A STUDY OF PORCINE INTESTINAL ADENOMATOSIS

VOLUME II

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Figure 1  Normal intestine, with terminal ileum, caecum and proximal colon opened. Although Peyer's patches are prominent in the ileum (arrowed) no thickening of the mucosa is seen.

Figure 2  PIA - terminal ileum - thickening of wall and marked reticulation of the serosal surface.
Figure 3  PIA – terminal ileum – exaggerated transverse folding of the mucosa.

Figure 4  Portions of normal intestine (right) and intestine from a case of PIA (left). The adenomatous mucosa is thickened, nodular and shows exaggerated folding.
Figure 5  PIA - close up of a portion of adenomatous mucosa of Figure 4 to show the nodular appearance of the surface.

Figure 6  PIA - terminal ileum - firm, thickened with numerous soft red nodules on the serosal surface.
**Figure 7** RI - terminal ileum - thickened and rigid conforming to the classical descriptive term of "hose-pipe gut". Opened portion shows a linear ulcer (arrowed).

**Figure 8** Cross-sections of intestine from cases of PIA (right), RI (centre) and normal intestine (left). In both PIA and RI the wall is thickened; due to mucosal proliferation in PIA, and muscular hypertrophy and granulation tissue proliferation in RI.
Figure 9  PIA/RI - terminal ileum - opened intestine from a case showing features of both PIA and RI. The mucosal surface is ulcerated and composed of granulation tissue with raised nodules of adenomatous mucosa (arrowed) also present.

Figure 10  NE - terminal ileum - the affected length of intestine is thickened and easily recognised.
Figure 11  NE - terminal ileum - opened to show the thickened, grey-yellow necrotic mucosa.

Figure 12  Normal pig (young) - mid small intestine - short crypts and long, slender villi.  H. and E.  x 100.
Figure 13  Normal pig - terminal ileum - villi attenuated over Peyer's patches, and crypts extend deep into the underlying lymphoid tissue. H. and E. x 80.

Figure 14  Normal pig - large intestine - elongate crypts opening onto a flattened mucosal surface. H. and E. x 300.
Figure 15  PIA - terminal ileum - adenomatous change involving the whole mucosa.  
H. and E.  x 100.

Figure 16  PIA - terminal ileum - a collection of adenomatous glands deep within a lymphoid nodule of Peyer's patches.  
H. and E.  x 80.
Figure 17  PIA - Adenomatous glands with large, immature, non-mucus secreting cells. H. and E. x 250.

Figure 18  PIA - an adenomatous gland with both cell types present; i.e., those with open vesicular nucleii and those with elongate spindle-shaped nucleii. H. and E. x 500.
Figure 19 PIA - terminal ileum - adenomatous mucosa. The apical region of the epithelial cells in the adenomatous glands are densely silver stained, giving some indication of the large number of argyrophilic vibrios present in this site. Levaditi x 100.

Figure 20 PIA - argyrophilic, vibrio-shaped bacteria are present in the apical cytoplasm of the adenomatous epithelial cells. Levaditi x 340.
Figure 21  PIA – terminal ileum – the bases of the glands are irregular due to the protrusion of adenomatous epithelial cells (arrowed) into the surrounding lamina propria.
H. and E.  x 200.
Figure 22  PIA - terminal ileum - cords of epithelial cells infiltrating into the underlying sub-mucosa. Masson's Trichrome  x 100.
Figure 23  PIA - higher power view of Figure 22. The infiltrating epithelial cells are arranged as groups or attenuated cords. A developing connective tissue reaction is also present. Masson's Trichrome  x 200.
Figure 24  PIA - terminal ileum - infiltrating epithelial cells, not surrounded by connective tissue. H. and E. x 250.

Figure 25  PIA - terminal ileum - a tongue of infiltrating epithelial cells (arrowed) is seen protruding into the lumen of a lymphatic vessel. Martius Scarlet Blue x 500.
Figure 26  PIA - terminal ileum - a mass of epithelial cells almost occluding a lymphatic vessel. Note goblet cell formation.
H. and E.  x 500.

Figure 27  Normal intestine - terminal ileum - glandular mucosa over-lying Peyer's patches in close association with lymphoid tissue.
H. and E.  x 300.
Figure 28  PIA - terminal ileum - a clump of dysplastic epithelial cells within a lymphoid nodule of Peyer's patches.
H. and E.  x 200.

Figure 29  PIA - Peyer's patches, terminal ileum - a group of necrotic epithelial cells (arrowed) resembling a foreign-body giant cell.
H. and E.  x 625.
Figure 30  PIA - Peyer's patches, terminal ileum - a group of necrotic epithelial cells (arrowed) resembling a Langhan's giant cell. H. and E. x 625.

Figure 31  PIA - large intestine - apparently normal gland in the sub-mucosa. H. and E. x 250.
Figure 32  RI - terminal ileum - marked hypertrophy of the external muscle layers. The sub-mucosa shows extensive granulation tissue proliferation, with isolated glandular elements visible. H. and E.  x 25.

Figure 33  RI - higher power of Figure 32 showing groups of glands. H. and E.  x 80.
Figure 34 HE - large intestine - a massive surface coagulative necrosis and adenomatous glands are clearly visible in the underlying mucosa. H. and E. x 80.
**Figure 35** PIA - terminal ileum - in sections of adenomatous intestine stained in a sandwich technique with hyperimmune mucosalis anti-serum and F.I.T.C. conjugated G.A.R. There is specific particulate fluorescence in the apical cytoplasm of the adenomatous epithelial cells. x 100.
Figure 36 Normal small intestine - transverse section of crypt showing lumen, brush border, apical secretory granules and a goblet cell. x 6000.
Figure 37 Normal small intestine - crypt - poorly developed membrane systems with granular cytoplasm, mitochondria and limited numbers of microvilli. Numerous secretory granules.

x 15,000.
Figure 38  Normal small intestine - villous epithelium - the mature villous absorptive cells show well developed microvillous brush-borders, membrane systems, less free ribosomes and an absence of apical secretory granules. An intra-epithelial lymphocyte is present in this field.  

x 6,000.
Figure 39  Normal large intestine - transverse section crypt - sparse microvilli, apical granules, but no bacteria in either lumen or cytoplasm.  

x 10,000.
Figure 40  Normal large intestine - upper gland epithelium - in the apical cytoplasm numerous granules and lysosomes are visible.  
$x\ 15,000$. 
Figure 41 PIA - vibrio shaped bacteria (arrowed) are visible in the apical cytoplasm of the adenomatous epithelial cells. Toluidene blue x 2,000.
Figure 42  PIA - terminal ileum - low power electron micrograph of an adenomatous gland. Vibrio-shaped bacteria are visible in the apical cytoplasm of the epithelial cells, together with numerous secretory granules.

x 6,000.
Figure 43 PIA - terminal ileum - adenomatous epithelial cells resembling immature crypt cells and bacteria (arrowed) are present in the cytoplasm. Microvilli are very poorly developed and the cytoplasm is granular.

x 10,000.
Figure 44  PIA - higher power electron micrograph of the apical regions of adenomatous epithelial cells. In addition to the apical secretory granules there are bacteria (arrowed) free within the cytoplasm. x 20,000.
Figure 45  PIA - bacteria undergoing septate division in the cytoplasm of an adenomatous epithelial cell. 
$\times 60,000$. 
Figure 46  PIA - spherical particles in the cytoplasm which are believed to be coated vesicles.  
\[ x \times 200,000. \]
Figure 47  PIA - terminal ileum - an electron micrograph of infiltrating adenomatous epithelial cells which have formed a gland, lumen (arrowed) to top left. x 6,000.
Figure 48  PIA - a higher power electron micrograph of a cell in the gland depicted in Figure 47. Bacteria (arrowed) are present in the cell. x 30,000.
Figure 49  PIA - impression smear of adenomatous mucosa showing acid-fast organisms intracellularly and free. Modified Ziehl Neilsen  x 1,360.

Figure 50  Plate showing 48 hr. growth of *mucosalis* (left) and *E. coli* (right).
Figure 51 Smear of *mucosalis*.
Gram's x 1,360.

Figure 52 Smear of *C. coli*.
Gram's x 1,700.
Figure 53  T.S.I. - villous atrophy and crypt hyperplasia. H. and E.  x 100.

Figure 54  L.I. - increase in cells in the lamina propria and some glands contain inflammatory cell debris. H. and E.  x 80.
Figure 55  Small intestine - cryostat section stained by the sandwich technique with hyperimmune mucosalis antisera and F.I.T.C. conjugated G.A.R. showing specific particulate fluorescence within cells in the lamina propria.

x 100.

Figure 56  Higher power of Figure 55 to show the particulate nature of the fluorescence.

x 200.
Figure 57 Ileo-caeco-colic lymph node - foreign body and Langhan's type giant cells are visible. H. and E. x 200.

Figure 58 L.I. - glands lined by flattened cuboidal epithelium. H. and E. x 100.
Figure 59 Pig 123/76 - small intestine - villous atrophy and crypt hyperplasia. H. and E. x 100.
Figure 60  Pig 123/76 - large intestine - epithelium cuboidal, some lumen debris and few goblet cells. H. and E.  x 250.
Figure 61 Pig 140/76 - the large intestine is enlarged and shows a reticulated appearance (arrowed) from the serosal surface. The mucosa of the opened caecum is thrown into exaggerated folds, the tips of which have undergone necrosis.

Figure 62 Pig 140/76 - large intestine - the epithelium under the area of necrosis is immature and proliferating. Surrounding areas have a substantial goblet cell population. H. and E. x 80.
Figure 63  Pig 140/76 - large intestine - higher power of Figure 62 to show the adenomatous appearance of the surviving epithelium. H. and E. x 100.

Figure 64  Pig 156/76 - portions of small intestine and large intestine showing changes of NE and PIA respectively. Minute foci of necrosis are visible on the surface of the large intestine.
Figure 65 Pig 156/76 - small intestine - necrotic debris overlying an adenomatous mucosa. H. and E. x 100.

Figure 66 Pig 156/76 - small intestine - higher power of Figure 65 to show the adenomatous appearance of the underlying surviving epithelium. H. and E. x 250.
Figure 67  Pig 156/76 - large intestine - marked variation in gland morphology, only some glands adenomatous. H. and E.  x 100.
**Figure 68** Pig 183/76 - terminal small intestine - thickening of the mucosa involving both Peyer's patches and non-lymphoid areas.

**Figure 69** Pig 183/76 - large intestine - thickened mucosa with plaque-like appearance of the surface.
Figure 70  Mid small intestine - shows an isolated adenomatous gland.

H. and E.  x 250.
Figure 71  Large intestine - although the glands have an adenomatous form many contain a considerable number of goblet cells.
H. and E.  x 80.
Figure 72 Large intestine - an isolated adenomatous gland is present surrounded by glands with large numbers of mucus-secreting cells. H. and E. x 100.
**Figure 73**  Small intestine - villous atrophy and crypt hyperplasia. Occasional adenomatous glands present. H. and E.  x 80.

**Figure 74**  Terminal small intestine - adenomatous glands "growing out" of the mucosa. H. and E.  x 125.
Figure 75 Large intestine - isolated adenomatous glands are present. Note the increased number of mononuclear cells in the lamina propria. H. and E. x 100.
Figure 76  Small intestine - enlarged, branched hyperplastic glands with an almost entirely goblet cell population (arrowed) are present in the mucosa. H. and E. x 100.
Figure 77 Small intestine - "microscopic adenoma". H. and E. x 80.
Figure 78  Large intestine - adenomatous glands "growing out" of the mucosa.
H. and E.  x 80.
**Figure 79** Small intestine - adenomatous gland. In the surrounding lamina propria there is an increased number of cells, and infiltrating cells are also present in the epithelium and gland lumen. Toluidene blue $\times 625$. 
Figure 80  Small intestine – mucosa from a recovering PIA case. Eosinophilic inclusions (arrowed) are present within the epithelium of the glands. H. and E.  x 200.
Figure 81 Higher power of Figure 80, to show the eosinophilic inclusions in the epithelium of the adenomatous glands. H. and E. x 500.
Figure 82  PIA - terminal small intestine - low power to show the large numbers of argyrophilic bacteria present within the apical cytoplasm of affected epithelial cells, in phagocytic cells in the lamina propria, and in both phagocytic cells and desquamated epithelial cells in the gland lumina. Levaditi  x 200.

Figure 83  PIA - terminal small intestine - higher power to show the vibrio-shaped argyrophilic bacteria present in the affected epithelial cells. Clumping of the bacteria (arrowed) in this site can be seen. Young's  x 500.
Figure 84. Small intestine— in areas where the adenomatous glands are "growing out" bacteria are present only in the adenomatous glands, and not in the underlying histologically normal glands. Levaditi x 250.
Small intestine - isolated adenomatous glands are present containing argyrophilic vibrio-shaped bacteria. Phagocytic cells in the surrounding lamina propria contain similar organisms. The adjacent histologically normal glands contain no bacteria.

Levaditi x 625.
Figure 86  Small intestine - early stage of the recovery phase. Occasional membrane-bound bacteria (arrowed) are seen.

x 10,000.
Figure 87  Small intestine - intermediate stage of the recovery phase. Many of the bacteria are more electron dense and shrunken in appearance. x 7,000.
Figure 88  Higher power electron micrograph to show the more shrunken, electron-dense appearance of the organisms.

x 60,000.
Figure 89  Electron micrograph to show the thickening and increase in density of part of the cell wall in an organism in a recovering PIA case.  
\[ \times 60,000. \]
Figure 90  Small intestine – a clump of bacteria are present within a membrane-bound vesicle in the apical cytoplasm of an intestinal epithelial cell.  
  x 20,000.
Figure 91  Higher power of Figure 90.

x 40,000.
Figure 92  Small intestine - bacteria within a phagosome or phagolysosome (arrowed).
          x 6,000.
Figure 93  Small intestine - complex phagolysosomes within the epithelium of a recovering PIA case.  
  x 10,000.
Figure 94  Small intestine - apoptotic bodies present at the base of the epithelium during the recovery phase of PIA.

x 6,000.
Figure 95  Small intestine - apoptotic bodies (arrowed) present within macrophages in the lamina propria. x 6,000.
Figure 96 Small intestine - low power electron micrograph to show an apoptotic body (arrowed) situated basally in the epithelium, and apparently passing into the lamina propria.

x 6,000.
Figure 97 A higher power of Figure 96 to show the apoptotic body in the process of passing into the lamina propria. 

x 30,000.
Figure 98  Small intestine - an apoptotic body (arrowed) is present within a macrophage in the gland lumen. x 18,000.
Small intestine - bacteria, identical to those in adenomatous intestinal epithelial cells, are present in macrophages in the lamina propria. x 10,000.
Small intestine - bacteria are seen in close proximity to the luminal surface of the epithelial cells, and also within the gland lumen, both free and in desquamated epithelial cells. 

x 6,000.
Figure 101. Small intestine - darker staining apoptotic cells (arrowed) present in the epithelium of adenomatous glands during recovery. 

x 6,000.
Figure 102 Higher power of Figure 101 to show apoptotic bodies in a macrophage in the lamina propria. x 15,000.
Figure 103 Higher power of Figure 102 to show the detail of the densely staining apoptotic bodies, which are present in macrophages in the lamina propria. x 20,000.
Figure 104 Small intestine - an apoptotic cell (arrowed) in the process of being shed into the gland lumen. x 6,000.
Figure 105 Small intestine - a light-staining, swollen cell present in the epithelium of an adenomatous gland, in a recovering PIA case. x 10,000.
Figure 106 Small intestine - a light-staining, swollen cell in the process of being extruded into the lumen. x 10,000.
Figure 107 Small intestine - phagocytic cells present within the gland lumen. A neutrophil can be seen phagocytosing an organism (arrowed). x 6,000.
Figure 108: Small intestine - bacteria present within phagosomes or phagolysosomes in a neutrophil polymorph in the gland lumen. x 15,000.
Figure 109 Small intestine - A macrophage in the process of apparently engulfing an epithelial cell, within the gland lumen.

x 10,000.
Figure 110 Small intestine - an electron micrograph to show the increased number of cells present in the lamina propria, including macrophages, eosinophils, neutrophils, plasma cells and lymphocytes. The outline of glands are present at the top left and bottom left of the picture. x 6,000.
Figure 111 Small intestine - an adenomatous gland in a recovering PIA case. In addition to the adenomatous epithelial cells there are mucus-secreting cells present, and more mature epithelial cells which do not contain bacteria. x 6,000.
Figure 112 Small intestine - more mature epithelial cells with only a few bacteria present and a well-developed microvillous brush-border and cytoplasmic membrane systems are evident. x 15,000.
Figure 113 Small intestine - in adenomatous glands with goblet cells the fluorescence is confined to the non-mucus-secreting epithelial cells. Cryostat section stained with mucosalis anti-serum and F.I.T.C. conjugated G.A.R. x 600.

Figure 114 Small intestine - cells containing specific fluorescence are present in the lamina propria and gland lumen. Cryostat section stained with mucosalis anti-serum and F.I.T.C. conjugated G.A.R. x 800.
Figure 115 In the adenomatous epithelium there are non-epithelial cells (macrophages) containing specific fluorescence. A cryostat section stained with mucosalis anti-serum and F.I.T.C. conjugated G.A.R.

x 350.
Figure 116 PBE - small intestine - a low power photomicrograph to demonstrate the underlying adenomatous appearance of the mucosa in these cases. H. and E. x 100.
Figure 117 PHE - small intestine - the glands at the base of the mucosa in this section contain a number of goblet cells.
H. and E. x 80.
Figure 118 PHE - small intestine - epithelial cells are being lost from the mucosa and in this area free red blood cells are seen in the gland lumen. H. and E. x 200.

Figure 119 PHE - small intestine - early villus formation is seen and goblet cells are present in the underlying adenomatous glands. H. and E. x 100.
Figure 120 PHE - small intestine - cells are present in the gland lumen and migrating through the epithelium.
Toluidine blue x 625.
Figure 121 PHE - small intestine - the apical cytoplasm of affected epithelial cells is packed with bacteria morphologically resembling mucosalis. The cells are damaged and bacteria are escaping from the luminal surface.

x 10,000.
Figure 122 PHE - small intestine - in some of the adenomatous glands there are goblet cells present. x 15,000.
Figure 123 PHE - small intestine - neutrophils and macrophages containing bacteria, identical to those present in the epithelium, are seen in the gland lumen.

x 6,000.
Figure 124 PHE - small intestine - higher power of Figure 123 to show bacteria within phagosomes or phagolysosomes in a neutrophil in the gland lumen. x 15,000.
Figure 125 PHE - small intestine - high power electron micrograph of the organisms in an intestinal epithelial cell. 

x 40,000.