Renal Neoplastic Response to Leukosis Virus Strains BAI A (Avian Myeloblastosis Virus) and MC29

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SUMMARY

Previous reports described the induction of avian renal neoplasms by leukosis virus strains BAI A [avian myeloblastosis virus (AMV)] and MC29, and illustrated morphological characteristics of the tumors. Continued studies in this work confirm evidence of the origin of the tumors from embryonal cells residual in the posthatched chick. The work further emphasizes differences in histopathology of the neoplasms caused by the two viruses and reveals differences in the histopathogenesis of the respective growths. Embryonal rests may consist of two types of cells, those of epithelial characteristics and a second element of differentiation between nephroblastema (mesenchyme) and epithelium and designated here as nephromesoblastoma. Infection by AMV induces tumors of epithelial characteristics and, in addition, derivatives of nephromesoblastoma consisting of cartilage, bone, areas of keratinization, and sarcoma. Keratinized structures in the nephroblastoma originate from nephromesoblastoma. In contrast, MC29 virus induces only epithelial growths representing principally aberrant and malformed glomerular and tubular structures with occasional cartilage derived from epithelial cells. MC29 tumors are completely lacking in nephromesoblastoma tissue and contain no bone, sarcoma, or keratinized formations. In MC29 tumors, occasional cartilage was derived from epithelium. Tumors caused by AMV exhibit the complex structure of nephroblastoma with all of the features of the growth in humans (Wilms' tumor) and designated as nephroblastoma, closely resemble the Wilms' tumor of man.

INTRODUCTION

Renal neoplasms occur frequently in chickens diseased with avian tumor viruses, both with agents passed repeatedly in the laboratory (2, 3, 9-11, 13, 14, 17, 19, 22) and, also, with strains newly isolated (7, 22) from field cases. Nevertheless, consideration of the histopathogenesis of the growths has been relatively limited. As an exception, the neoplasm in birds diseased with BAI strain A (AMV) has attracted much attention (2, 10, 12). Studies by light (12) and electron microscopy (10) revealed complex growth comprising epithelial structures mimicking, to varying degrees, normal nephric elements; deposits of cartilage and bone; and, "pearl"-like formations of keratinizing cells; and spindle-cell masses resembling fibrosarcoma. Such neoplasms, designated as nephroblastoma, closely resemble the Wilms' tumor of man.

In contrast, renal tumors associated with infection with MC29 (myelocytomatosis virus) (13, 19) consisted principally of epithelial structures, with only occasional small deposits of cartilage, and thus were strikingly different from those induced by AMV. Virus-induced avian neoplasms with the features of the nephroblastoma have been reported thus far only in association with AMV, whereas other types of renal growths in birds diseased with other avian tumor viruses (3, 14, 16, 22), and often improperly termed (22) nephroblastomas, are similar in principle to the neoplasms found in chicks with MC29 myelocytomatosis. Growth such as those found in MC29-diseased birds are designated as renal adenoma and renal adenocarcinoma by many pathologists (6, 18).

To learn more of the nature of the growths and the basis for the striking differences between the 2 types of neoplasms, further studies have been made on both the AMV nephroblastoma and on the tumors induced by strain MC29. This report describes aspects of histopathogenesis not previously emphasized and illustrates additional characteristics of histopathology, especially that of the MC29 growth. Moreover, the large number of growths provided the material for further exemplification of the potentials of primordial renal cells for alteration and abnormal differentiation. The findings are of significance, also, in their bearing on oncogenic specificity of individual avian tumor virus strains.

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J. W. Beard et al.

MATERIALS AND METHODS

Viruses. Derivation of MC29 virus and the experiments yielding the renal tumors induced by the agent were described (13, 19). Virus in most of the specimens of plasma from MC29-diseased birds was passed through 0.2-Selas filters (Selas Corporation, Philadelphia, Pa.). Fluids from tissue cultures of the virus in chick embryo cell monolayer cultures (11, 15) were passed through 1.2-µm Millipore filters (Millipore Filter Corporation, Bedford, Mass.). Preparations of AMV and their application to the production of renal tumors were also described (10, 12). Except for 1 series of experiments, designated as Experiment 2, growths used in the present work were of the same group (Experiment 1) previously examined (10, 12). The agent for production of the other AMV neoplasms (Experiment 2) was derived from fluid of chick embryo cell cultures infected by virus-free extracts of AMV ribonucleoprotein (26). Virus transmitted in vitro by certain fractions of the ribonucleoprotein extract and inoculated i.v. in young chicks (Experiment 2) induced myeloblastosis and, as the untreated agent, tumors of the kidney and other growths as well. In some of the experiments of this series (Ref. 26, Table 1), cells of the tissue cultures producing virus transmitted by the ribonucleoprotein extracts were inoculated into the test chickens.

Numbers of virus particles in blood plasma of birds diseased with AMV were estimated by ATPase activity (12). Enumeration of virus particles in the blood plasma of birds with myelocytomatosis or in the supernatant fluid of chick embryo cultures infected with MC29 virus was effected by sedimentation on agar and counts of the particles in the electron microscope (25).

Chickens. Test birds used in the experiments with MC29 virus were either line 15 inbred White Leghorns (Regional Poultry Research Laboratory, East Lansing, Mich.) from the laboratory laying flock (5) at Duke University, or Shaver strain White Leghorns (Shaver Poultry Breeding Farms, Ltd., Galt, Ontario, Canada), obtained from the Central Carolina Farmer’s Exchange, Durham, N. C. Except for special studies, inoculations of the materials were made i.v. in volumes of 0.1 to 0.5 ml in chicks 1 to 5 days old. Blood smears were made daily or at other intervals appropriate for following changes in the circulating cells indicative of the course of the disease. Chickens used in the study of AMV, including the work with virus transmitted in chick embryo cell cultures by ribonucleoprotein extracts (26), were also line 15 White Leghorns.

Specimen Preparation. Autopsy specimens from birds dying spontaneously or killed by bleeding from the heart were fixed in Zenker-formol solution, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Specimens of MC29 growths taken for electron microscopy were fixed in 2% glutaraldehyde buffered at pH 7.2 with 0.1 M sodium cacodylate (24), postfixed with 1% osmic acid buffered at pH 7.2 with Veronal (20), and embedded in Maraglas (8). Sections were cut with glass knives on a Porter-Blum ultramicrotome, stained with uranyl acetate and lead citrate (23), and examined in a Siemens Elmiskop I.

In most of the earlier studies (Experiment 1), AMV growths were fixed with 1% osmic acid and embedded in methacrylate or Epon, and sections cut with glass knives on a Porter-Blum ultramicrotome were stained with lead acetate or uranyl acetate. Specimens from Experiment 2 were embedded in Maraglas, and the sections were stained routinely with both uranyl acetate and lead citrate.

RESULTS

Specimens of AMV nephroblastoma were available from 64 birds, about 8% of a group of 792 chickens (Experiment 1), as previously tabulated (12). This incidence involves only the number of birds not dying early of myeloblastosis and thus does not reflect the susceptibility of the total population to development of nephroblastoma (see Ref. 12, Text-Figure 1). For this reason, a relationship between incidence of growths and the number of virus particles in the inoculum of blood plasma was not clearly discernible despite 100-fold variations (from $10^4$ to $10^6$ particles per dose per bird) in different experiments. Another series of nephroblastomas in 33 birds was derived from the studies on transmission of AMV by ribonucleoprotein extracted from the agent (Experiment 2), as indicated in Table 1 of Ref. 26.

MC29 growths were obtained from the same series of approximately 3086 birds providing primary hepatic tumors of the type described in Ref. 1. From the group of 100 chickens in a single experiment (1), renal growths occurred in 22 of the birds inoculated. Nevertheless, the values cited represent only general approximations, since the incidence of the growths induced by either AMV or MC29 varied greatly with the conditions of study, including age and genetic constitution of the chickens and route of inoculation, as well as the dose of the respective agents. Survival of birds with myelocytomatosis was relatively long (Table 1), and the influence of dose on renal tumor incidence could be clearly distinguished. As an example, 4 groups of 10 birds inoculated, respectively, with $10^4$, $10^5$, $10^6$, and $10^7$ MC29 virus particles from tissue culture yielded 8, 4, 3, and 2 birds with growths in the respective groups. Other like experiments gave similar results.

Gross Characteristics. Occurrence and gross characteristics of the neoplasms reveal at once major differences between the AMV (Fig. 1) and MC29 (Figs. 2 and 3) renal growths. In a series of 1760 animals inoculated with AMV or transplanted i.m. with renal tumor tissue as described (12), growths occurred in 180 birds. Of these, tumors were unilateral in 105 birds, with an approximately equal distribution between the right and left organs. Growths were bilateral in 75 growths. In a series of 1760 animals inoculated with AMV or transplanted i.m. with renal tumor tissue as described (12), growths occurred in 180 birds. Of these, tumors were unilateral in 105 birds, with an approximately equal distribution between the right and left organs. Growths were bilateral in the other 75 chickens with 1 tumor or 2 or more tumors in each organ. Essentially all neoplasms were in the superficial cortex or even pedunculated (12). Some encroached on adjacent renal tissue with destruction due to pressure rather than invasion or erosion. Size varied from minute nodules to masses several inches in diameter. Some growths were soft, and others were hard with much cartilage (Fig. 11). Many were lobulated, and others contained small cysts with serous or hemorrhagic fluid. The survey
Table 1

Primary tumors in the kidneys of 22 of 100 chicks (M1 to M100) inoculated i.v. with strain MC29 avian leukosis virus in Experiment 1159 (March 26, 1971)

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* DPI, days postinoculation; GRO, neoplastic alterations of embryonic-rest structures; ADE, adenocarcinoma; SOL, compact growth without discernible pattern; TUB, tubular carcinomas. L, R, and B indicate growths in left, right, or both kidneys.

pictures (Figs. 11 to 13) showed the broad spectrum of neoplastic tissues, ranging from masses of cartilage, bone, epithelial growth of tubules, and various epithelial structures, to the ubiquitous nephromesoblastic tissue (Figs. 11 to 14). The growths consisted of varying proportions of the different tissues, some with large or-sparse growth extending deeply into separate interlobular fissures (Figs. 28 and 31).

Histogenesis. Histological studies of many primary renal tumors have consistently indicated that the growths induced by both AMV and MC29 arise in nephrogenic postembryonal rests. Such growths can be readily traced from inception as barely recognizable foci of aberrant cells through the processes resulting in well-developed neoplasms (12, 19). Although the tumors originate from residual embryonal structures, it is of critical significance to recognize that the host cell type responding is characteristic for the respective AMV and MC29 agents. This feature of origin probably accounts for the major distinctions in the pathomorphology of the 2 types of neoplasms described here.

AMV Nephroblastoma. Embryonal rests in the post-hatched chick closely resemble analogous structures in man (4). The most primitive formations (Ref. 21, Fig. 2) are remnants of collecting ductules immediately surrounded by nephrogenic cells embedded in a matrix of nephromesoblastic elements (Fig. 4). From these develop the more differentiated S-forms like those (Fig. 5) in the human embryo (Ref. 21, Fig. 3). The most primitive precursors of the AMV nephroblastoma (Figs. 6 and 7) consist of differentiating epithelial structures, together with a matrix of nephromesoblastic cells like those seen in Fig. 4. Morphology of the structures in Figs. 4 to 7 (Ref. 10, Figs. 24 and 25) is more evident in the survey electron micrographs (Figs. 8 and 9) of a nephroblastoma from a 2-year-old child. Fig. 8 shows the epithelial features of a collecting tubule, together with primitive nephroblastoma and cells exhibiting characteristics transitional between mesenchymal and epithelial elements derived by differential alteration of nephroblastema. This type of growth, derived by an essentially specific aspect of differentiation of nephroblastema and designated as nephromesoblastoma, is a neoplastic characterizing feature of the nephroblastoma from which a variety of structures originate. Morphology of the nephromesoblastoma growth in the human nephroblastoma (Fig. 10) is indistinguishable from that in the chick (Figs. 4, 6, and 7).

Earlier studies (10, 12) revealed the variety of neoplastic tissues comprising the nephroblastoma, including structures closely mimicking all aspects of the nephron as well as cartilage, bone, spindle-cell growths, and “epithelial pearls” embedded in the ubiquitous nephromesoblastoma tissue (Figs. 11 to 14). The growths consisted of varying proportions of the different tissues, some with large amounts of cartilage (Figs. 11 and 14) and others with more or less prominent tubular formations mixed with nephromesoblastoma (Figs. 12, 13, 19, and 20). A notable feature of the nephroblastoma are the epithelial pearls (Figs. 15 to 17), which were initially (10, 12) regarded as derivatives of epithelial elements. The present studies have demonstrated origin of the structures by alteration of cells of the nephromesoblastoma to epithelial type and squamous cells which progress to keratinization. Figs. 15 to 17 illustrate the pro-
gressive changes of the nephromesoblastoma to epithelial cell differentiation preceding onset of squamous cell development and keratinization. A particularly illuminating example of alteration of nephromesoblastoma to cartilage is demonstrated by the minute growth shown in Fig. 18.

Diversity of epithelial structures also reveals the remarkable capacity of derivatives of nephroblastoma for alterations in morphology and organization. This is evident in tubular formations (Figs. 19 and 20) and in the tubular and papillary carcinomas illustrated in Figs. 21 to 24. Manifestations of abortive glomerular differentiation (see Ref. 10, Fig. 1, for structure of a normal glomerular corpuscle) are shown in Figs. 25 to 27. Some of the structures strongly resemble squamous cells, as discussed later. The formations in Figs. 25 to 27 exhibit pronounced aberrations in the differentiation of tissues simulating the analogous features of the developing normal glomerular corpuscle (10).

**MC29 Nephroma.** MC29 renal tumors differ strikingly from AMV growths in the display of a somewhat less complex histogenesis and variety of histomorphology than the corresponding features of the AMV tumor. In contrast to the organs with AMV neoplasms, the kidneys are frequently massively involved and almost completely replaced by neoplastic tissue, as seen in the photographs of slices (Fig. 28) of a single kidney taken at different levels. The significant aspect of the MC29 growths is the derivation of this alteration of epithelial cells of the embryonal rests without indication of participation of nonepithelial cells such as the nephromesoblastoma shown in Figs. 4, 6, and 7.

As already mentioned, a singular feature of renal response to MC29 virus is the enormous number of foci of embryonal rests, which must number in the hundreds or thousands in some organs, to judge from those seen both around the cortex and deep within the renal tissue in a single section. The onset of hyperplasia (Fig. 29) consists of the appearance of tubular or primitive glomerular processes (Figs. 29 to 31) resembling analogous structures in the embryonal rests associated with AMV growths. A conspicuous feature of the progressive neoplasia is the absence of the mesenchyme-like nephroblastoma or nephromesoblastoma in all of the MC29 growths thus far studied. Embryonal rests responding to MC29 virus varied from minute foci of a few pseudoglomeruli and abnormal tubules (Figs. 29 and 30) to lengthy groups and strips of primitive growth of these characteristics extending long distances in the cortex or along lobular surfaces deep in the kidney tissue (Fig. 31). Primitive glomeruli (Figs. 29 to 31) frequently occur in very large numbers including not only the parietal cells but, also, outstanding growth of visceral cells and central mass cells which form large tumors such as the growth illustrated in Fig. 31. A minute growth (Fig. 32) shows hemorrhage within a pseudoglomerular corpuscle which accounts for many of the small red growths seen in some kidneys (Fig. 3).

In the same manner as in the nephroblastoma, epithelial cells responding to MC29 virus show remarkable capacity for variation in differentiation to yield formations of singular morphology. Fig. 33 represents the principal features of a very aberrant glomerular corpuscle consisting of highly abnormal columnar cells. Analogous malformations (Fig. 34) occur in the distorted forms of differentiation of tubule cells with a distinct resemblance to squamous epithelium and marked metaplastic alterations (Fig. 35). Diversity of tubule cell differentiation and growth result in tubular or papillary carcinomas (Figs. 36 and 37) and in solid tumors or adenocarcinomas (Figs. 38 and 39) which may occupy or replace large portions of the kidney (Fig. 28). Tubular growths occur frequently (Fig. 28), and the form and distribution of some cells suggest resemblance to extremely malformed glomerular corpuscles.

The histology of neoplasms derived by neoplastic development of the pseudoglomeruli as seen in light micrographs, such as those in Figs. 30, 31, and Fig. 40, inset, is revealed in the survey electron micrograph of low magnification in Fig. 40. The picture shows the major part of an aberrant glomerulus with essentially all elements (10), including Bowman's capsule, primitive podocytes, capillaries and, in large numbers, the accumulation of central mass cells as exemplified by the light micrograph of the inset.

Cartilage occurred in a few MC29 growths (Fig. 28), but the origin differed from that formed in the AMV nephroblastoma. In the MC29 growth, cartilage arose by morphological alteration of epithelial cells (Fig. 41) instead of from the nephromesoblastoma in the AMV tumors, as indicated by a comparison of Figs. 40 and 18. Walls of the cystic structures enclosing many MC29 growths (Fig. 2) consisted of endothelial cells (Fig. 42). Other growths occurring rather frequently in MC29 neoplasms were hemangiomas and endotheliomas (Fig. 43).

The extremes of alteration of tubular cells from the normal morphology to the primitive differentiation of representative structures of distal (Fig. 44), proximal (Fig. 45), and unidentified tubules (Fig. 46) are illustrated in the electron micrographs of the figures indicated. Loss of the differentiation of the normal structure is greater in these growths than in those previously described (19).

**DISCUSSION**

Comparisons of AMV and MC29 renal tumors have confirmed and emphasized major differences (10, 12, 19) between the 2 types of growths and the remarkable variations in the morphological alterations and organization of the cells comprising the neoplasms. Although renal growths in birds diseased with avian tumor viruses arise from embryonal rests, AMV and MC29 neoplasms differ significantly in histology dependent, apparently, on the character of the cells responding to the respective agents. In the AMV growths, it would appear that both residual epithelial and nephromesoblastoma cells respond, whereas the MC29 tumors consist only of epithelial structures with occasional cartilage but without evidence of nephromesoblastoma. Hyperplastic response of embryonal rests in MC29-affected kidneys was much more extensive than in birds with AMV disease due, probably, to far greater susceptibility and growth response of the primitive cells to MC29 virus than to AMV. This would suggest that the number of embryonal rests in the young chick might far exceed the number identifiable by microscopic methods or response to AMV.

It is not unexpected that epithelial growths would arise...
from epithelial elements in the embryonal rests. In previous work (10, 12), it was shown that bone and cartilage were derived from the mesenchymal (nephromesoblastic) tissue, but it seemed apparent that spindle cell tumors also might arise from altered epithelial cells. An unexpected finding in the MC29 growths was evidence of the origin of cartilage from epithelial structures. Derivation of epithelial pearls with keratinization was initially obscure (12), but in the present work, these AMV tumor structures were traced to morphologically altered nephromesoblastoma tissue without evidence of a relationship to recognizable epithelium. This might well explain the absence of such formations in the MC29 tumors, which lacked the nephromesoblastic tissue.

In the AMV nephroblastoma, epithelial growth varied from complete though aberrant glomerular cupules through the range of essentially all forms of nephron tubules. Epithelial growth in the MC29 tumors likewise resulted in malformed glomeruli and tubules, many of which lost identity and developed solid carcinomatoses neoplasms with little evidence of residual tubules. The remarkable capacities of the nephrogenic cells for variation were particularly evident in the abortive attempts of the cells to form glomerular cupules. Cells of some exceptional malformations were columnar or cuboidal, and some exhibited the staining and morphological appearance of squamous cells. Resemblance of some elements to squamous cell growths may not be too surprising. Squamous cell carcinoma is a prominent neoplasm of the renal pelvis, and collecting tubules occur also in the body of the kidney (6). Potentials for this type of growth might be conferred by the collecting tubules in their influence on nephroblastoma or might be due to ductule cells displaced during ontogenesis. Tubular adenocarcinomas, papillary cyst adenocarcinomas, and solid adenocarcinomas were of frequent occurrence, especially in the MC29 tumors.

With respect to the etiological viruses, the findings revealed a marked specificity in host-virus interaction and response to the respective AMV and MC29 agents. Such specificity with respect to MC29 virus, compared with other avian tumor viruses, was outstanding also in the induction of primary tumors of the liver (1). In the liver, apparently fully differentiated parenchymal cells responded, but cells of the biliary system did not. A distinct parallelism in the kidney was the response of both epithelial and nephromesoblastoma cells to AMV, compared with the response of only epithelial nephrogenic cells to MC29. Pronounced variations in hepatocyte morphology in the formation of different tumor types were the same in principle as those manifested in the renal growths. In both liver and renal tumors, virus specificity with respect to etiology was limited to initiation of growth. However, predominant characteristics of the growths were governed and directed principally by the genetic characteristics (4) inherent in the nephroblastoma. This is shown further by the similarity of tumors caused by many agents (9) to neoplasms produced by the viruses. It has been a matter of experience (9) that renal tumors are of similar morphology in the varieties of animals observed. Among these, the predominant type is by far the adenomatous or epithelial growth, compared with the nephroblastoma or Wilms'-like neoplasm, which is relatively rare except under special conditions. B1 strain A virus invariably induces nephroblastoma, whereas growths associated with avian tumor viruses other than AMV are always described, although not always designated, as adenoma or adenocarcinoma such as those induced by the MC29 agent. The MC29 and other analogous strains have never produced tumors of the morphology of the nephroblastoma.

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Figs. 1 to 46. All figures, except electron micrographs, were stained with H & E. DPI, days postinoculation.

Fig. 1. Nephroblastoma from bird diseased with AMV (C879; DPI, 102) shows structural irregularities and tumor masses in the surface of the growth cut in half. × 1.6.

Fig. 2. Kidneys from bird (×681; DPI, 30) diseased with MC29 virus illustrate cystic covering of the large growths in the organ from the right side and the smaller growths on the left. × 1.5.

Fig. 3. Growths in both MC29-infected kidneys (X970; DPI, 112) showing involvement of whole organs and illustrating small red nodules (see Fig. 32) protruding above the surface of the kidney on the left and the numerous growths in the organ on the right. × 1.2.
Renal Tumors Induced by MC29 and AMV Leukosis Viruses

Fig. 4. Primitive formation of embryonal rest in bird (C205; DPI, 94) with AMV nephroblastoma showing ureteral bud (CT) (see Fig. 8) surrounded by nephromesoblastoma (see Fig. 25). x 800.

Fig. 5. S-form of primitive nephron in a bird with AMV nephroblastoma (C205; DPI, 94) attached to collecting tubule (AT) enclosed in developing Bowman's capsule (K) x 800.

Fig. 6. Embryonal rest in newly hatched normal chick illustrating early differentiation resembling S-form of developing glomerulus (CT), epithelial cells of primordia (N), and associated incompletely differentiated nephroblastoma (nephromesoblastoma) (EO). x 750.

Fig. 7. Micrograph of another structure in same chick as that of Fig. 6 showing a primitive glomerular corpuscle (arrow) surrounded by partly differentiated nephroblastema (nephromesoblastoma) (EO). x 350.

Fig. 8. Electron micrograph of primitive collecting tubule (CT) and nephromesoblastoma (EO) derived from undifferentiated blastema (arrows) in a nephroblastoma from a 2-year-old child. x 400.

Fig. 9. Survey electron micrograph of nephromesoblastoma (EO) from same human growth as that of Fig. 8. x 6000.

Fig. 10. Light micrograph of nephromesoblastoma (EO) of human nephroblastoma. x 400.

Fig. 11. Photographs of sections of AMV nephroblastoma (C205; DPI, 94) illustrate large amounts of cartilage (a), nephromesoblastoma (eo), bone (os), and the location of an epithelial pearl (pe). x 5.

Fig. 12. Photograph of section of AMV nephroblastoma (C555; DPI, 90) consisting of tubular growths (arrow; see Fig. 19) and nephromesoblastoma (eo). x 4.

Fig. 13. AMV nephroblastoma (C333; DPI, 105) consisting of widely distributed tubular growths (arrow; see Fig. 20) and massed, well-differentiated tubules in another area of the same growth. x 4.

Fig. 14. Survey micrograph of AMV nephroblastoma (C884; DPI, 77) illustrating variety of growths including bone (OS), cartilage (C), epithelial pearls (pe) (see Fig. 17), altered nephromesoblastoma cells (a), tubules and glandular structures, and basic growth of nephromesoblastoma (EO). x 80.

Fig. 15. The micrograph of an AMV nephroblastoma (C833; DPI, 105) with inset (C884; DPI, 77) illustrates alteration of nephromesoblastoma cells to epithelial elements (a) with transformation to squamous-type cells (b, c, and inset) followed by death and keratinization of central cells (d). x 400.

Fig. 16. A very small focus of altered nephromesoblastoma cells (W010; DPI, 84) illustrates squamous-type cells and onset of keratinization. x 800.

Fig. 17. A characteristic epithelial pearl formation represents a higher magnification of the structure (pe) in the nephroblastoma of Fig. 14 and illustrates epithelial elements (arrow) transitional in differentiation from nephromesoblastoma to the squamous cell type associated with keratinization. x 400.

Fig. 18. A minute growth (C884; DPI, 77) shows alteration of nephromesoblastoma cells directly to cartilage (c) without transitional stages of differentiation. x 400.

Fig. 19. Massed tubular growth in AMV nephroblastoma like that of Fig. 12 (W05; DPI, 84) consists of well-differentiated structures embedded in nephromesoblastoma tissue. x 400.

Fig. 20. Groups of tubules are sparsely distributed in the nephromesoblastoma (EO) of C933 (DPI, 105) as indicated (arrow) in the portion of the tumor to the left in Fig. 13. x 400.

Fig. 21. A tubular type of adenoma in an AMV nephroblastoma (C368; DPI, 97) illustrates papillary processes bounded by columnar or cuboidal cells. x 200.

Fig. 22. Characteristics of the growth of Fig. 21 are illustrated at higher magnification. x 400.

Fig. 23. Another type of tubular adenoma in an AMV nephroblastoma (W03; DPI, 102) is entirely different from that of Figs. 21 and 22. x 400.

Fig. 24. Tubules (C928; DPI, 92) in an unusual formation in an AMV nephroblastoma are bounded by walls of squamous-type cells. Inset, abortive glomerular formation of the same type of cells. The structure at the right (arrow) in a portion of a different type of tubule (see Fig. 27) associated with abortive glomerular formation. x 800.

Fig. 25. An exceedingly aberrant differentiation of cells resembling the squamous type in an AMV nephroblastoma (C971; DPI, 141) has the appearance of a carcinoma of a glomerular corpuscle with Bowman's capsule (K) and the layer of squamous-like cells simulating the visceral (VL) layer of podocytes. x 400.

Fig. 26. Mass of squamous-like cells in pseudoglomerular corpuscle in another region of the specimen of Fig. 25. x 400.

Fig. 27. An unusual type of pseudoglomerular corpuscle formation in an AMV nephroblastoma (C928; DPI, 92) with columnar-cell structure simulating the parietal boundary (K) and the presumably visceral layer of undifferentiated podocytes (arrow). x 400.

Fig. 28. Photographs of transverse sections of a single kidney from a bird (Y17; DPI, 115) with MC29 virus disease show extent of involvement with different growths: (a) small masses of cartilage; (b) tubular carcinoma resembling the growth shown in Fig. 36; (c) tubular adenocarcinoma like that in Fig. 37; (d) solid adenocarcinoma of packed tubule alterations as in Figs. 38 and 39; (e) remnants of essentially normal renal tissue; (f) cyst wall consisting of endothelial cells (see Fig. 42); (g) small hemangioma (see Fig. 43); (h) beginning embryonal rest alterations (see Figs. 29, 30, and 32); and (i) a minute tubular carcinoma (see Figs. 36 and 37). x 24.

Fig. 29. An initial stage of MC29 tumor growth (Y95; DPI, 35) illustrates malformed primitive S-forms (arrow) (see Fig. 5) and aberrant glomerular corpuscles immediately beneath the cortex. x 400.

Fig. 30. An MC29 virus growth (U398; DPI, 29) analogous to that of Fig. 29 shows more primitive forms of glomerular corpuscles (G) lacking organization and differentiation of component structures (see Figs. 40 and inset). x 600.

Fig. 31. A mass of MC29 growth consists of undifferentiated primitive glomerular corpuscles (see Figs. 29 and 40) (U418; DPI, 39) located deep in kidney substance. x 80.

Fig. 32. A primitive glomerular corpuscle in a beginning MC29 growth (V774; DPI, 32) illustrates hemorrhage into a developing pseudoglomerular corpuscle responsible for most of the "red nodules" in the superficial cortex (see growths in kidney at the left in Fig. 3). x 200.

Fig. 33. An abortive form of a glomerular corpuscle in an MC29 growth (Y56; DPI, 44) resembling the caricature of the analogous AMV tumor structure (Fig. 25) shows parietal layer of columnar and cuboidal cells corresponding to Bowman's capsule (K) and the malformed visceral layer (arrow) consisting of cells of similar morphology. x 400.

Fig. 34. Tubules in the MC29 growth in Z296 (DPI, 63) are bounded by elements of squamous-cell appearance resembling some structures seen in the AMV nephroblastoma (see Figs. 24 and 25). x 400.

Fig. 35. A portion of an MC29 growth (V99; DPI, 45) shows developing disorganization of a tubule structure with morphology transitional between that of Figs. 34 and tubular carcinoma. x 400.

Fig. 36. Micrograph illustrates a type of tubular carcinoma (Z306; DPI, 35) occurring often in MC29 renal tumors (see Fig. 28). x 400.

Fig. 37. Micrograph shows an example of an MC29 papillary tubular carcinoma (Z296; DPI, 63) somewhat similar to analogous growths in some AMV nephroblastomas (see Fig. 23). x 400.

Fig. 38. MC29 adenocarcinoma (U759; DPI, 39) has developed from tubular structures (see electron micrographs, Figs. 44 to 46). x 400.

Fig. 39. Another MC29 adenocarcinoma (Z14; DPI, 35) was derived from tubular structures resembling those in Fig. 38 (see Figs. 44 to 46). x 400.

Fig. 40. Survey electron micrograph (U398; DPI, 29) of an abortive glomerular corpuscle representing all usual components including Bowman's capsule (K), malformed podocytes (P), and mass cells (M). Large numbers of virus particles (V) are trapped in the structure. The electron micrograph illustrates the structures (G) shown in the inset (U743; DPI, 24) and in Figs. 30 and 31. x 3000.

Fig. 41. The micrograph shows derivation of cartilage (C) from epithelial cells (ep) of a disrupted tubule. x 800.

Fig. 42. Electron micrograph of a disrupted tubule (EN) line the walls of the cyst surrounding the MC29 tumor in V760; DPI, 56 (see Figs. 2 and 28). x 800.

Fig. 43. The micrograph shows the structure of a small hemangioma with associated endothelium (EN) in V285; DPI, 26 (see Fig. 28). x 400.

Fig. 44. An electron micrograph of an adenocarcinoma in V306 (DPI, 31) consists of disorganized, greatly altered cells of a distal convoluted tubule. The tissue contains many virus particles (V). x 6000.

Fig. 45. An adenocarcinoma in V793 (DPI, 48) shows disorganization and greatly altered differentiation of proximal convoluted tubule with loss of brush border. x 6000.

Fig. 46. An adenocarcinoma (V306; DPI, 31) of an unidentified tubular structure illustrates marked alterations of cell structure and organization and the presence of masses of virus particles (V). x 6000.
Renal Tumors Induced by MC29 and AMV Leukosis Viruses

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Renal Neoplastic Response to Leukosis Virus Strains BAI A (Avian Myeloblastosis Virus) and MC29

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