STAGE REPORT - 2012

Epidemiological study of the research

During the project were investigated 121 dog's cadavers with different pathological disorders to identify the eventual renal disorders in the context of the disease. Thus, were macroscopically, histological and electron microscopically examined the kidneys from 163 dog's cadavers with various pathological processes:

Diseases	**Pathogen agent (disease)**	**The observed Gl.**	**N.**	**%**
Virosis	Carré disease	Membranous/ membranoproliferative Gl.	24	19.83
	Rubarth (HIC) disease	Membranoproliferative Gl.	12	9.92
	Herpes virosis	Membranoproliferative Gl.	10	8.26
Neoplasm	Mammary carcinoma	Membranous Gl.	28	23.14
	Fibrosarcoma	Membranous Gl.	2	1.65
	Mixt renal Carcinoma	Membranoproliferative Gl.	1	0.83
	Cholangiocarcinoma	Membranous Gl.	1	0.83
	Mastocytoma	Membranous Gl.	3	2.48
Bacteriosis	Pyometra	Membranoproliferative Gl.	17	14.04
	Pyodermitis(*Staphylococcus intermedius*)	Proliferative /purulent Gl.	7	5.79
Toxicosis	Ethylene glycol	Membranous/ membranoproliferative Gl.	6	4.96
Parazitosis	Dirofilariosis *(Dirofilaria immitis)*	Membranous/ membranoproliferative Gl.	4	3.31
	Ascaridiosis	Membranoproliferative Gl.	6	4.96
Total cases			**121**	**100**

The pathogenesis of the glomerulonephritis produced by accumulation of the circulatory immune complexes

The study of the spontaneous and experimental glomerulonephritis proved that the immune mechanism plays an important role in glomerular pathology. For inducing the immune glomerulonephritis, the Atg-Atc immune circulatory complexes are the main factor.

These complexes may contain bacteria, viruses, parasite antigens or neoplasm antigens.

The pathogenesis and the way the immune complexes accumulate on and in glomerular membranes depend on quantitative and qualitative aspects: Atc-Atg quantity of complexes, the dimension of complexes, molecular configuration, the antibody affinity to antigen, electrical charge and solubility.

The big complexes, insoluble and excessively formed are rapidly removed from blood at kidney level and phagocytised by monocytes-macrophage system (MMS) or partially taken by the glomerular mesangium.

On the other hand, the immune complexes by intermediary dimensions formed in presence of excessively antigens remain in liquid and may accumulate on basal membrane of the glomerular membrane, of the rounded tuft of blood capillaries or at the level of mesangium.

By the mean of the electron microscopy the accumulated immune complexes are emphasized under the shape of unregulated accumulations, electron-dense disposed in subendothelial position (*subendothelial GN*) or subepithelial (*subepithelial GN*), in thickness of the basal membrane (*intramembranous GN*) or in mesangium (*mesangial GN*).

The pathogenicity of the circulatory immune complexes rest in their ability to trigger some phenomena that have as result the alteration of the basal membranes (membranous and membranoproliferative GN.) and proliferation of the mesangial cells (proliferative GN.).

The accumulation in subendothelial position is usual for the circulatory immune complexes with increased anionic charge that is not allowing the passage through glomerular basal membrane and with high affinity of the antibody for antigen that makes them difficult to dissociate.

On the contrary, the subepithelial position is usual for the complexes with cationic charge and with low affinity of the antibody to antigen, which allows the dissociation of the immune complex and independent migration of the antigen and antibody through glomerular basal membrane, reforming the complex on its subepithelial side.

The intra-membrane accumulation of the immune complexes is less usual, in some cases representing an intermediary phase of migration through thickness of the glomerular basal membrane.

The accumulation in glomerular mesangium is characteristic to immune complexes with neutral charge.

These complexes rich in antigens produce a significant activation of the complement that is the reason why they prove a reduced ability to produce glomerular lesions.

It is also very important that every disease with chronically evolution that is exposed for long time to an antigen may stimulate the continuous formation of circulatory immune complexes involved in the pathogenesis of immune inflammations.

The glomerulonephritis formed by formation of the immune complexes "*in situ*" is sustained by the findings in *Dirofilaria immitis* infestations in dogs. The *Dirofilaria immitis* antigens were directly implanted in basal glomerular membrane. Subsequently, the circulatory antibodies have reacted with the antigens accumulated in basal membrane, forming in the end, at its level (in situ) the Atg-Atc immune complexes.

Thus, the feed-back of the glomerulus to these injuries is monomorphous being generally represented by thickening of the glomerular basal membranes, by cell proliferation and eventually by sclerosis.

Membranous glomerulonephritis is an unspecific lesion determined by circulatory immune deposits, very discrete, on the epithelial surface of the glomerular basal membrane and without any inflammatory signs, at first.

Afterwards, a slight thickness of the basal membrane and diffuse or focalised fusion of the podocytes processes takes place over the immune accumulations present at membrane level. The podocytes are tumefied and podocytes processes contain a granular material.

In advanced progressive stages, the membrane spiculi are fusing with the immune membrane accumulations, the capillary wall being considerable thickened. The thickness of the basal membrane becomes obvious due to the new synthesized membrane material.

For the examined cases, this type of glomerulonephritis was observed in dogs predominantly in neoplasm diseases. Thus, were identified glomerulonephritis in bitches with mammary carcinoma and in dogs with fibrosarcoma, liver cholangisarcoma and mastocytoma. Yet, the lesion was also underlined as part of the lezional aspects of the Carré disease, in infestation with *Dirofilaria immitis* and in intoxication with ethylene glycol. The membranous glomerulonephritis may be the expression of geriatric age, as a consequence of continuous synthesis of membranous material.

Histological, the glomerular basal membrane appeared thicker (of approximately 3-4 time more than normal), especially at the level of the peripheral glomerular capillaries (solitary), being distorted and having a *wire loop* aspect. The lumen of the capillaries was normal, or even distained and empty. A slight proliferation of the mesangial cells was also noticed and the increase of the mesangial matrix. Moreover, it was noticed steatonephrosis and tubular granular dystrophy, resulted from the permeability alteration of the glomerular membranes.

As evolution, the glomerular basal membrane is losing its polyanionic charge and becomes very permissive, especially for the serous proteins. Thus, appears proteinuria and nephritic syndrome.

Some of the cases, the evolution is favourable, mostly, the lesions being reversible, in other cases is observed a lent progressive evolution to glomerular sclerosis, as a result of obliteration of the capillary lumen.

From clinically point of view, membranous glomerulonephritis are integrated part of the nephritic syndrome.

Proliferative glomerulonephritis. This type of immune glomerulonephritis is frequently encountered, being dominated by the cellular and matrix modifications of the glomerular

mesangium, morphologically expressed through an increase more or less notable of the cell number from its structure, as a result of the proliferation of mesangial and endothelial cells associated with inflammatory cells (polynuclear, mononuclear cells), increase of the mesangial matrix and of the mesangial deposits.

In histological examination, the glomeruli were increased in volume, occupying most of the glomerular cavity. The capillaries had thin basal membranes. The lumens of the capillaries were pressed, without blood, sometimes lacking.

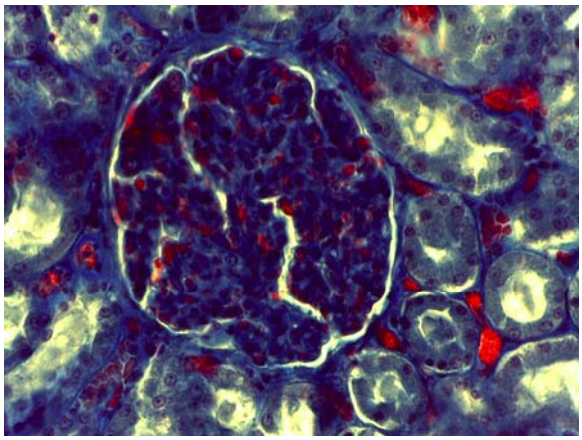
The mesangial proliferations led to separation tendency of the glomerular lobules.

This type of glomerulonephritis was observed in pyodermitis, parallel evolving with a metastatic netrophilic glomerulonephritis (Fig.).

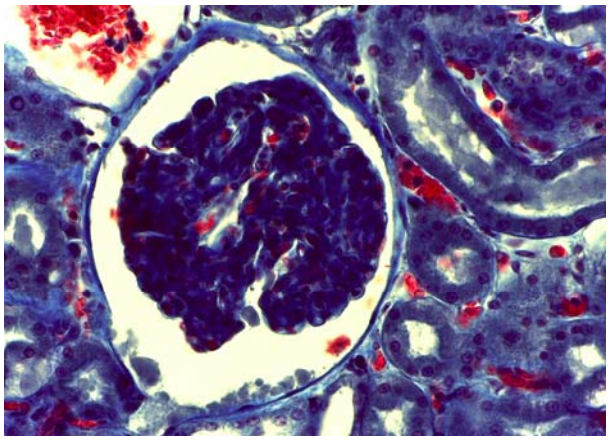
Membrane proliferative glomerulonephritis (MPGN), also called mesangio-capillary glomerulonephritis represent a morpho-clinical entity characterised by proliferation of the resident cells (endothelial and mesangial) and at the same time by thickness and duplication of the glomerular basal membrane, hence fulfilling both aspects of the membranous and mesangio-proliferative glomerulonephritis.

Moreover, were emphasized other changes represented by leucocytes afflux, micro thromboses and proliferations of the parietal epithelium of the Bowman's capsule. The interstitial lesions depend on duration and gravity of the glomerulonephritis (alteration of the permeability of the glomerular capillaries).

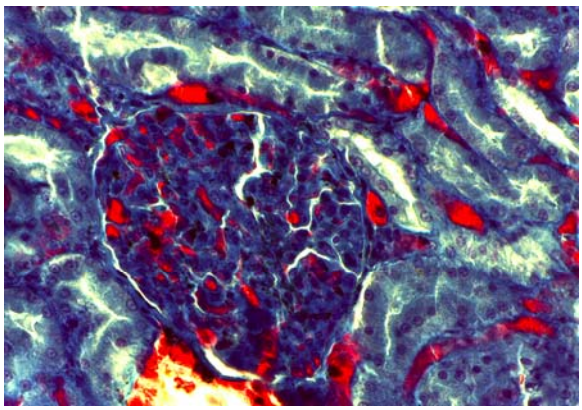
The lesion was histological diagnosed in Carre disease, Rubarth disease (HIC), herpes Virosis, mixed renal carcinoma, ethylene glycol intoxication, dirofilaria and ascaris infestation and purulent endometritis in bitch. In bacterial and viral diseases, due to persistent antigemia at the level of the kidneys were emphasized major glomerular lesions consisting in membranous type glomerulonephritis and membrane proliferative.



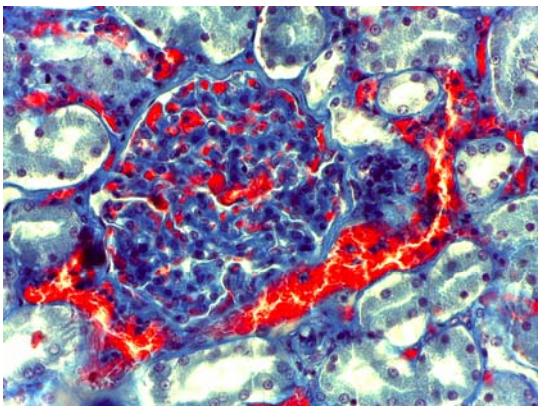
Dog. Membrane-proliferative Gl.
Carré disease. Col. HEA, x400



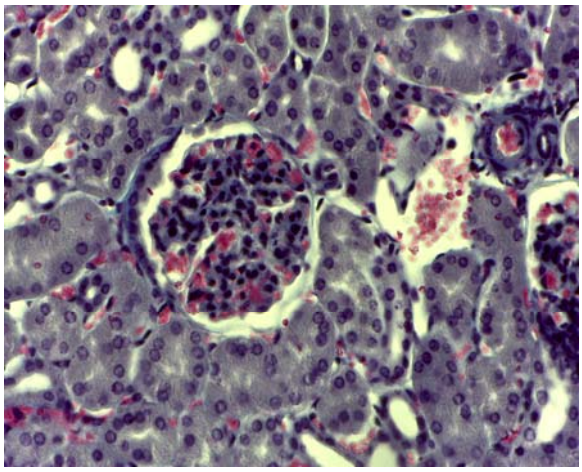
Dog. Membranous Gl. Carre disease.
Col. HEA, x400



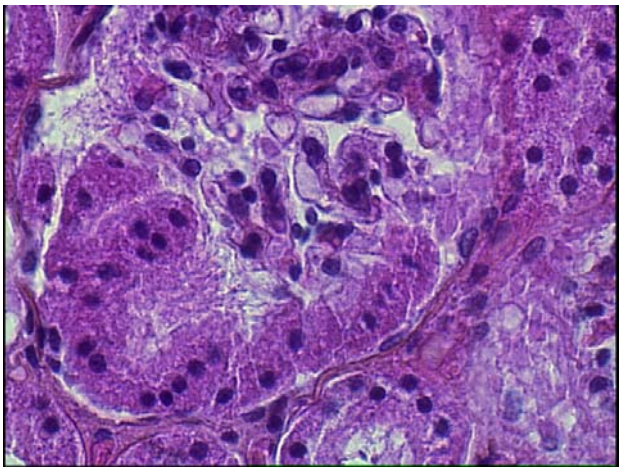
Dog. Membrane-proliferative Gl.
Rubarth disease. Col. HEA, x400



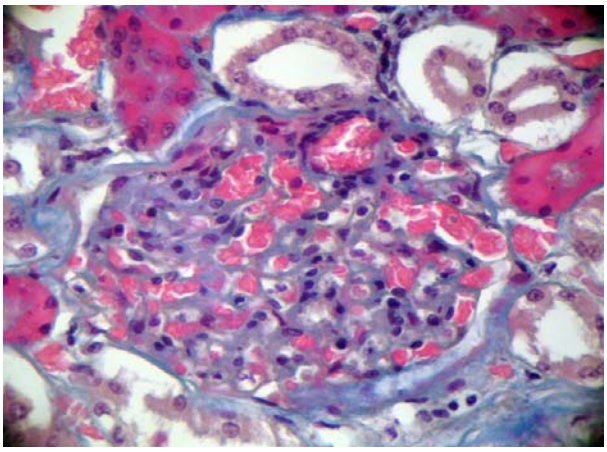
Dog. Membrane-proliferative Gl. Herpesvirosis.
Col. HEA, x400



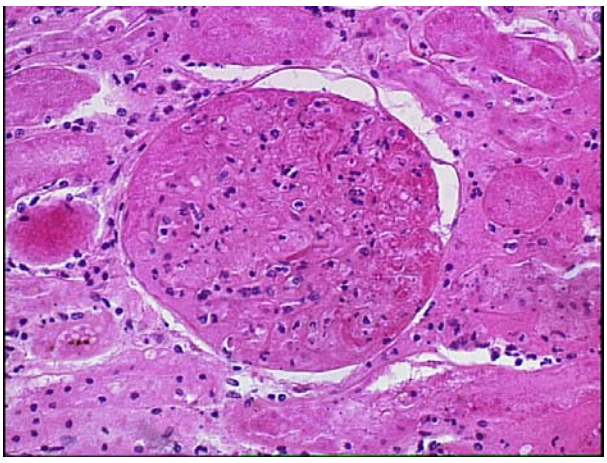
Bitch. Proliferative Gl. Mammary carcinoma. Col.
HEA, x400



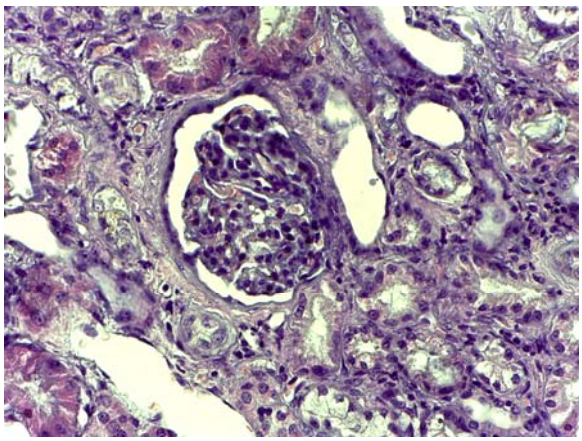
Dog. Proliferativ Gl.. Pyodermitis. Col. HE, x1000



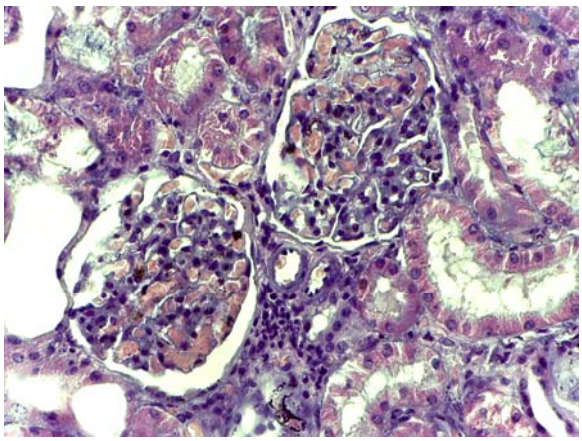
Dog. Membrane-proliferative Gl.
Mixed renal carcinoma. Col. HEA, x400



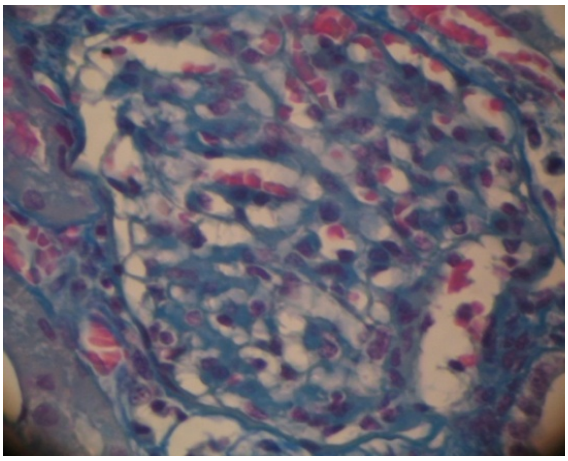
Bitch. Purulent Gl. Col. HE, x400



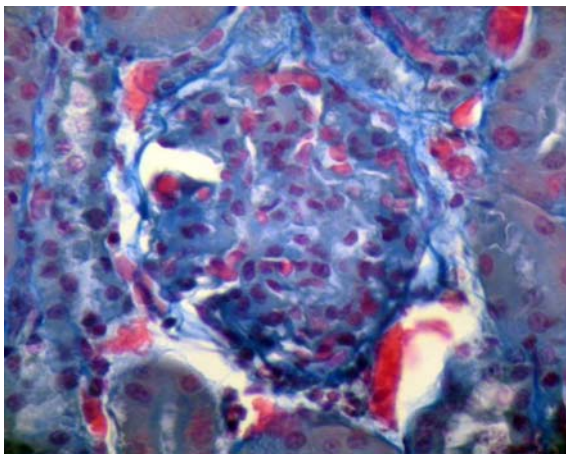
Dog. Membranous Gl. Calcium oxalate crystals in uriniferous tubules. Ethylene glycol intoxication. Col. HEA, x400



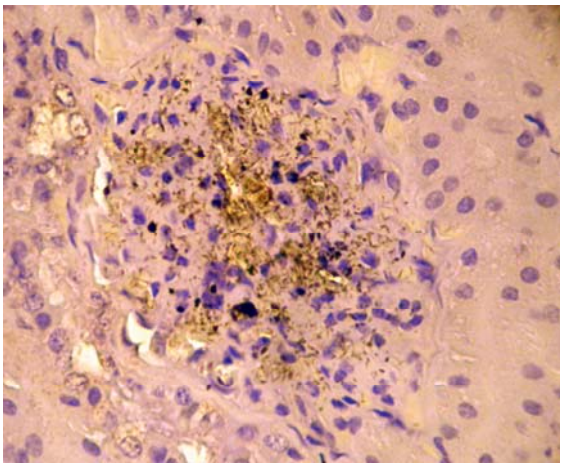
Dog. Proliferative Gl. Separation of the glomerular lobules. Calcium oxalate crystals in uriniferous tubules. Ethylene glycol intoxication. Col. HEA, x400



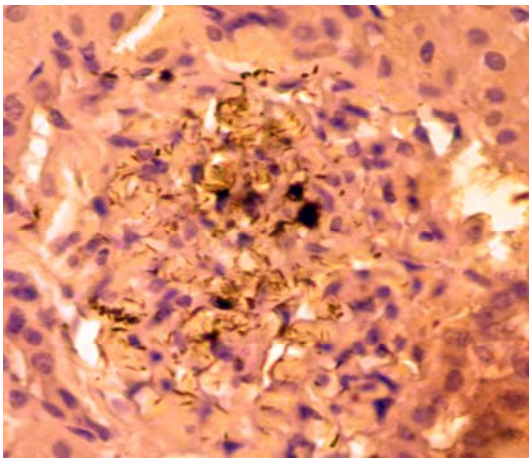
Dog. Membranous Gl. Dirofilarisis. Col. HEA, x1000



Dog. Membranous Gl. Dirofilarisis. Col. HEA, x400



Dog. Membrane proliferative glomerulonephritis. IgG emphasized in glomerular mesangiom. Col. Hematoxylin, x400



Dog. Membrane proliferative glomerulonephritis. IgG emphasized in glomerular mesangiom. Col. Hematoxylin, x400

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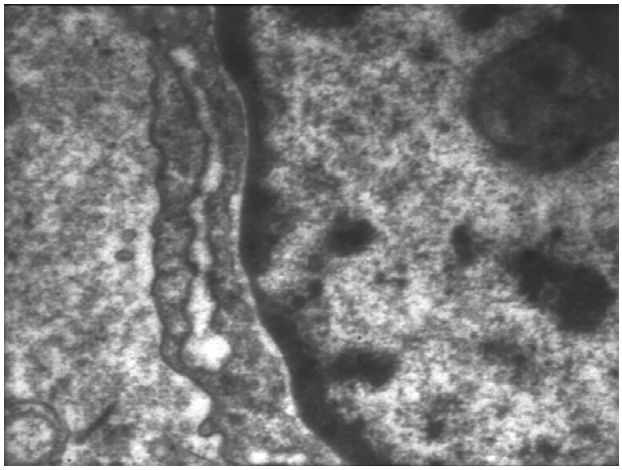
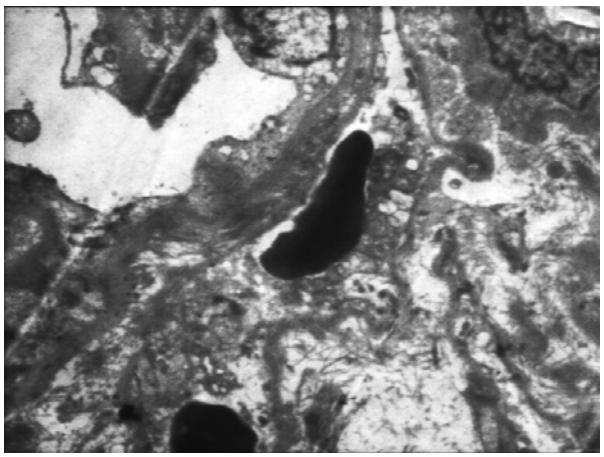
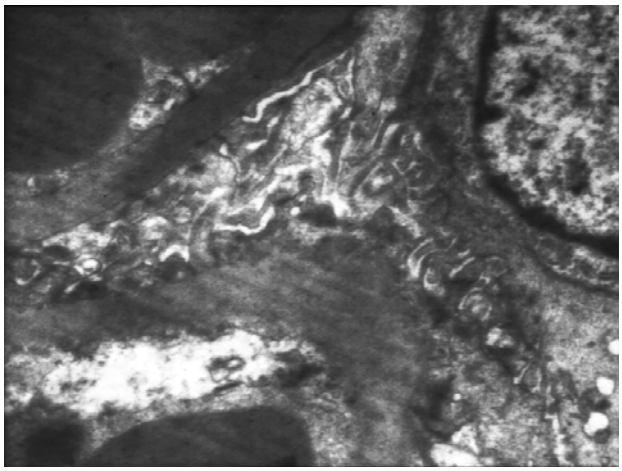


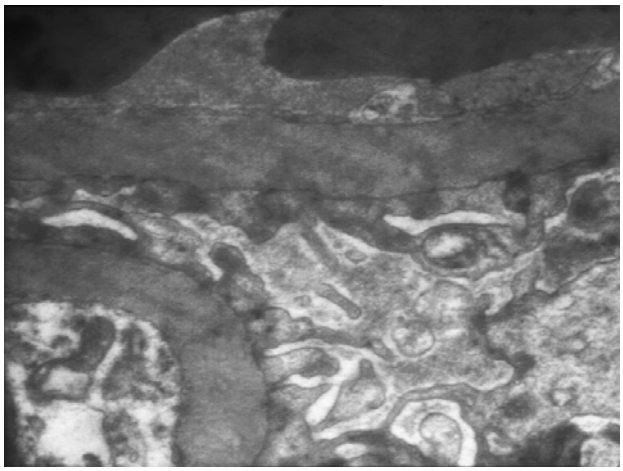
Dog. Double layer of Immune complexes which give a double shape to the glomerular basal membrane ("train railways").Carre disease. Col. Uranil acetate, x8700



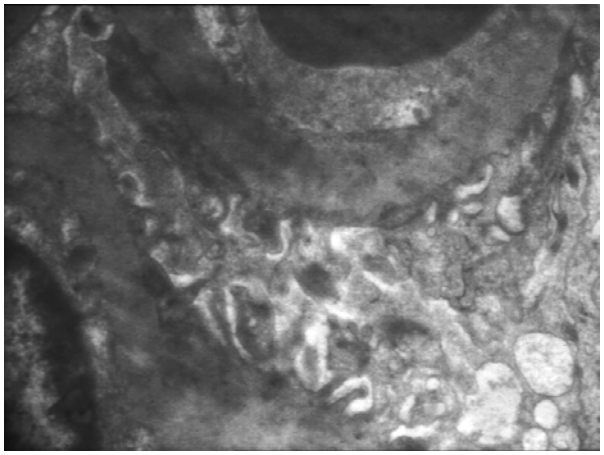
Dog. Basal membrane of the glomerular capillary wavy and thickened; immune complexes on the epithelial and intra membranare side. Rubarth disease. Col. Uranil acetate, x1250



Dog. Basal membrane of the glomerular capillary wavy and thickened; immune complexes on the epithelial side between the podocyte processes. Rubarth disease. Col. Uranil acetate, x3400;



Dog. Basal membrane of the glomerular capillary wavy and thickened; immune complexes on the epithelial side and intra membranare. Rubarth disease. Col. Uranil acetate, x6200;



Dog. Basal membrane of the glomerular capillary. Immune complexes on both sides (endothelial and epithelial) and intra membranare. Col uranil acetate, x4400;