of the thymus. We must therefore view the lateral thyroid as a portion of the thymus which is now united with the thyroid. In lower animals the secondary union of the gland from degenerating clefts with the median thyroid does not take place, and they remain in the tissue of the neck, as in the auxiliary thyroid glands, which have perplexed so many investigators. According to Kastschenko the lateral thyroid of mammals plays a very minor part in the formation of the mature organ, while according to His it forms the major part. A true blending of the two does, however, take place, as shown by the investigations of Born and of His (Fig. 5241).

The further development of the thyroid is by means of sprouting, so that the enlarged organ is a plexiform mass of cylinders of epithelial cells. Blood-vessels grow in between them, and soon the cylinders show constrictions which cut them up again and again. They now become hollow, and at the same time there is a secretion of the colloid substance. The cut-up cylinders become more and more distended, and thus the adult thyroid is composed of a mass of hollow spheres covered with a layer of epithelial cells and filled with colloid substance. When half of the thyroid is removed by an operation or otherwise, the remaining portion soon loses its colloid and returns to its "embryonic state." It enlarges to its former size and again forms the colloid spheres much after the fashion it did in the embryo.[31]

In the human embryo Sudler[32] finds the thyroid rudiment in the earliest one studied, an embryo at the end of the second week. It appears as a rounded eminence on the ridges uniting the first pair of visceral pouches. Its outline is elliptical, being broader from side to side than it is ventrodorsally. This is the rudiment of both the thyroid gland and the ductus thyreoglossus.

In an embryo of the fourth week the rudiment appears as a solid body extending dorsally from the apex of the

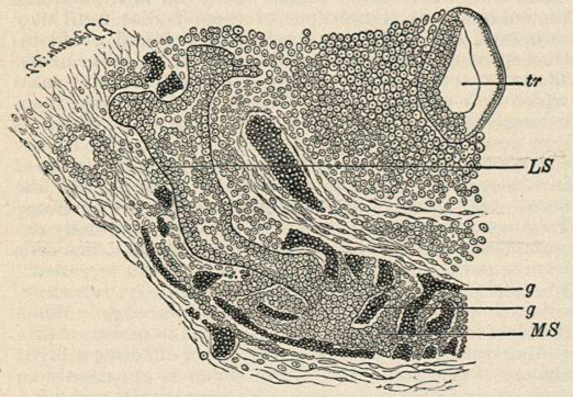

Fig. 5241.—Section through the Thyroid of the Embryo of the Pig, 21.5 mm. long. × 80. (From Hertwig, after Born.) *tr*, Trachea; *LS.*, lateral thyroid; *MS*, median thyroid; *g*, *g*, blood-vessels.

angle formed by the meeting of the first visceral pouches (Fig. 5242). Just oral to it is the hollow cavity representing the inner of the second visceral arches and directly aboral is the hollow cavity representing the tuberculum impar. Its appearance is that of a knob on a short slender stem. The fourth visceral pouch at this stage shows no thickening or development into the lateral thyroid rudiment.

In an embryo of four and one-half weeks the thyreoglossal duct remains as a small conical eminence on the

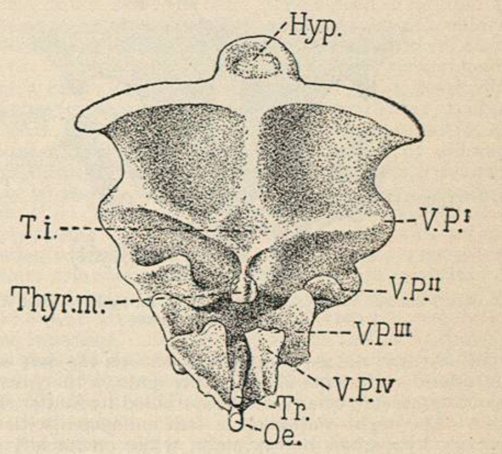

Fig. 5242.—Ventral View of a Model of the Pharynx of an Embryo Four Weeks Old (No. 2). (After Sudler.) *Hyp.*, Hypophysis; *Oe.*, œsophagus; *T.i.*, depression of the tuberculum impar; *Thyr.m.*, median thyroid rudiment; *Tr.*, trachea; *VP*i–*VP*iv, first to fourth visceral pouches.

ridge connecting the first visceral pouches. It is at the junction of the tuberculum impar and the two dorsal rudiments of the tongue (Fig. 5243). The median thyroid rudiment has become entirely disconnected and has sunk to the level of the third visceral fold. It has spread out laterally and has a bilobed structure. The left lobe

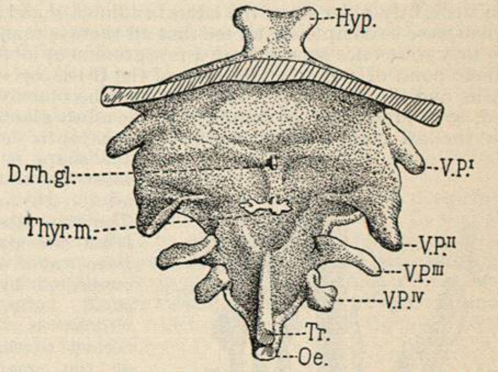

Fig. 5243.—Ventral View of a Model of the Pharynx of an Embryo Four and One-half Weeks Old (No. 163). (After Sudler.) *D.Th.gl.*, ductus thyreoglossus.

is much the longer and approaches closer to the floor of the mouth than the right. In this the fourth visceral pouches appear as two ventral projections with enlarged knobs bent sharply dorsal.

In an embryo of five weeks the median thyroid rudiment has become **U**-shaped, though the left arm is much longer than the right (Fig. 5244). Its outline is quite irregular. In this the transverse part of the **U** which runs across the middle line has sunk to the level of the fourth visceral pouch. This part shows the usual network structure formed by cords of solid cells. The arms are crescentic in cross section, with the hollow looking away from the middle line and embracing the thymus, although the two do not come in contact. The lateral thyroid rudiments, which consist of hollow tubes surmounted by solid expansions, are still connected with the pharynx. The two sides are unsymmetrical. On the right side the ventral knob is smaller than the dorsal, while on the left they are about equal in size and placed on the same level.

In an embryo only slightly older the median thyroid is still **U**-shaped, though the right arm is still smaller than

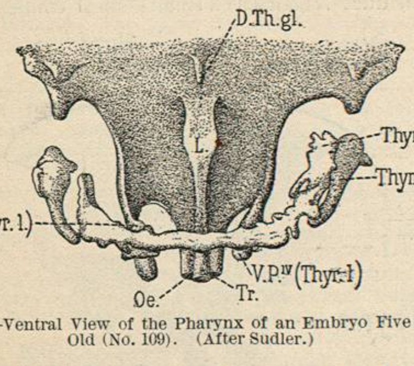

FIG. 5244.—Ventral View of the Pharynx of an Embryo Five Weeks Old (No. 109). (After Sudler.)

in the last and not so long as the one on the left side. The lateral rudiments show in this embryo the greatest lack of symmetry of any of those studied by Sudler (Fig. 5245). The right rudiment is still connected with the pharynx by a small hollow stalk, while on the left side this connection has entirely disappeared. On the right side the ventral knob touches the middle of the right arm of the median rudiment, but there is no histological continuity, whereas on the left side the ventral knob not only touches the median rudiment, but there is actual continuity. As in the embryo described before, the ventral knob on the right side is much smaller than the dorsal one, while on the left side they are of almost the same size.

The median and lateral thyroid rudiments have united on both sides in an embryo of the sixth week, and all connection with the pharynx has disappeared. They still appear as distinct rudiments.

In a slightly older stage the lateral rudiments and the median have so completely united that all there is to show that they were once separate are a few prominent lobules at their point of union. The loop of the **U** has become smaller and the arms larger, and they have become lobulated, so approaching the condition of the adult gland.

In the last embryo studied, one of the seventh week, the shape is almost that of the adult thyroid. The two lateral lobes are pyriform and are connected by a small isthmus, which is attached to them at the smaller end.

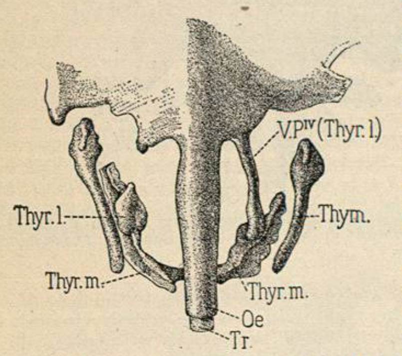

FIG. 5245.—Dorsal View of the Pharynx of an Embryo 13 mm. long (No. 175). (After Sudler.) The lateral thyroid on one side is attached to the pharynx and on the other is separated from it.

In the human embryo, as well as in the bird and some of the mammals, the pharynx develops more slowly on the right side than on the left, and the most striking example of this is in the thyroid. This may be due to the development of the heart and the bending of the head to the left.

From these different embryos Sudler draws the conclusion that "the thyroid arises in the human embryo from the union of a median rudiment situated at the point of junction of the tuberculum impar and the two dorsal rudiments of the tongue with a paired rudiment arising as a differentiation of a lining of the fourth visceral pouch."

Franklin P. Mall.

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TICK FEVER, OR SPOTTED FEVER.—A disease known by the latter of these two names is found in the States of Montana, Idaho, Nevada, Wyoming, and Oregon. As two other diseases (viz., typhus fever and cerebro-spinal meningitis) are already known as spotted fever, it would be well, as suggested by Anderson, to call the disease under discussion tick fever.

ETIOLOGY.—Tick fever or spotted fever is found in the mountainous districts in the above-named States at an elevation of over three thousand feet. It does not seem to be prevalent outside the latitude of 40° to 47° N. The disease is only found in persons whose occupation causes them to be exposed to the bite of the tick; such are lumbermen, ranchmen, and sheep-herders. Males in the prime of life are most liable to the disease; this would be expected from the occupations just mentioned. Beyond this, age and sex have no etiological significance. The disease is in all probability caused by a parasite.

The Parasite.—"Wilson and Chowning noticed ovoid intracorpuscular bodies in stained preparations of the blood from their earlier cases. They did not determine the character or significance of these bodies until they examined the fresh blood, when they found ovoid intracorpuscular bodies showing amœboid movements. These observations they confirmed in all the later cases which they examined. To Wilson and Chowning, then, belongs the credit of discovering a parasite which is very *probably* the cause of spotted (tick) fever." Anderson further says that in his studies upon the cause of this disease he "had the opportunity of examining the blood, both fresh and stained, in a number of cases. Two cases were in a hospital in Missoula, and daily examinations were made. In the fresh blood a few cells were found to contain parasites. Three forms were seen. The most common was a single ovoid body, refractile, situated within the cell, usually near its edge. When the slide is warmed this body possesses the power of projecting quite rapidly pseudopodia and of effecting a slight change of position. This form, which is apparently an early or young form, is about 1.5–2 μ in length, and 0.5–1 μ in width at its widest part. It closely resembles the earliest intracorpuscular parasites of æstivo-autumnal malaria.

"Another form, not so common, was larger, being about 2–2.5 by 1–1.5 μ, larger at one end and showing in the larger end a dark granular spot; this was also amœboid.

"The third form noted was arranged in pairs, distinctly pyriform, with the smaller ends approaching, and in two cases a fine thread uniting the small ends was seen. Motion was not observed in this form, but the spot mentioned in the second form was seen.

"The parasites are never found in very large numbers, it being usually necessary to search several fields of the slide to find one. Sometimes they occur in groups, two or three infected cells being found in one field. In both fresh and stained preparations extracorpuscular bodies closely resembling the small single intracorpuscular form were seen. I was unable definitely to decide the character of these bodies, but am strongly inclined to think that they are the young form of the parasite which has not yet invaded the red cells.

"In the cases of spotted (tick) fever which I had the opportunity of examining I had no great difficulty in finding both in fresh and in stained preparations the bodies above described. Their constancy in the blood of persons suffering with spotted fever, their persistence for some time in the blood of these persons after recovery, their absence from the blood of persons suffering from other diseases and of healthy persons make it very probable that they are the cause of the disease, and that one more has been added to the rapidly growing list of diseases of man due to animal parasites." (Anderson: "Spotted Fever (Tick Fever) of the Rocky Mountains.")

Method of Infection.—"The life history of the organisms of malaria and Texas fever naturally suggested that some insect was concerned in the transmission of the disease. On investigation it was found that the ticks appeared in the valley about the last of February, but were inactive until the middle of March or 1st of April, the first cases of fever appearing about the last of March. The ticks begin to diminish greatly in number from about June 1st, and after the middle of July very few are seen; the cases of fever also begin to diminish about June 1st, the latest date on which the disease has been known to occur being July 20th.

"Mosquitoes do not appear in the valley until after the first cases of fever develop, and remain some time after the last cases appear. Bedbugs and other house insects, I think, were well excluded, by the fact that there has never been known an instance in which two cases occurred the same year in the same house.

"On a closer study of the cases of spotted (tick) fever it was always found that there was a history of tick bites about one week before the onset. In four cases there was a history of a single bite two, three, five, and seven days, respectively, before the initial symptoms. The usual time between the bite and the onset of the fever is about seven days. If the tick transmits the disease, it may be asked, Why do not more persons become infected, and why is the infection confined to the west bank of the Bitter Root River? I think this may be answered by the very obvious fact that the tick is unable to travel any great distance, unless carried on some person or object. Again, it is very unusual for a tick to bite a person and not be discovered in a short while, and the result is the death of the tick. If, as in Texas fever, the development of the parasite takes place in the female tick and the young ticks transmit the infection, the very small number of ticks which escape detection in persons explains the small number of infected ticks. Where do the female ticks get their infection? I examined a recovered case twenty-four days after discharge by the physician and had no trouble in finding the parasite in the fresh blood. This child had been out of doors for over two weeks, and if a female tick (ticks were quite numerous near the house) had bitten her and escaped destruction the parasites in the blood taken in by the tick would have undergone development, and the young ticks, when hatched out, would be ready to infect prospective victims.

"While the above facts and conclusions tend strongly to the belief that the ticks are necessary for the transmission of the disease, the actual fact cannot be proved scientifically until carefully controlled experiments are made on non-immune persons." (Anderson, *ut supra.*)

The tick in question is in all probability *Dermacentor reticulatus.*

MORBID ANATOMY.—Rigor mortis is intense, and appears early. The skin is jaundiced, has a mottled appearance, and the wounds caused by the tick bites may be present. Petechial spots, bright to dark purple in color, and from 1 to 3 cm. in diameter, are found, chiefly on the wrist, ankle, arm, and leg. The spleen, liver, and pancreas are much enlarged; the kidneys are also enlarged.

SYMPTOMS.—There is a period of incubation of about a week. The patient complains of nausea, general malaise, and a chill; this latter is followed by a fever which reaches its highest point about the tenth day, is characterized by evening rise and morning remissions, lasts about two weeks, and may be followed by subnormal temperature. In severe cases the morning remissions may be absent, and the fever remains high (from 104° to 106° F.). There are general pain and soreness, particularly during the first week, coated tongue with red edges, sordes, constipation, nausea which persists in severe cases, scanty urine with albumin and casts, and epistaxis. The liver and spleen may be enlarged. The pulse is high, and out of all proportion to the fever; the respiration is also increased. An examination of the blood shows: (1) the parasite described above; (2) a decrease in the percentage of hæmoglobin; (3) a decrease in the number of the red blood cells; (4) a slight leucocytosis, chiefly of the large mononuclears. Bronchitis is present during the second week; and in severe cases lobar pneumonia supervenes, with a grave prognosis.

"*The eruption* appears usually on the third day, first on the wrists and ankles, then on arms, legs, forehead, back, chest, and, last and least, on the abdomen. It is never very abundant on the abdomen, but the other portions of the body, in some cases, are literally covered by the eruption.

"At first the spots are of a bright red color, macular at all times, from a pin point to a split pea in size. At first they disappear readily on pressure and return quickly, but if the case is a severe one they soon become darker and in some cases are almost purple. From about the sixth to the tenth day of the disease they fail to disappear on pressure and are distinctly petechial in character. In favorable cases, about the fourteenth day, they begin to lose their petechial character and disappear slowly on pressure. In some cases the eruption consists of small, brownish spots, giving a turkey-egg appearance.

"As the fever declines the eruption begins to fade; but a slight return of fever or a free perspiration will cause it to show distinctly.

"When convalescence is well advanced desquamation begins and extends over the entire body. In very severe cases there may be gangrene of the fingers or toes, and still more frequently of the skin of the scrotum and penis. The skin is always jaundiced to a greater or less degree. This is usually first noticed in the conjunctivæ, the vessels of which are congested from the outset." (Anderson, *ut supra.*)

	Tick fever or spotted fever.	Typhoid fever.	Typhus fever.
Contagion	Non-contagious	Not contagious in the ordinary acceptation of the term.	Very contagious.
Geographical distribution.	From 40° to 47° N.	Universal	Almost universal.
Season	March to July	All the year; chiefly July to November.	Generally in the winter.
Eruption—			
Date of occurrence.	Third day	Second week	Third to fifth day.
Site of first appearance.	Wrists and ankles, arms and legs.	Abdomen and back.	Abdomen, flexor surfaces of forearms, and general, except on face.
Blood examination.	Shows parasite	Eberth's bacillus in cultures from blood. Widal reaction.	Negative.