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From the Department of Surgery and Department of Clinical Biochemistry, Royal Veterinary College, Stockholm, Sweden.

COMPARATIVE PATHOPHYSIOLOGICAL ASPECTS OF THE GLOMERULONEPHRITIS ASSOCIATED WITH PYOMETRA IN DOGS

By

Åke Åsheim

Morphological stigmata of glomerulonephritis have been detected by light and electron microscopical examination of kidneys from bitches with polyuria and polydipsia associated with pyometra (*Obel et al.* 1964). There are some morphological features which this type of glomerulonephritis shares with glomerulonephritis in human beings and nephrotoxic serum nephritis in dogs, lesions commonly considered to be the result of immunobiological processes.

What will be attempted in this paper is to relate the pathophysiological disturbances (and the absence of disturbances) with each other and with the histopathological changes in pyometra glomerulonephritis. For this purpose, pyometra glomerulonephritis can be compared with some known types of glomerulus damage — acute and chronic glomerulonephritis and pregnancy toxaemia in human beings and nephrotoxic glomerulonephritis in dogs.

1. *Acute glomerulonephritis (human beings).*

This disease generally occurs as a complication to infection, particularly with streptococci. The morphological changes in the glomerulus comprise proliferation of the endothelial cells, some swelling of the basement membrane, and deposition of electron-dense material between the basement membrane and the endothelial cells (*Farquhar* 1960; *Allen* 1962; *Movat et al.* 1962). The most obvious clinical signs are oedema, hypertension and haematuria (*Miller & Hayman* 1959; *de Wardener* 1961). The serum protein content is normal or somewhat

reduced. The cholesterol level in the serum is usually normal but in children can be increased (*Heymann & Wilson* 1959). The protein content of the urine can be negligible or reach as much as 300 mg/100 ml (*Stetson et al.* 1955; *Allen* 1962). Albumin represents most of the protein in the urine (*Squire et al.* 1962). There is often oliguria. A normal renal concentrating ability is usually maintained but the glomerular filtration rate and filtration fraction tend to be reduced (*Earle et al.* 1944; *Earle et al.* 1951; *Parrish et al.* 1961).

2. *Chronic glomerulonephritis (human beings).*

Chronic glomerulonephritis can succeed the acute phase. Morphologically, the changes are still predominantly intracapillary with proliferation of endothelial cells, thickening of the basement membrane, and varying amounts of deposite to give gradual occlusion of the capillary lumina (*Farquhar* 1960; *Steiner et al.* 1962).

The clinical signs are persistent proteinuria, haematuria and oedema. In some patients the haematuria disappears but heavy proteinuria remains and a pronounced oedema occurs. This, the nephrotic stage of glomerulonephritis, can persist for a long time (*Miller & Hayman* 1959). The nephrotic stage is often accompanied by an increase in the serum cholesterol content. A reduction in the max. osmotic U/P ratio with polyuria often occurs, unlike the case in the acute phase. The reduction in the max. osmotic U/P ratio has been attributed by some (*Bricker et al.* 1959) to increased osmotic loading of remaining functioning nephrons. Others (*Baldwin et al.* 1955; *Adams et al.* 1961) believe that there is an absolute reduction in the concentrating ability which does not depend on a possible osmotic diuresis. The glomerular filtration rate, just as in the acute phase, is often reduced but the filtration fraction is generally within normal limits.

3. *Toxaemia of pregnancy (human beings).*

The glomerular changes are principally intracapillary with swelling of the endothelial cytoplasm. The epithelial cells can also become swollen but swelling of the basement membrane occurs only when the glomerulus damage is severe (*Pollak & Nettles* 1960). Oedema, hypertension, and proteinuria, generally between 300 and 600 mg per 100 ml urine, dominate the clinical appearance (*Pollak & Nettles* 1960). The serum protein content is generally normal (*de Wardener* 1961) but the serum cholesterol content can be increased.

The concentrating ability is usually normal. Oliguria is common (*Pollack & Nettles* 1960). Both the glomerular filtration rate and the filtration fraction are generally reduced (*Bucht & Werkö* 1953).

4. *Nephrotoxic glomerulonephritis (dogs).*

Naturally-occurring glomerular lesions are generally believed to be uncommon in dogs (*Bloom* 1954) and there are apparently no descriptions of the morphological and physiological abnormalities associated with this state. There are, on the other hand, numerous

reports dealing with experimentally-induced glomerular damage in dogs. Most of these are concerned with morphological studies and the pathophysiology is scarcely mentioned. *Seegal et al.* (1955), however, have described the functional abnormalities in dogs in which acute glomerulonephritis was induced with a nephrotoxic serum (*Bevans et al.* 1955). This type of renal damage is characterized by swelling of the basement membrane to a greater degree than in the human types of glomerulonephritis listed above. Just as in the human types there is also intracapillary cell proliferation and deposition of electron-dense material between the endothelial cells and the basement membrane (*Movat et al.* 1961). Clinically, the dogs were depressed and anorexic and had bouts of emesis. Slight oedema and some hypertension were also detected. The leukocyte counts were normal, the erythrocyte counts depressed, and the erythrocyte sedimentation rate increased. The serum cholesterol content increased steadily to about 300 mg/100 ml. Total serum protein levels were not reported but hypoalbuminaemia and a drop in the albumin/globulin ratio were mentioned. There was proteinuria (about 300 mg per 100 ml urine) and various degrees of haematuria.

5. *Glomerulonephritis in pyometra bitches.*

The morphological changes in this type of nephritis seem to be practically identical with those of nephrotoxic serum nephritis in dogs. Both, for example, include a greater degree of thickening of the basement membrane than is encountered in the human types of glomerulonephritis.

Many of the functional abnormalities characterizing the renal damage associated with pyometra have been described previously (*Åsheim* 1963; *Åsheim* 1964 a, b, c). The max. osmotic U/P ratio and often the glomerular filtration rate and filtration fraction as well, are reduced. The reduction in the max. osmotic U/P ratio in pyometra bitches represents a functional depression of the concentrating segments of the nephron and is independent of a possible osmotic diuresis.

In order to give a more complete presentation of the pathophysiology of pyometra glomerulonephritis, a number of pyometra bitches have been examined morphologically and clinically in those respects which, in nephritis, generally reveal deviations from the normal.

MATERIAL AND METHODS

The results of various renal function tests (*Åsheim* 1963; *Åsheim* 1964 a, b, c) and bacteriological examination of the uterus (*Åsheim* 1964 d) for 79 bitches with pyometra and polydipsia have been published previously. The mean age of the bitches was 8.4 years with a standard deviation of $\pm$ 2.0 years and a range of

4 to 12 years. All these bitches had been examined clinically in the usual manner and blood and urine samples taken for examination as described below. Special laboratory studies were carried out on some of the bitches.

a. Serum cholesterol content (Swedin 1946).

Twenty-two bitches, all with a max. osmotic U/P ratio less than 3.7, were examined. GFR had been determined for eight of the animals and five had a rate of less than 55 ml/min/m^2.

b. Plasma volume.

Plasma volume was determined for six normal bitches (16 to 28 kg) and five pyometra bitches (17 to 42 kg) after the injection of 5 mg Evans blue intravenously. Plasma samples were taken 10, 20, 30 and 40 minutes after injection. The initial plasma content of Evans blue was estimated by extrapolation on semilogarithmic paper (*Frank & Carr* 1955).

c. Blood pressure.

Mean arterial pressure has been measured by connecting an open mercury manometer to a polythene catheter placed in a femoral artery (*Persson et al.* 1961).

Some of the pyometra bitches were re-examined in the same manner 9 to 15 days after ovariohysterectomy.

All these special studies were repeated on twenty-one normal, medium-sized bitches with a mean age of 2.5 years (range 1—6).

Student's t-test has been applied for comparing the results obtained for normal bitches and pyometra bitches. The results are given as P-values.

LABORATORY DETAILS

The *blood* was examined for the number of leukocytes and erythrocytes, the erythrocyte sedimentation rate (ESR), haemoglobin content, haematocrit, and non-protein nitrogen (NPN). The total CO_2 content has been determined by van Slyke's method, plasma sodium and potassium levels by flame photometry, and plasma osmolarity by freezing-point depression. The technique and the error of the method for the latter has been given previously (*Åsheim* 1963). The total protein content and amounts of the various protein components were determined as described in an earlier paper (*Åsheim* 1964 d).

The *urine* was examined for sediment, osmolarity, and the presence of glucose and protein. Since the vagina often contains abundant

exudate from the uterus all urine samples were taken by catheterization of the bladder. In spite of this precaution the possibility of contamination cannot be ignored, particularly in regard to the sediment. The degree of proteinuria was graded by Heller's method from 0 to +++ and in some instances quantitatively determined by Goa's method (*Goa* 1953) in conjunction with paper electrophoresis of the urinary protein. These determinations were made by M. Piscator, M.D., the National Institute of Public Health, Stockholm, according to the method given in his paper (1962).

The reduction in renal concentrating ability means that the urine is more diluted than normally and that the protein content per unit volume is reduced. Since the course of the disease did not permit measurements of daily protein excretion for comparison of the pyometra bitches with normal bitches, urinary protein levels are given here both as the amount found and as the amount calculated to be present if the urine had a concentration of 1000 mOsm/l with unchanged protein excretion. This concentration (1000 mOsm/l) is close to the mean value for osmolarity of the urine of normal bitches (Table 6).

RESULTS

The clinical appearance of the animals was characteristic for the disease; the bitches showed all or some of the usual clinical signs of depression, anorexia, emesis, diarrhoea, and discharge from the vulva. The body temperature was usually normal or only slightly increased. The abdomen was often distended because of the great enlargement of the uterus. None of the bitches was obviously oedematous. From three to five days after ovariohysterectomy the general condition of the animals began to improve rapidly and most animals were clinically healthy when discharged between nine and fifteen days after surgery.

Blood.

When examined before operation the animals generally had leukocytosis and anaemia (Table 1). The ESR was usually greatly increased but some animals had quite normal ESR values. The total CO_2 content ranged from normal to greatly reduced values. NPN levels were increased in only eight of the seventy-nine animals examined. There was usually a moderate increase in the serum cholesterol content. No relationship could be demonstrated between the degree of reduction of GFR and increase in cholesterol values.

The values obtained nine to fifteen days after ovariohysterectomy are also included in Table 1. The anaemia was more

Table 1. Blood values in normal bitches and in pyometra bitches before and after ovariohysterectomy.

	White cells 10^3/ccm	Red cells 10^6/ccm	Haemoglobin g/100 ml	Haematocrit vol %	Erythrocyte sedimentation rate mm/1 hour	NPN mg/100 ml	Total-CO_2 vol %	Serum cholesterol mg/100 ml
NORMAL BITCHES								
Number of bitches	21	21	21	21	21	21	21	12
Mean	8.3	6.4	15.8	47.2	1.7	28.8	51.0	214.8
Range	4.8—16.2	5.0—8.1	11.8—18.1	34—53	0—8	21—42	40—58	138—267
Standard error	0.59	0.18	0.34	0.98	0.44	1.00	1.09	12.12
Standard deviation	2.7	0.8	1.5	4.5	2.0	4.6	5.0	42.1
PYOMETRA BITCHES								
Preoperative								
Number of bitches	79	79	79	79	79	79	36	22
Mean	36.3	5.9	13.8	41.0	28.2	32.0	39.2	363.0
Range	16.6—91.8	3.4—8.7	8.8—17.3	24—53	1—127	18—66	22—59	225—539
Standard error	1.81	0.14	0.33	0.80	3.74	1.46	1.67	16.97
Standard deviation	16.1	1.2	2.9	7.1	33.2	13.0	10.0	79.6
P-value	<0.001	>0.05	<0.01	<0.001	<0.001	>0.05	<0.001	<0.001
9—15 days postoperative								
Number of bitches	30	30	30	30	30	17	13	
Mean	28.0	4.6	11.1	33.6	24.8	28.4	44.5	
Range	7.2—80.0	3.0—5.9	6.7—15.2	21—46	5—86	17—41	34—54	
Standard error	3.40	0.16	0.40	1.04	5.48	1.46	1.76	
Standard deviation	18.7	0.9	2.2	5.7	20.8	6.0	6.3	

Table 2. Serum cholesterol in pyometra bitches before and 11—15 days after ovariohysterectomy.

Pyometra bitches no.	SERUM CHOLESTEROL mg/100 ml Preoperative	Postoperative
202	347	265
241	494	176
245	365	200
267	394	190
315	327	177
346	338	297
347	287	238
361	467	326
372	261	197
375	225	192
416	363	164
Mean:	352	220

accentuated but the other values began to approach normal values.

The pre-operative and post-operative serum cholesterol values for eleven pyometra bitches are compared in Table 2. In the short interval between samples the mean pre-operative value of 352 mg/100 ml had declined to a mean post-operative level of 220 mg/100 ml, a value within the normal range (see Table 1). Only a few bitches retained a cholesterol level over the normal.

The values for total serum protein and the different protein fractions in the seventy-nine pyometra bitches together with normal values are listed in Table 3. The total protein content was greatly increased in the pyometra bitches and mainly reflected the absolute and relative increase in the globulin fraction (with the exception of alpha-1). At the same time the albumin content was reduced and this helped in producing the low albumin/globulin ratio.

Post-operative blood samples were taken for electrophoresis from thirty-four of the bitches included in Table 3 and the results are compared with the pre-operative values in Table 4. After ovariohysterectomy there was a definite tendency towards normal values.

The plasma volume in the pyometra bitches ranged from 25 to 36 ml per kg bodyweight with a mean of 29 ml per kg. Cor-

Table 3. Total serum protein content and serum electrophoresis values for pyometra bitches before ovariohysterectomy compared with normal values.

	Total protein	Albumin		Globulin								A/G ratio
				alpha-1		alpha-2		beta		gamma		
	g/100 ml	rel. %	g/100 ml	rel. %	g/100 ml	rel. %	g/100 ml	rel. %	g/100 ml	rel. %	g/100 ml	
NORMAL BITCHES												
Number of bitches	23	23	23	23	23	23	23	23	23	23	23	23
Mean	7.0	57.0	4.0	4.5	0.3	10.7	0.7	15.0	1.0	11.0	0.8	1.34
Range	5.6—9.0	41.4—67.8	2.3—5.9	2.7—8.4	0.2—0.5	6.9—14.0	0.5—0.9	6.4—23.4	0.5—1.4	5.5—16.3	0.5—1.2	0.77—1.95
Standard error	0.19	1.66	0.16	0.33	0.02	0.49	0.04	0.85	0.06	0.56	0.04	0.08
Standard deviation	0.9	7.9	0.8	1.6	0.1	2.4	0.2	4.1	0.3	2.7	0.2	0.37
PYOMETRA BITCHES												
Number of bitches	79	79	79	79	79	79	79	79	79	79	79	79
Mean	8.4	30.8	2.6	4.5	0.4	18.0	1.5	20.8	1.7	25.5	2.2	0.47
Range	6.4—10.8	15.2—46.1	1.1—4.7	1.5—8.8	0.2—0.7	8.5—30.3	0.8—2.4	11.4—41.2	0.8—3.9	11.7—57.1	0.9—5.7	0.09—0.98
Standard error	0.11	1.00	0.08	1.55	0.01	0.62	0.05	0.64	0.06	1.09	0.11	0.02
Standard deviation	0.9	8.9	0.75	1.4	0.1	5.5	0.5	5.7	0.5	9.7	1.0	0.22
P-value	<0.001	<0.001	<0.001	>0.05	>0.05	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 4. The mean values (g/100 ml) for total protein and the different protein components in serum from 34 pyometra bitches before and after ovariohysterectomy compared with normal values.

		PYOMETRA BITCHES		NORMAL BITCHES
		Preoperative values	Postoperative values	
Total protein		8.5	7.6	7.0
Albumin		2.5	2.9	4.0
Globulin	alpha-1	0.4	0.3	0.3
	alpha-2	1.5	1.1	0.7
	beta	1.7	1.4	1.0
	gamma	2.3	1.9	0.8
A/G ratio		0.42	0.65	1.34

responding values for the normal bitches were 40 to 51 ml per kg with a mean of 43 ml per kg. The values for the two groups are not fully comparable, however, since the pyometra bitches were much fatter than the normal bitches and in the normal group there was an obvious tendency for a smaller plasma volume per kg bodyweight in the fatter animals.

The post-operative plasma volume was determined for five pyometra bitches and compared with the pre-operative plasma

Table 5. The total amount of circulating plasma protein for five pyometra bitches before and after ovariohysterectomy calculated on the basis of plasma volume and plasma protein content.

Pyometra bitches no.	Day postop.	Plasma volume ml	Protein content g/100 ml	Calculated total plasma protein g	△ Calculated total plasma protein * g
241	preop.	954	7.7	73.5	7.3
	14	894	7.4	66.2	
245	preop.	1083	8.5	92.1	8.0
	13	1121	7.5	84.1	
267	preop.	570	9.5	54.2	9.7
	15	593	7.5	44.5	
347	preop.	666	8.5	56.6	0.1
	12	743	7.6	56.5	
398	preop.	957	8.8	84.2	16.0
	12	947	7.2	68.2	
				Mean:	5.2

* △ = difference between the calculated total amount of circulating plasma protein before and after ovariohysterectomy.

Table 6. The urine protein content for five normal bitches and nine pyometra bitches has been determined by the Heller and Biuret methods. With the determined urine osmolarity as a basis, the amount (mg) of protein per 100 ml urine with a concentration of 1000 mOsm/l has been calculated.

Normal bitches no.	Urine				Serum				
	Uosm mOsm/1	Protein			Total protein g/100 ml	Albumin g/100 ml	Globulin		
		Heller 0-3+	Biuret mg/100 ml	Calculated content			alpha g/100 ml	beta g/100 ml	gamma g/100 ml
F 17	1027	0	31	30	7.8	4.2	1.8	1.1	0.7
F 22	1103	trace	47	43	7.8	4.1	2.0	1.0	0.7
F 23	970	0	17	18	7.4	4.1	1.5	1.4	0.5
F 32	1030	trace	21	20	6.6	3.8	0.9	1.1	0.8
F 33	928	0	22	24	6.5	3.9	1.0	0.9	0.7
Pyometra bitches no.									
202	607	trace	25	41	7.2	1.8	2.0	1.3	2.1
203	590	+	72	122	7.8	2.6	1.7	2.0	1.6
206	405	++(+)	320	790	8.5	3.7	1.4	1.7	1.7
207	604	++	340	563	9.9	1.9	1.0	1.3	5.7
210	450	trace	48	107	8.3	2.5	1.9	1.4	2.5
211	907	trace	48	53	10.8	2.6	2.4	1.9	3.8
212	975	+++	410	420	9.6	2.3	3.2	1.7	2.4
213	390	0	23	59	8.3	1.7	2.7	2.1	1.9
214	670	++	152	227	8.2	3.4	1.8	1.4	1.7

volume (Table 5). Plasma volume was reduced in two of the bitches and increased in the other three. Calculated total plasma protein was reduced in all these bitches after ovariohysterectomy.

Urine.

The urine samples often contained bacteria and red and white blood cells in numbers ranging from very few to very numerous. The possibility of contamination with uterine exudate has been dealt with above. In no instance were there sufficient numbers of erythrocytes present to produce visible discolouration of the urine. Urine from three of the seventy-nine bitches contained traces of glucose.

All the bitches were examined for proteinuria by Heller's method.

0	(+)	46	bitches
+	(+)	20	„
++	(+)	8	„
+++		5	„

Because Heller's method gives only a rough estimate of the amount of protein in the urine quantitative protein determinations were carried out on urine samples from nine of the pyometra bitches. The results obtained with both methods on urine samples from pyometra bitches and normal bitches as well as urine concentration are given in Table 6. The *calculated* amount of protein in 100 ml urine with a concentration of 1000 mOsm/l has been established in the manner described under Methods.

Three of the nine pyometra bitches had a *calculated* protein content in the urine which fell within normal limits. For the other six bitches the *calculated* protein content exceeded 100 mg per 100 ml urine.

The urine protein were also separated by paper electrophoresis. The protein content in urine from normal bitches is so small that the different fractions are difficult to distinguish (Fig. 1 A). Separation became more distinct as the protein content increased (Fig. 1 B—F). In urine from six of the nine pyometra bitches (203, 206, 207, 212, 213, 214) the albumin fraction was greatly increased to give an A/G ratio approaching or exceeding unity (Fig. 1 C, D, E). The two bitches (207, 211) with the highest level of gamma-globulin in the serum also had a

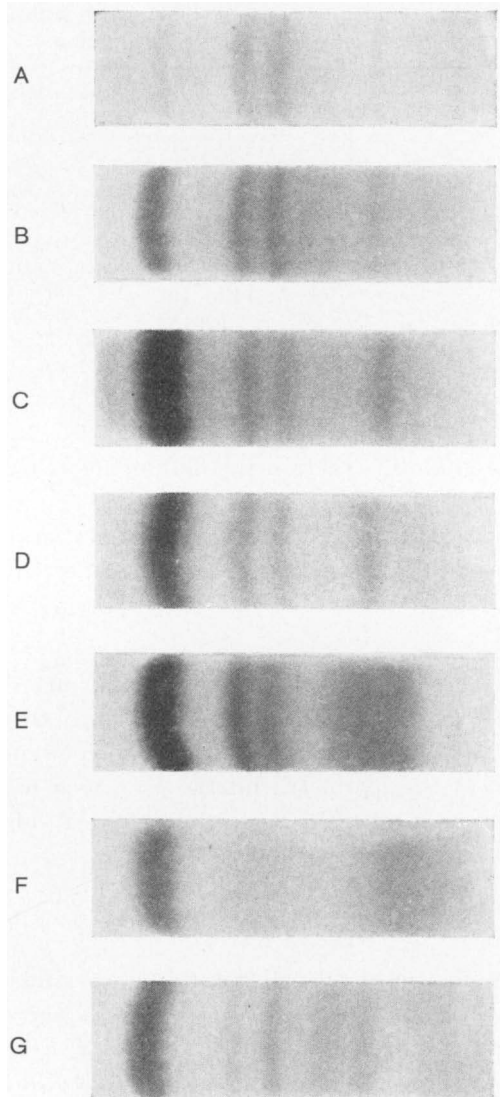

Fig. 1. Paper electrophoresis of protein in the urine of a normal bitch (A) and bitches with pyometra (B—F). Serum protein fractions from a normal bitch are illustrated in G.

Table 7. Mean arterial pressure in pyometra bitches compared with the pressure in normal bitches.

	MEAN ARTERIAL PRESSURE mm Hg	
	Pyometra bitches	Normal bitches
Number of bitches	12	11
Mean	133	130
Range	112—166	104—150
Standard error	4.3	4.6
Standard deviation	15	15
P-value	>0.05	

definite gamma-globulin fraction in their urine (Fig. 1 E and F, Table 6).

The electrophoretic patterns for the urinary protein and for normal blood serum protein resemble each other (Fig. 1 G).

Blood pressure.

There were no obvious differences in mean arterial pressure between pyometra bitches (133 mm Hg) and normal bitches (130 mm Hg); see Table 7. Post-operative blood pressure was taken for seven of the pyometra bitches to give a mean value of 129 mm Hg compared with the pre-operative mean of 127 mm Hg for these seven bitches.

DISCUSSION

The changes in the blood cell counts and serum protein patterns in the pyometra bitches with polydipsia accord with the results reported by others (*Boguth & Rieck* 1953; *Freudiger* 1955; *Rüsse* 1955; *Eikmeier & Moegle* 1959; *Christoph* 1961).

When evaluating the differences between pyometra nephritis and the renal injuries taken for comparison (see introduction) it ought to be kept in mind that at the time of examination the pyometra bitches were exposed to the effects of an infectious process. The renal injuries chosen as comparisons either represent a post-infection complication or do not have any obvious relationship with an infection. In the pyometra bitches, the leukocytosis, increased ESR, anaemia, and reduction in the serum albumin fraction and an increase in the globulin fraction are

undoubtedly associated with the infection and, accordingly, are not relevant to a comparative discussion of the renal injury. The following points are worth discussing in this context.

A. Reduction in glomerular filtration rate and its relationship with the morphological changes.

The degree of reduction in the glomerular filtration rate in pyometra bitches is correlated to the degree of the histopathological changes in the glomerulus (*Obel et al.* 1964). In this respect, renal dysfunction in pyometra bitches fits in with the renal dysfunction in human beings with acute pathological changes in the glomerular capillaries (*Parrish et al.* 1961). Reduction in the filtration fraction (*Åsheim* 1964 a) also suggests that the glomerular damage is of an acute type (*Allen* 1962).

B. Proteinuria and its relationship with the morphological changes.

If the degree of proteinuria is taken as a measure of the pathological increase in protein permeability of glomerular capillaries the increase in permeability in pyometra nephritis is relatively moderate. On the other hand, in human beings with mixed membranous and proliferative glomerulonephritis — the type of renal damage which most closely resembles the glomerulus injury in pyometra bitches — the degree of proteinuria is often severe. It is tempting to ascribe this difference in capillary permeability to the fact that there is a much greater degree of thickening of the "true" basement membrane in pyometra nephritis. In the human lesion, much of what appears under the light microscope to be thickening of the basement membrane in reality, as seen by electron microscopy, represents deposits. There is, however, another possible explanation to the difference between human beings and pyometra bitches in the degree of proteinuria and that is that dogs may have a greater capacity for resorption of filtered protein.

In types of renal damage in human beings accompanied by heavy proteinuria, the foot processes of the epithelial cells are usually extensively fused (*Movat et al.* 1959; *Farquhar* 1960). In states with moderate or slight proteinuria the changes in these structures are correspondingly less severe (*Allen* 1962). In pyometra bitches only slight and focal fusion of the foot processes has been observed. The one pyometra bitch with extensive fusion

of the foot processes was the only one with heavy proteinuria (*Obel et al.* 1964). Thus the combination of only slight or moderate proteinuria and well-preserved foot processes which is a characteristic of pyometra nephritis suggest that there is the same correlation between proteinuria and fusion of the foot processes in pyometra bitches as in human beings.

C. Absence of oedema and hypertension in glomerulonephritis in dogs.

The absence of oedema and hypertension in the clinical manifestations is one of the most striking differences between pyometra nephritis and glomerulonephritis in human beings. The absence of oedema in pyometra bitches does not necessarily imply that there is a fundamental difference between the renal injuries. Dogs simply seldom develop oedema in clinical states, cardiac insufficiency for example, which in human beings are almost invariably associated with oedema. The same applies to the absence of hypertension in pyometra bitches. It has been demonstrated that a normal blood pressure is maintained by dogs with other types of nephropathies (*Persson et al.* 1961). Hypertension is uncommon in naturally-occurring diseases of dogs.

D. Hypercholesterolaemia.

An increase in the serum cholesterol content accompanies acute glomerulonephritis in children (*Heymann & Wilson* 1959), the nephrotic syndrome in adults (*Allen* 1962) and nephrotoxic serum nephritis in dogs (*Seegal et al.* 1955). An increase in serum cholesterol is also associated with pyometra nephritis but the increase is more moderate than in the nephrotic syndrome of human beings.

The cause of the hypercholesterolaemia of glomerulonephritis is unknown. Some have proposed that the hypercholesterolaemia is associated in some way with the hypoalbuminaemia which occurs at the same time (*Rosenman et al.* 1956). On the other hand, hypoalbuminaemia not caused by renal damage is not accompanied by hypercholesterolaemia (*Gordon* 1959). The fact that serum cholesterol values in pyometra bitches return to normal after ovariohysterectomy more rapidly than the albumin values suggests that there is no direct relationship between the changes in these two serum components.

E. Possible relationship between hyperproteinaemia and plasma volume.

The hyperproteinaemia of pyometra bitches could result from either an increase in plasma protein synthesis or a reduction in plasma volume. Since there was no comparable control series for the plasma volume determinations, the results obtained have limited absolute value. But since the serum protein levels after ovariohysterectomy regularly approached normal values regardless of whether the plasma volume increased or decreased, it seems unlikely that the hyperproteinaemia of pyometra results from a decrease in plasma volume.

F. Reduction of renal concentrating ability.

The renal concentrating ability is often normal in human beings with glomerulonephritis. Only when the damage to the renal parenchyma is extensive does the max. osmotic U/P ratio decline and polyuria occur. There is no extensive parenchyma damage in the kidneys of pyometra bitches to explain the reduction of the max. osmotic U/P ratio (*Obel et al.* 1964). This represents a clear difference between pyometra nephritis and glomerulonephritis in human beings. The difference is not necessarily a species difference in the manner in which the kidney tissue reacts in pathological states. There is, in fact, experimental evidence suggesting that the polyuria of pyometra is induced by toxins absorbed from the uterus and which — probably by increasing blood flow through the kidneys — reduces the sodium gradient in the medulla and with it, the concentrating ability (*Åsheim* 1964 d). There is probably no state in human beings in which the body is exposed to toxins to the same extent as is the case for bitches with pyometra.

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SUMMARY

This report deals with some clinical features of bitches with pyometra accompanied by polyuria. According to previous morphological studies a glomerulonephritis often acompanies pyometra in bitches. The renal dysfunction of pyometra has been compared with observations made on human beings with morphologically similar nephropathies.

Reduction of the glomerular filtration rate and filtration fraction, the occurrence of proteinuria, and hypercholesterolaemia are clinical features in common.

The reduced concentrating ability of pyometra bitches — probably the result of toxin released from the uterus — gives polyuria, a clinical sign which does not appear in human beings with glomerulonephritis.

Other differences are the absence of oedema and hypertension in pyometra bitches. These differences do not necessarily imply a difference in the nature of the renal damage; they more likely represent species differences in reaction patterns.

Possible causal relationships between the different functional abnormalities and between the functional abnormalities and the morphological changes are discussed.

ZUSAMMENFASSUNG

Komparative pathologisch-physiologische Gesichtspunkte über die Glomerulonephritis in Zusammenhang mit der Pyometra beim Hund.

Der Autor hat Hunde die infolge einer Pyometra an Polyurie erkrankten klinisch untersucht. Seinen früheren morphologischen Untersuchungen gemäss, wurde bei den Tieren mit Pyometra in Nieren

oft eine Glomerulonephritis festgestellt. Die Resultate wurden in Hinsicht auf die beobachtete Funktionsstörungen verglichen mit solchen Nephropathien beim Mensch die ein ähnliches morphologisches Bild hatten.

Hinsichtlich der Reduktion der Glomerulifiltration und der Filtrationsfraktion, des Vorkommens von Proteinurie und Hypercholesterolämie, übereinstimmt die Pyometranephritis klinisch mit den Verhältnissen beim Mensch.

Da die Konzentrationsfähigkeit bei der Pyometranephritis vermindert ist — möglicherweise von der Toxinaussonderung aus Gebärmutter abhängig — entsteht bei Pyometrahunden eine Polyurie als Unterschied von der Glomerulonephritis beim Mensch.

Die andere Unterschiede bei den Pyometranephriten bestehen im Mangel an einer Ödemtendenz und Hypertonie. Es bestehen jedoch Gründe zur Annahme, dass die letztgenannten Unterschiede nicht bedingt werden müssen durch Unterschiede in der Art der Nierenschädigung, sondern könnten sich auch auf die artspezifische Reaktionsweise beziehen betreffend die extrarenale Funktionen bei Mensch bzw. Hund.

Der eventuelle kausale Zusammenhang teils zwischen den verschiedenen beobachteten Funktionsstörungen untereinander, teils zwischen diesen und den bestehenden morphologischen Veränderungen, wird diskutiert.

SAMMANFATTNING

Komparativa patofysiologiska synpunkter på glomerulonefriten i samband med pyometra hos hund.

Författaren har utfört kliniska undersökningar på hundar som visat polyuri i samband med pyometra. Enligt författarens tidigare morfologiska undersökningar föreligger i njurarna hos pyometradjuren ofta en glomerulonefrit. Resultaten ha med avseende på iakttagna funktionsstörningar jämförts med sådana nefropatier hos homo som förete en likartad morfologisk bild.

Med avseende på reduktion av glomerulusfiltration och filtrationsfraktion, förekomst av proteinuri och hypercholesterolämi överensstämmer pyometranefriten kliniskt väl med förhållandena hos homo.

Genom att koncentrationsförmågan vid pyometranefriten är nedsatt — troligen beroende på toxinutsådd från uterus — uppstår hos pyometrahundarna en polyuri vilket skiljer den från glomerulonefriten hos homo.

Andra skillnader är avsaknaden av ödemtendens och hypertoni vid pyometranefriten. Det finns emellertid skäl som tala för att sistnämnda skillnader ej behöva betingas av skillnader i njurskadans *art* utan kunna hänföra sig till artspecifika reaktionssätt vad gäller extrarenala funktioner hos homo resp. hund.

Eventuella kausalsammanhang dels mellan de olika iakttagna funktionsstörningarna inbördes dels mellan dessa och de föreliggande morfologiska förändringarna diskuteras.

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