

## No. 4.

REPORT ON THE SO-CALLED ENTERIC OR TYPHOID FEVER OF THE PIG,  
by DR. KLEIN.

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I propose to give in this memoir a preliminary account of the results of an inquiry into the disease commonly called Pig-typhoid. Dr. Budd, in a lecture to the Members of the Royal Agricultural Society in 1865, and in his well-known treatise on Typhoid Fever, speaks of this disease in the pig as of the "exact counterpart of typhoid fever in man;" and Professor Wortley Axe, in his recent remarks on typhoid fever in pigs (the "Veterinarian," July 1875, p. 489) concurs with this assertion of Dr. Budd, by trying to show that in etiological, clinical, and anatomical respects both diseases are identical.

Being myself engaged in studying the anatomy of typhoid or enteric fever in man (see No. VI. of this series of Reports, 1875), I was naturally anxious to see whether more light could be thrown on this disease by an experimental and anatomical inquiry into its "counterpart" in the pig. I was therefore greatly disappointed when at the very outset of this inquiry I found that in an anatomical sense the two diseases are essentially different from each other.

It is admitted by all pathologists that the anatomical lesions in human typhoid are of so definite and specific a character that by them, and by them alone, the disease can be recognised in most cases. As I shall show, the anatomical lesions in pig-typhoid are likewise of a very specific nature, being not only very characteristic of this and no other disease in the pig, but also essentially distinct from the human typhoid. It is true the pig-typhoid bears some resemblance to real typhoid in man, but this resemblance is not greater than that amongst infective diseases in general. As is well known, pig-typhoid is a highly infectious disease, associated with an eruption of the skin and ulceration of the large intestine. It has been assumed that the intestinal discharges are the carriers of the contagion, but this assumption seems not to have rested on any direct experimental proof; though from Professor Axe's experiments, it appears that lymph from the pustules of the skin of diseased animals has the power of producing the disease when inoculated into the skin of healthy animals.

I have succeeded in proving, experimentally, that the disease can be produced by inoculating into healthy animals matter obtained from the ulcerations of the intestine; and likewise that the blood of the diseased animals, at a stage when all symptoms are well developed, does not necessarily contain the contagium. In the latter respect the pig-typhoid is essentially different from anthrax, with which it is usually confounded by continental writers on account of a certain similarity of the anatomical appearances in the two diseases; for in anthrax the blood, as is well known, is pre-eminently loaded with the contagium.

A.—The experiments to be recorded in the following have been carried out in conjunction with Mr. W. Duguid, veterinary surgeon at the Brown Institution. They were all performed on young animals.

*Experiment 1.*—Two perfectly healthy pigs were fed on a piece of large intestine full of ulcers; the material was used perfectly fresh, just as it was removed from the animal that had been killed for the purpose of the research. The animals remained perfectly healthy.

*Experiment 2.*—Small pieces of the spleen of a typhoid pig, full of whitish nodules of different sizes (*see* the following chapter), were rubbed up with three-quarters per cent. saline solution; of this material one healthy pig received a considerable quantity as food; a few divisions of a Pravaz syringe of the same material were injected into the skin of the groin of another healthy pig. The first animal died on the eighth, the other on the twelfth day; in both cases the “typhoid” symptoms were very well marked.

*Experiment 3.*—A healthy pig received into the skin of its right groin half a syringe full of the blood and juice of a swollen lymphatic gland, taken from an animal recently dead of the disease, and in which all the anatomical appearances were very well marked. The infected animal showed no signs of the disease for sixteen days, except a small hard nodule (the skin not adherent) in the subcutaneous tissue at the seat of the injection; so that we are quite justified in assuming that the result of the experiment was negative. And this is of very great importance, inasmuch as it tends to furnish direct additional proof of the difference between anthrax and the disease in question; the former being pre-eminently infectious through the blood.

*Experiment 4.*—From the same pig as in preceding experiment, fresh material was obtained (by scraping) from an ulcer of large intestine, and this material, having been suspended in three-quarters per cent. saline solution, was injected into the skin of the groin of a healthy animal. After ten days, the animal died, with exceedingly well-marked appearances of pig-typhoid in skin, intestine, lung, and lymphatic glands. The inguinal lymphatic glands near the seat of inoculation were especially enlarged, and deep red. The soft palate was swollen and contained follicular ulcerations.

*Experiment 5.*—Ulcerated parts of intestine of the same animal as that used in experiments 3 and 4 were kept macerating in water for three days, and then swallowed by a healthy animal. This animal died after thirteen days, under very marked symptoms of pig-typhoid: the appearances of skin, intestine, lung, lymphatic glands, &c., being exceedingly well developed, much more than in experiment 4.

The experiment does not, however, prove, as it seems to do, contrary to the experience of experiment 1, that the disease may be communicated by the food; for the very important fact of the infective material having had to be introduced by force must not by any means be lost sight of, as rendering more than possible that in the struggle superficial injuries to the mucous membrane of the mouth may have been the means of effecting inoculation, and that, therefore, this experiment 5 may belong to the same category as experiment 4, *i.e.*, inoculation through direct injection into the connective tissue of the integument. Whether this is so or not we intend to determine by new experiments.

*Experiment 6.*—The last experiment for the present, but not the least important one, is this: The same animal that had been inoculated with blood and juice of lymphatic glands, and, as we have seen, remained healthy, was again inoculated into the left groin on October 19, but this time not with blood, but with material obtained (by scraping) from an intestinal ulcer of the animal that had died in consequence of experiment 5.

The animal showed very little marked alterations while alive, but, being killed after 12 days, was found to present the following changes: At the seat of the second inoculation there was an abscess in the subcutaneous tissue, this being at the same time closely adherent to the skin. The inguinal glands of the same side much enlarged and very red, so also the lumbar, sternal, and bronchial

lymphatic glands. The two last named had the very characteristic aspect of the lymphatic glands in pig-typhoid : *see* the following chapter. The mucous membrane of the intestine pale, except at the ileo-cæcal valve, which contained a few very small defects of the mucosa ; and microscopic examination proved unmistakably that the mucosa at the ileo-cæcal valve was diseased, only though a mild degree : *see* the last chapter.

The appearance of the lymphatic glands, and the microscopic examination of the intestine (ileo-cæcal valve) in this case, leave no doubt about the animal having been suffering under a very slight degree of pig-typhoid. This experiment contrasts in an important manner with experiment 3 : for both were performed on the same animal ; but in experiment 3, where blood and juice of lymphatic gland had been used as inoculation-material, no disease was produced, whereas in experiment 6, where material of an ulcer had been inoculated, the animal became smitten with pig-typhoid. It might be argued that the condition of the lymphatic glands and intestine as found after the animal was killed may be, perhaps, referred to the first inoculation ; this objection can easily be disposed of, for the microscopic examination proved the changes of the lymphatic glands and intestine to be of recent date ; and besides the characteristic typhoid changes of the inguinal glands near the seat of the second inoculation are quite conclusive.

It is, however, clear to us that in order to arrive at definite conclusions we have to repeat the experiments. As far as they go at present we are inclined to assume—

(1.) That the skin of the diseased animals contains the contagium, as appears from the experiments of Professor Axe.

(2.) That the ulcers of the large intestine, and likewise the diseased spleen, contain the contagium, as appears from my experiments 2, 4, 5, and 6.

(3.) That the contagium is probably not contained in the blood and lymphatic glands at a late stage of the disease, but before this negative conclusion is accepted, additional experiments are particularly requisite.

(4.) That the disease can be produced by inoculation from intestinal ulcers into the skin, as appears from my experiments 4 and 6.

(5.) That whether the same can be achieved by simple feeding with matter of the intestinal ulcers is doubtful, *see* experiments 1 and 5.

Whether the contagium is also contained in the lung, and whether the disease can be produced by inoculating directly into the blood, are questions which cannot be answered without additional experiments.

B. The following are the appearances presented by our animals at the post-mortem examination :—

(a.) *Skin*.—In most of the 12 animals that were examined the skin was affected. The skin about the perineum, symphysis, and groins is swollen and of diffuse red colour, so is also the skin of the neck. The ear-lobes much swollen, especially near the tips, and red. The same of the skin of the nose. In two cases there was no distinct rash, and in one case there were in skin of groins, and especially in both ear-lobes, (a few in former, numerous in latter place) smaller or larger necrotic patches of the superficial part of the skin, including epidermis and corium.

(b.) *Intestine*.—Small intestine shows, as a rule, hyperæmia, and in some cases ecchymosis in the mucous and submucous tissue, and the serous covering. In some rare cases the same is seen also in the stomach. Large intestine shows always the most characteristic appearances. There are at least smaller or larger, isolated or confluent,

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generally roundish, ulcerations at and around ileo-cæcal valve, the rest of the mucous membrane being hyperæmic, even to ecchymosis. In the highest degree the whole large intestine down to the rectum contains ulcers; in the cæcum they are confluent, and measure several inches, extending transversely as well as longitudinally; while the whole remaining mucous membrane of the large intestine is much thickened, and in some parts the submucous tissue contains large accumulations of blood. The ulcers are of various aspects. The following forms may be seen: very minute, well-defined, prominent, yellowish-whitish specks of the size of a millet or hempseed; then somewhat larger, more flattened, prominent, circular or oval yellowish patches (with which in one case the whole mucous membrane of the cæcum seemed quite covered), of the size of a hempseed, up to about  $\frac{1}{8}$  of an inch in diameter; next, flat, circular, or slightly oblong patches, situated on the crest of a fold of the mucous membrane, in size from  $\frac{1}{8}$  to 1 inch in diameter, generally black or grey (from bile pigment), except a very conspicuous and, I may almost say, characteristic prominent rim which is yellow. The ulcer generally shows a pale, central, or eccentric disc, around which the rest of the ulcer is arranged as concentric rings. Between these flat ulcers with concentric layers and those uniform, yellowish-white, prominent patches and nodules there are all intermediary form; this is easily understood if it is borne in mind that as the latter increase in size the central part is transformed into that black or greyish mass. Besides these there are very often found on the surface of the mucosa minute whitish specks, just perceptible by the unaided eye. In one single instance have I seen ulcerations of the lower part of ileum. This case had exceedingly numerous ulcerations of the large intestine. The two ulcers of the ileum were quite different from the ulcers generally found in the large intestine, for they were oblong, deep pits, surrounded by a thick, prominent wall of swollen mucous membrane, very much the same as ulcers of human typhoid; on the peritoneal surfaces there was an elevation corresponding to them.

The above-described ulceration of the large intestine of the pig cannot in any way be confounded with the characteristic ulcers of human typhoid; the differences are really striking on the most superficial inspection. The only similarity may be said to exist between those early cases of human typhoid which French writers call *la forme bouttoneuse* (where the mucosa of the lower part of ileum and cæcum is studded with small papular structures due to enlargement of solitary lymph-follicles and local accumulations of lymphatic tissue), and the forms of pig-typhoid where the mucosa of the cæcum is covered with slightly elevated papules or patches; but under any circumstance the microscope reveals a marvellous difference in the two diseases, for in the pig-typhoid these patches whether nodules or ulcers, *have absolutely nothing whatever to do with lymphatic follicles*, whereas in human typhoid we find in the first stage round or generally oblong, prominent, papules or patches of swollen lymph-follicles, surrounded by swollen mucous membrane, after which stage the greater part of the swollen lymphatic patches dies and is finally discharged as a slough, leaving behind a pit-like excavation bordered by elevated overhanging mucosa.

Besides the intestine, the following lymphatic glands present very characteristic appearances; the mesenteric glands, especially those of the large intestine; the bronchial glands; the chain of glands along the thoracic (descending) aorta; the sternal glands; and the submaxillary lymphatic glands. The glands are much swollen, slightly firmer than normal or more or less red, in severe cases dark purple or even black and when cut into letting a considerable amount of red fluid ooze out.

At the same time it may be seen that the chief seat of red colourisation is the cortical part of the gland, from which it extends for a greater or smaller distance into the medullary part according to the greater or smaller severity of the change.

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In a few cases we observed ulceration also of the organs of the throat. In one case these were symmetrical ulcerations of the mucous membrane of the gums and cheeks, of the front part of the tongue, of the hard and soft palate, and of the epiglottis. The ulcers were of a dark grey colour; and what was most conspicuous about them was their marvellously symmetrical distribution on the two sides of the above organs. In another case we found follicular abscesses in the soft palate; they were very numerous, and the whole organ was much increased in thickness; there was an extensive ulcer in the median line of the epiglottis next the free edge. In a third case we found ulcerations of the gum and cheeks, of the tongue and hard palate; the soft palate contained numerous follicular abscesses; the epiglottis and the mucous membrane at the entrance of the larynx showed hyperæmia and œdema. The epiglottis in addition was possessed with an ulcer. It is noteworthy that these three animals in which we found affections of the throat came all from the same place. In a fourth case, produced by inoculation of matter from intestinal ulcers into the skin, we found follicular abscesses of the soft palate, the organ being much swollen.

The morbid condition of the lymphatic glands is sometimes, to naked-eye inspection, very slight indeed; besides the swelling of the gland there may be only what appears a slight hyperhemic condition; but even here the microscope reveals in all cases a very characteristic state, namely, a bursting of blood vessels in the cortical tissue, and hæmorrhage into the lymphatic follicles and sinuses of that part, amounting in severe cases to total destruction of the adenoid tissue by blood. In severe cases the medullary sinuses, and partly also the medullary lymphatic cylinders become filled with extravasated blood. In so far this condition is similar to what is found in anthrax. Now, this state of the lymphatic glands is, as I said, very characteristic, and, combined with the disease of the intestine, is of paramount importance for the diagnosis.

Further important symptoms, and which have not hitherto received due attention, are affections of the lung and serous membranes. Especially the lung-affection has shown itself to be as constant as any of the preceding, even more constant than that of the skin. The state of the lung is this: the slightest degree consists in a distinct mapping out of the lobes and lobules by œdema of interlobular tissue, the lung-tissue of the corresponding parts being at the same time hyperæmic. Then these parts become hepatised and transformed into a heavy, airless, red, transparent tissue; and subsequently smaller or larger opaque or white specks and patches appear in the red substance, and, as they increase in size, become gradually confluent. On a section it may be seen that this is due to the fact that the bronchial tubes become gradually filled with a white, brittle, cheesy mass, progressing gradually from the finest ramifications on to the larger branches of the affected lobules and lobes. Finally the whole lobule is transformed into a discoloured, dry, hard, friable mass. The pleura of the corresponding parts is of course inflamed, being in some cases exceedingly thick, and covered with false membranes. In severer cases the greater part of one lung and portions of the other may be thus changed, and on the external surface there may exist smaller or greater ulcerations. Except in very light cases there is generally a certain amount of pleural exudation; and in severer cases the pleura contains a considerable quantity of a thick, offensive, yellowish, or discoloured exudation. In some severer cases the pericar-

dium is also inflamed, containing a large quantity of exudation, and its walls being much thickened by false membranes. The same is also the case with the peritoneum, this being in some cases hyperæmic in parts, or even covered with solid lymph and pus. We have had cases where there was no skin eruption, slight intestinal change, and extensive pleuro-pneumonia, pericarditis, and pleuritis.

The next organ of importance is the spleen. The spleen is of dark colour and sometimes enlarged; in some cases it appears not altered in size. In one case it was remarkably enlarged, having throughout it irregular nodular structures, from the size of a pin's head to that of a pea or even larger, whitish in appearance and of firm consistency.

The liver is in severe cases enlarged and very full of blood. The kidney is sometimes also changed: there is hyperæmia of the pyramidal parts, and underneath the capsule, which may be easily stripped off, there are visible on the surface of cortex hæmorrhagic round spots of the size of a pin's head, while similar spots, but scarcer, are met with in the cortex and pyramids. The severer the case the more numerous the hæmorrhagic spots.

Thus we may say that the skin, large intestine, lymphatic glands, and lungs are the organs most commonly affected, and that changes of the serous membranes, the spleen, liver, and kidney, and likewise of the organs of the throat, are of less constant occurrence.

#### (C.) Microscopic examination.

(1.) *Skin*.—I have examined the microscopic character of those parts of the skin which show the diffuse redness, and in which the skin is being at the same time thicker than in normal parts. The longer the animal lives the more swollen become these parts, as is best shown on the ear-lobes: the pendent parts of these becoming transformed into deep-red, thick, puffy masses, from the surface of which the epidermis peels in greater or smaller flakes. Not seldom are there to be seen smaller or larger roundish or irregular brownish blotches and scabs on the ear-lobes as well as groins and skin of haunch, which blotches and scabs correspond to a necrosis of the corresponding parts of corium. The microscopical characters are these: in the lighter cases as in the earlier stages the corium is œdematous, as is very beautifully shown in the skin of the ear-lobes near the apex by the exceeding distinctness of the lymphatic vessels and the distended interfascicular lymph-spaces which are easily traced to open into the lymphatic vessels. The blood vessels of the corium (including arteries) are more or less distended and filled with blood or plugged with fibrin. Generally the fibrinous plug does not fill up the whole length or breadth of the vessel, nor does it present the ordinary aspect of fibrin in the blood vessels *i.e.*, a felt-work of fibres, but resembles a yellowish cylinder, of so dense a structure that the constituent fibrils are hardly distinguishable; other parts of the vessel contain blood. It is clear from this that there has been existing in the vessels stasis of blood, and that this latter has undergone conglutination.

Around the vessels we find lymphoid cells; besides these we find in some cases a very great number of large coarsely-granular cells very deeply staining in hæmatoxylin, with a relatively large, clear, vesicular nucleus; the same cells will be mentioned as occurring in the intestine. The sweat glands are greatly distended, and often filled with blood more or less charged. The connective tissue of the corium contains, in a more advanced stage, in its distended interfascicular lymph-spaces, fibrinous exudations, and in still later cases the tissue becomes more or less flooded with lymph-cells starting from around the vessels and extend-

ing into the interfascicular spaces. And finally the superficial parts of the corium change into a necrotic decolourised mass, the elements of which break down and are transformed into débris. On the ear-lobes, and also in other parts of the skin, I have seen the epidermis becoming very much thickened when the inflammation has reached a high degree.

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(2.) *Intestine.*—The mucous membrane of the large intestine shows the following changes. The capillary vessels next the surface very much distended and filled with blood, occasionally ruptured, so that blood is extravasated in the mucosa underneath the epithelium. Generally the epithelium at the mouth of Lieberkühn's crypts detached and in the act of breaking down. The same is the case with the epithelium covering the mucosa around the mouth of the crypts; at these places the epithelium is raised from the mucosa by the presence of cavities filled with fluid, in which are suspended cells, granular matter, and blood. The epithelium of these parts is quite different from the normal condition, the cells being much shorter, and their nuclei swollen up; this leads to the cells breaking up into small elements; and finally the epithelium is altogether discharged. The mucosa is at the same time much thickened by the presence of lymph-corpuses. The lymph spaces around Lieberkühn's crypts distended. In the superficial parts of the mucosa, as well as in the submucosa, there are in most parts present large uninuclear cells, which are conspicuous by their coarse granulation, and staining very deeply blue in hæmatoxylin. They are present also in great numbers in the connective tissue of the lymphatic glands, and also occasionally in the skin (see above). In the mucosa of the large intestine, and in the lymphatic glands, they are seen to be of the most different shapes: spherical, oval, spindle-shaped, branched, or irregularly drawn out; and this difference in shape makes it very probable that the cells in question are amœboid. The Lieberkühn's crypts are, as a rule, full with mucous secretion; the cells of the epithelium, especially in the outer portion of the crypts, are goblet-cells filled with mucus. In parts more affected the epithelium of crypts is loosened, and at some places perfectly removed from the glands. In other glands the nuclei of the epithelial cells are enormously enlarged, and the cells changed into spindle-shaped or irregular bodies. In this condition we find the mucous membrane over most parts of the large intestine. In some cases there is copious hæmorrhage in the submucosa, or rather the lymphatic vessels of the submucosa are very much distended and filled with blood, derived, no doubt, from broken vessels. In that blood we find, however, hæmatoidin crystals, and besides a peculiar arrangement of the blood corpuscles; these are arranged around spherical larger or smaller masses, which possess a very uniform and finely granular aspect.

The muscular coat of the intestine is also much swollen, varying to œdematous condition. The fat cells of submucous tissue are mostly filled with a mucous matter.

From the above condition of distension of blood vessels, loosening and partial or total removal of epithelium, we have all intermediary forms to the necrosis and disintegration of the most superficial portions of the mucosa, commencing as very small circumscribed opaque spots in which the tissue is disintegrating, and rapidly increasing in breadth and depth. There is no doubt whatever that the "ulcerations" of the large intestine are merely due to a necrosis of the most superficial part of the mucosa. That part in which the necrosis started remains, as has been mentioned, discernible for a long time as a more or less well-defined speck, around which successive new layers of mucosa have more or less concentrically undergone necrosis.

The submucosa shows at the same time, next the muscularis mucosae, a reactive inflammation: being full of pus-corpuscles. As the necrosis spreads, the infiltration of the deeper parts with pus-cells increases. Generally the muscularis mucosa seems to be the boundary up to which the necrosis proceeds. In some cases, however, the corresponding part of the submucosa appears likewise involved in the process.

From and even before the first signs of necrosis of the mucosa, viz., when the epithelium begins to break down and be shed from the surface, there are found masses of micrococci, which in some ulcers occupy a great portion of the débris. Also ova of nematode worms I have found in the débris of some of the smaller ulcers.

What we have said hitherto is, I think, quite sufficient to convince anyone that the "ulceration" of the mucosa of large intestine in the pig has absolutely nothing in common with the ulceration of the intestine in typhoid fever of man: the latter being a process entirely limited to the lymphatic follicles of the intestine, which have previously become highly inflamed and hypertrophied.

There are several other points which must be mentioned here, both of great histological interest, and also because of their importance to a right interpretation of the naked-eye appearances of the disease. In some cases when the ulcerations of the intestines are very numerous, the solitary lymph-follicles are seen to be enlarged and peculiarly changed. On the naked-eye inspection we perceive in those cases, in the mucous membrane, translucent spherical nodules, from about the size of a pin's head to hemp seed, or larger, which possess an opaque white centre. Examining them under a microscope we find that in the submucosa there is a larger or smaller saccular cavity, lined by columnar epithelium, and filled with more or less broken-down pus-cells, mucous matter, and granular débris; the wall of the sac containing a few rudiments of Lieberkühn's crypts, is surrounded by adenoid tissue; the cavity of the neck is in communication with the free surface of the intestine by a broad canal occupied by a plug of the same substance as found in the cavity. The plug of the neck and sac generally falls out during preparation. Mr. W. A. Shoobred, late of St. Bartholomews' Hospital, who examined for me these structures in mucous membrane less changed, found the following: There exist numerous flask-shaped invaginations of the mucosa into the submucous tissue, which flask-shaped cavities are lined by epithelium like the mucosa; the body of the flask situated in the submucosa contains Lieberkühn's crypts like the other parts of the mucosa, with the difference that they are much larger at their blind ends. The flask-shaped invaginations are, as a rule, imbedded in, or surrounded by, a lymph-follicle.

Now it is easy to understand the above condition described as translucent nodules with an opaque centre. One has only to bear in mind: that when the mucosa of the surrounding parts is much inflamed, the cavity and neck of the flask-shaped bodies become filled with pus-cells (gradually breaking down) mucous and granular débris; that under these conditions this cavity becomes more and more distended; and that also the Lieberkühn's follicles in their wall, through stretching, become gradually lost. The tissue of the lymphatic follicle becomes compressed into a narrow zone as the flask-shaped body becomes more distended. Where, however, the flask-shaped bodies do not become plugged up we find this condition: abundant mucous secretion taking place in the Lieberkühn's crypts of the neck, enlargement of the lymphatic follicle around the body of the flask-shaped gland, and penetration of the adenoid tissue into the cavity of the gland, the progressing adenoid issue, however, breaking down when in the cavity of the gland. At



these places the epithelium of the bottom of the Lieberkühn's crypts appears to be changed into a uniformly granular mass with numerous nuclei; the outlines of the individual epithelial cells having disappeared these masses split into several "giant cells," *i.e.*, huge granular masses, with a great number (5, 20, or more) of small vesicular nuclei; whether these giant cells originate from the epithelium of the Lieberkühn's follicles in the manner just described or not, it is certain that at these places the lymph-follicle contains them. But also in other parts of the intestine have I seen "giant cells:" that is to say, where the intestinal mucosa has been moderately thickened, and the surface epithelium at some places has become disintegrated, I have observed in the distended lymph-spaces around Lieberkühn's follicles, huge cylindrical or irregular shaped, finely and uniformly granular masses, at one peripheral place of which were embedded very numerous small elliptical or staff-shaped, or spindle-shaped nuclei, deep stained in hæmatoxylin. The corresponding crypts were much changed, the epithelium being transformed into a thin granular layer in which the nuclei might still be seen, and the cavity of the crypts being distended at some places, and containing masses of lymph-cells, which, however, were in the act of disintegration. Generally at the place where the "giant cell" was found the wall of the crypt was seen to be broken, and in communication with the lymph-space around. Similar giant cells I have found in lymph-spaces in the deeper parts of the mucosa, even extending into the submucosa through the muscularis mucosæ; and finally near the epithelium of the surface where they presented, however, more the round aspect of "giant cells," *i.e.*, their nuclei more like vesicular structures and distributed through the greater part of the centre. I find the giant cells not in all cases, but chiefly in those in which the above-named nodular structures, *i.e.*, swollen flask-shaped glands and enlarged lymph-follicles, are numerous; and generally they are to be found not far from parts containing the flask-shaped glands and lymph-follicles.

With regard to the ulcerations of the mucous membrane of the mouth, gum, hard palate, and tongue, I have to state that here also the ulceration consists in a necrosis of inflamed mucous membrane, in a breaking down of the superficial parts of the mucosa into a coloured débris.

There is one more point which I believe deserves careful attention. In the ulceration of the tongue just mentioned, and at a time when the superficial scab has not become removed, I have seen masses of micrococci situate chiefly in the tissue of the papillæ, but at some places reaching as far deep as the inflammation extends. That they are micrococci was proved by their forming lumps of uniform granules; these lumps stain deep purple-blue in hæmatoxylin, and are thus very conspicuous, and besides resist the action of caustic potash, with which all the rest of the tissue disappears. These heaps of micrococci in locality correspond to the papillæ, and are on the surface of the scab, but underneath the covering epithelium, some parts of this having changed into a dry, hard, discoloured mass, others containing larger or smaller vesicles filled with fluid.

In the soft palate we generally find the lymphatic follicles greatly increased, and the mucous glands much inflamed and infiltrated with pus-cells: the number of these latter increasing, the tissue of the mucous glands becomes destroyed, and minute abscesses are formed which discharge their contents through the duct of the mucous gland, which duct has naturally become greatly distended.

(3.) *Lymphatic glands.*—Corresponding to greater or lesser redness of the lymphatic glands we find the cortical parts occupied by greater or

smaller masses of blood, the adenoid tissue becoming at the same time destroyed. But this destruction, of course, depends on the amount of blood present. In the most acute cases we find not only great portions of the cortical follicles transformed into an almost uniform red mass, *i.e.*, swamped with blood, but also some of the medullary cylinders saturated with it. All the lymph-sinuses are in this case also filled with blood, and hence a very striking appearance is produced in some parts: the adenoid cylinders being still intact, while the lymph-sinuses between them and the connective-tissue trabeculæ, are much distended and filled with blood. We may say we have in some parts a very good injection of the lymph-channels with blood. In the cases in which I found (as above mentioned) in the extravasated blood of the sub-mucosa of the intestine the peculiar spherical granular lumps, I met also in the lymph-sinuses of the medulla the same spherical granular lumps. In some mesenteric glands some of the cortical as well as medullary sinuses are filled and distended by fibrin and granular débris, which materials also extend on to the adjacent adenoid tissue. I have seen glands, in which large portions of the adenoid tissue were entirely replaced by fibrin and granular débris.

In the glands from cases of somewhat longer duration, and where there has been extravasation of blood into the cortical adenoid tissue, we find the adenoid tissue in general considerably hypertrophied, and the lymph-sinuses filled with cells of different sizes and aspect. In mesenteric glands of some cases I have found enormous numbers of the giant cells filling up the lymph-sinuses of the medulla. These "giant cells" I can trace down to small granular cells with two or three elliptical clear nuclei, looking very much like epithelial cells. A very striking appearance is produced in some parts, when the lymph-sinuses of the medulla contain giant cells of various sizes closely arranged one at the side of the other: some of the larger ones, containing 20, 30, and more nuclei, seem to break down at their edges into small granular fragments. The connective tissue trabeculæ contain ordinary lymph-cells, and in some cases a great number of the coarsely granular deeply stained wanderers.

(4.) *Organs of Respiration.*—As has been mentioned, the epiglottis showed ulcerations only in a few cases. I have before me preparations through the epiglottis, the submucosa of the posterior surface being in a state of necrosis, and near the edge so broken down as to leave there a deep ulcer, while the mucous membrane of the anterior surface is only slightly inflamed in its submucous tissue: in this I find lymphatic vessels filled with micrococci, *i.e.*, uniformly granular masses stained conspicuously blue by hæmatoxylin, the "granules" becoming more distinct after treatment with caustic potash.

In addition to what has been said of the changes presented by the lungs, I have to mention that the lung is the seat of lobular pneumonia. The walls of the air-cells thickened by round cells and the cavities of the former containing lymph-cells, changed epithelial cells, and in some instances also smaller or larger "giant cells." In the last stages or higher degrees the inflamed tissue becomes transformed into a necrotic disintegrating mass. In the infiltrated, firm, more or less disintegrating parts I find great masses of micrococci filling up capillaries and veins and also contained in lymphatics around arteries. They may be found also in minor bronchi which have become completely blocked up by cheesy inflammatory products, but there the masses of micrococci, conspicuous by their blue colouration in hæmatoxylin preparations, are generally present in greater or smaller lumps between the outer surface of the plug and the wall of the bronchus. In one case I found ova

of Nematode worms in the tissue of the inflamed parts, and in the larger bronchi bundles of the worms themselves.

The pleura is much swollen, and contains great numbers, continuous layers, of lumps of micrococci. The free surface of the membrane is in many parts covered with them. The exudation fluid is also charged with them, as has been mentioned above. The lymphatic vessels of the surface of the lung (the subpleural vessels) are greatly distended and filled with fibrin; also the different trunks situated in the septa of lobes.

With regard to other organs, as particularly the liver, spleen, and kidney, my investigations are yet too incomplete for me to make definite statements; except as regards the liver, that its interlobular connective tissue is greatly altered, by infiltration with lymph-corpuscles, which at some parts form considerable accumulations, amounting almost to nodular new-growths. Similar accumulations of lymph-cells may be observed within the acini of the liver of more advanced cases.

APP. No. 4.

On Enteric or  
Typhoid Fever  
of the Pig, by  
Dr. Klein.