EXPERIMENTAL AND CLINICAL OBSERVATIONS
ON THE URINE AND BLOOD
IN NEPHRITIS

BY

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The following observations have been carried out as follows:-

I. On two dogs and eight Rabbits in which experimental nephritis had been induced by the hypodermic injection of Potassium Chromate.

In each of these a qualitative and quantitative analysis of the urinary constituents was carried out and observations were made on the blood.

II. Similar observations on the human subject were carried out in
one case of acute parenchymatous nephritis
one case of subacute parenchymatous nephritis and on
one case of interstitial nephritis.

These experiments and the analyses were conducted at the College of Physicians' Laboratory, Edinburgh.

Methods

In the animal experiments the toxins commonly used, Cantharidis, Corrosive Sublimate and Oxalic acid are difficult to regulate and when the changes in the blood are to be noted, the results are undesirable on account of their haemolytic effect on the blood.

The toxin found most suitable for prolonged administration was a salt of chromic acid, the salt used in these experiments was the potash salt.

Chromic salts were found suitable by Hall and Herxheimer (Brit. Med. Journal 1903). They state, that apart from the toxic action on the organism the changes in the kidney, etc., are so regular that any direct effect, i.e., the effect on the tissues produced directly by the salt, as opposed to the effect due to the nephritis, is minimal.

The strength of the solution used in these experiments was 0.1 gramme of Potassium Chromate dissolved in 20 c.c. of water.

The dose varied with the weight of the animal, the usual standard taken was 10 cc (0.05 gr. Pot. Chrom.) for an animal of 1500 grammes.

The first rabbit got 0.1 gramme but the action was so severe that the animal died in two days.

In several rabbits the injection was repeated three times, 0.05 grm. of Potassium Chromate given on each occasion.

The animals were kept in a ^{wood} mice cage, the floor of which inclined to a central drain. This drain was filled with glass wool through which the urine filtered free from faeces etc. to a receptacle below.

The diet during the whole experiments

I. Rabbits.

A constant green vegetable diet, in the form

of cabbage, was given, as upon such the daily excretion is more abundant and regular than on the usual laboratory diet of meal and water.

II. Dogs.

The dogs were fed with oatmeal porridge without salt, along with milk.

Experiment I.

Rabbit - 1960 grammes.

22nd Dec. 1905 - 0.1 grm. of Pot. Chromate
in 20 c.c. of water injected hypodermically.

First day after injection there was no urine
excreted, on the second day the amount was 200 c.c.

The urine contained albumen 3.5 per mille.

Deposit - Renal epithelium and granular tube casts.

Died on 24th Dec. 1905.

Urinalysis

	Daily amount in cc	Sp. gr.	Reaction
17th	90 cc	1022	Alkaline
18th & 19th	380 cc	1022	Alkaline
23rd	no urine	-	-
24th	200 cc	1017	Acid

Total Nitrogen in grammes per diem

17th	.6
18th & 19th	.85
23rd	-
24th	.39

Urea Nitrogen in grammes per diem

17th	.43
18th & 19th	.56
23rd	-
24th	.23

Urea Nitrogen as percentage of Total Nitrogen

17th	70
18th & 19th	70
23rd	-
24th	58

Proteid

Total Proteid - .35%

Separate Proteids - Serum albumen - .27%

Serum Globulin - .07%

Deposit - Granular Tube casts.

Histological changes in Organs

Spleen.

Malpighian Bodies are large and present no special features. Pulp shows acute congestion and throughout it are numerous small rounded and irregularly shaped granules of a dark brown coloured pigment; this for the most part is lying free but is sometimes found intracellular. Here and there throughout the pulp are large cells which have ingested red blood corpuscles to such an extent as to obscure their characteristics.

Marrow

Also congested; no haemoblastic increase, slight increase of the leucoblastic cells. Giant cells are numerous and in some cases somewhat

degenerated, in one or two instances the nucleus appearing to be undergoing fragmentation.

Kidney

Glomeruli show signs of early congestion. Epithelium of convoluted tubules and collecting tubules is swollen but nuclei stain distinctly. There is no desquamation of cells, but there is a considerable amount of exudation forming casts in the convoluted tubules, more marked in the collecting tubules. Henle's tubules are not so severely affected.

Liver

Shows no gross changes.

Experiment II.

Rabbit - 1460 grms.

2nd Jan. 1906 0.025 grms of Pot. Chrom. in 5 cc of water was injected.

The urine passed on 3rd January contained .078% albumen. Deposit - few renal cells and granular tube casts.

Urine on 4th Jan. contained less albumen, deposit similar.

Blood before injection

Red cells	White cells	Polymorphs (1)	Lymphocytes	Basophile
4,830,000	5600	57	40	2

After injection

4,500,000	7000	62	35	3
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Rabbit killed 5th Jan. 1906.

(1) In these and the following differential counts in rabbits no attempt has been made to separate the pseudo-eosinophile (the common polymorph in the rabbit) from the Eosinophile.

Urinalysis

	Daily urine in cc	Sp. gr.	Reaction
Jan. 1st	260 cc	1014	Alkaline
" 2nd	300 cc	1010	"
" 3rd	230 cc	1017	"
" 4th	370 cc	1011	"

Total Nitrogen in grms per diem

Jan. 1st	.42
" 2nd	.56
" 3rd	.96
" 4th	.75

Urea Nitrogen in grms per diem

Jan. 1st	.3
" 2nd	.4
" 3rd	.72
" 4th	.56

Urea Nitrogen as percentage of Total Nitrogen

Jan. 1st	78%
" 2nd	71%
" 3rd	75%
" 4th	74%

Total Proteid - .078% Jan. 3rd
 .07% " 4th

Separate Proteid	Serum Albumen	- .05	} Jan. 3rd
	Serum Globulin	- .028	
	Serum Albumen	- .06	} Jan. 4th
	Serum Globulin	- .01	

Histological Changes in Organs

Spleen

Malpighian Bodies are large. Pulp is congested and shows slight amount of pigment, as seen in Rabbit I.

Marrow.

Shows no erythroblastic activity but slightly of the leucoblastic portion. Giant cells normal. No great changes except the increase of the leucoblastic tissue.

Kidney

Glomeruli are slightly congested. Epithelium of Convoluted tubules and collecting tubules shows early desquamation and early formation of casts. Henle's tubules practically unaffected.

Liver

Shows no gross changes.

Experiment III.

Rabbit - 2120 grms.

5th Feb. 1906 0.05 grms of Pot. Chrom. in
10 cc of water was injected.

6th Feb. - urine contained no albumen.

7th Feb. - Albumen amounted to 10 per mille.
Deposit renal epithelium and granular tube casts.

The albumen gradually diminished and on 13th
Feb. was 0.5 per mille.

A second injection (0.025 grm. Pot. Chrom.)
was given on the same day. The urine for the
following four days contained albumen amounting to
0.5 per mille.

A third injection (0.05 grm. Pot. Chrom.) was
given on 20th Feb. Albumen on Feb. 21st amounted
to 3. per mille. 23rd and 24th 1.75 per mille
and on 27th Feb. had fallen to .3 per mille.

Fourth injection (0.05 grm. Pot. Chrom.) was
given on 27th Feb. Urine on 28th Feb. albumen
was .5 per mille, rose to 10 per mille on March
1st. Deposit - Renal epithelium, hyaline and
granular casts in great quantities.

March 2nd - 5 per mille

" 3rd - 2 per mille.

On March 4th Rabbit was killed - weight 1275
grms.

Changes in the Blood

	Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
Before					
in-jection	5,160,000	5800	46	46	5
13.2.06	5,900,000	5800	63	25	12
24.2.06	5,000,000	5400	24	54	22

Histological Changes in the OrgansSpleen

Malpighian Bodies are small. Pulp is enormously congested and full of lymphocytes. Here and there in the sinuses are large cells full of a golden brown pigment. Endothelium lining some of the sinuses is prominent and almost cubical in shape.

Marrow

Shows advanced gelatinous degeneration. Fat cells in large part are shrivelled and in many cases altogether disappeared. Giant cells are scanty and degenerated. Capillaries have lost the defined arrangement found in normal marrow of rabbit and red cells form the bulk of the tissue. Erythroblastic action is less than normal. Leucocytes are less than normal and are found singly or in small groups, and for the most part comprise eosinophiles and pseudo-eosinophiles. Few large lymphocytes and very few polymorphs to be seen.

Table of Experiment III.

	Daily urine in cc	Albumen per mille	Weight in grms.
Average before injection	168	-	2120
Feb. 6th	73	nil	
" 7th	90	10	
" 8th	82	8	
" 9th	62	2	
" 10th	130	1	
" 11th & 12th	270	.5	1640
" 13th	225	.5	
" 14th	120	.5	
" 15th	100	.5	
" 16th	122	.5	
" 17th	142	-.5	
" 18th	171	nil	1810
" 20th	250	.5	
" 21st	164	1	
" 22nd	160	3	
" 23rd	130	1.75	
" 24th	110	1.75	
" 25th	140	.5	
" 26th	210	.3	
" 27th	210	.3	1595
" 28th	123	.5	
Mar. 1st	40	10	1445
" 2nd	65	5	
" 3rd	98	2	1275

Experiment IV

Rabbit - 2300 grms.

22nd Feb. 0.05 grms of Pot. Chrom. was injected in 10 cc water.

Resulting nephritis was slight. There were traces of albumen (.5 per mille) in the urine for the following four days. Deposit - few renal epithelial cells.

Feb. 27th - .05 grms Pot. Chrom. injected.

Feb. 28th albumen amounted to 1 per mille. 2nd and 3rd March - 2 per mille on each day.

And injection was repeated on 30th March when 0.075 grm. Pot. Chrom. was injected, followed by no urine on March 31st and on April 1st heavy precipitate on boiling. Deposit - hyaline casts. Rabbit was killed on 2nd April. Weight - 1780 grms.

Changes in the Blood

	Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
Before in-jection	5,790,000	7600	52	41	7
After in-jection					
26.2.06	5,600,000	8400	71	26	3
3.3.06	5,600,000	8200	69	28	3
9.3.06	5,400,000	8000	63	34	3

Histological Changes in the Organs

Spleen

Congested. Malpighian Bodies are atrophied and inconspicuous. The most striking feature is the packing of the pulp with large cells containing disintegrating red blood corpuscles, or a yellow pigment derived from them, in a few cases these are enormously large. Cells in pulp are almost all lymphocytes.

Marrow

Is in an advanced state of gelatinous degeneration. The fat has practically disappeared from the cells leaving the capsules collapsed. Throughout the marrow there seems to be an increase of fibrous tissue. Leucocytes, chiefly pseudo-eosinophiles and pseudo-eosinophile myelocytes, are present in rather less than normal amount. Giant cells are scanty and degenerated.

There is a very large number of large cells packed with a golden brown pigment.

Kidneys

Show very marked fibrous interstitial changes. Many of the convoluted tubules have altogether disappeared and are replaced by fibrous tissue. Some of the glomeruli have disappeared likewise. Casts in tubules are numerous. Collecting tubules and Henle tubules are similarly, but to a less extent, affected.

Liver.

Shows marked fatty-degeneration of cells.

Pigmentary changes are similar to rabbit V. but not so conspicuous in the endothelial cells.

Table of Experiment IV

	Daily urine in cc	Albumen per mille	Weight in grms.
Average before injection	242	-	2300
Feb. 23rd	210	Trace	
24th	-	-	
25th	171	.5	
26th	120	1.	2230
27th	220	.5	
28th	120	1.	
Mar. 1st	nil	-	2040
2nd	265	2.	
3rd	160	2.	
4th & 5th	216	.5	1945
6th	140	.5	
7th	298	.5	
8th	130	.5	1900
9th	198	.4	
10th	140	Trace	
11th & 12th	180	Trace	1890
13th	142	Trace	
14th	290	nil	
15th	380	nil	
16th	290	nil	
17th & 18th	450	nil	
30th	270	.5	
31st	-	-	
April 1st	84	^{heavy} Many ppt.	1780

Experiment V.

Rabbit - 2230 grms.

13th March 1906 - .05 gm. of Pot. Chrom. in 10 cc of water was injected.

On March 16th the urine contained albumen 2.5 per mille, renal epithelium and Granular tube casts. For the next three days albumen was .5 per mille. Deposit - few renal cells and portions of tube casts. Weight - 2170.

March 22nd injection (0.75 gm. of Pot. Chrom. in 15 cc of water) was repeated. On March 25th and 26th albumen amounted to 2.5 per mille. Deposit as before.

April 6th - no albumen. Weight - 2220 grms. .1 gm. of Pot. Chrom. was injected.

7th April albumen 3. per mille and 2 per mille on 8th. Deposit of renal epithelium with granular and hyaline tube casts.

The nephritis gradually subsided till 18th April when the rabbit was found dead.

Changes in the Blood

Before injection

Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
6,870,000	7,800	39	54	6

After injection

	Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
26.3.06	6,440,000	18,000	47	47	6
22.3.06	6,150,000	10,000	37	57	6
24.3.06	6,130,000	8,100	46	48	6
5.4.06	6,500,000	7,800	44	50	6
7.4.06	5,520,000	13,400	63	52	5
13.4.06	6,280,000	7,200	50	44	6

Histological changes in the Organs

Spleen.

Pulp is markedly congested. Malpighian Bodies are small. In the sinuses are large cells, both endothelium and leucocytes, which are engorged with slightly altered red blood corpuscles, or with a golden brown pigment derived from them. In addition to this there is a small quantity of a darker brown pigment in small granules, for the most part free and to a less extent intracellular.

Some of the sinuses show a remarked prominence of the endothelial cells lining them. This change was also seen in the case of rabbit IV.

Marrow.

Shows marked congestion, loss of normal arrangement of blood vessels. Increase of cellular elements encroaching upon the tissues, especially the fat cells. Leucocytes seem diminished in

number and seem more widely scattered among the erythrocytes than usual, a very few show mitosis.

Giant cells scanty and degenerated.

Erythroblastic tissue is not active.

Kidney.

Glomeruli show slight fibrous thickening.

Bowman's capsule shows active proliferation. In some of the glomeruli there is accumulation up to the capillaries.

In convoluted tubules, the epithelial cells are swollen and nuclei not visible. Casts numerous. In loop tubules active cell proliferation is seen.

Liver.

Throughout the liver there is a moderate quantity of a granular brown pigment, this is rather more in amount towards the periphery than the centre of the lobules.

In addition to this, the endothelium lining the capillaries are in many cases packed with a similar pigment.

There is no evidence of congestion.

Table of Experiment V.

	Daily urine in cc	Albumen per mille	Weight in grms.
Average before injection	250	-	2230
March 14th	140	-	
15th	54	Trace	
16th	110	2.5	
17th	90	.5	
18th & 19th	160	.5	2170
20th	300	.4	
21st	278	.5	
22nd	320	.25	
23rd	200	2.5	
24th	190	.5	
25th & 26th	120	2.5	
27th	80	2	
28th & 29th	110	.6	
30th	106	.5	
31st	246	Trace	1990
April 6th	120	.5	
7th	110	3.	
8th & 9th	210	2	1910
10th	140	.5	
11th	200	.5	
12th	260	.4	
13th	106	.25	
14th	210	Trace	
15th & 16th	420	"	
17th	204	"	1410

Experiment VI.

Rabbit - 1845 grms.

May 30th injected with .05 grms. of Pot. Chrom. in 10 cc of water.

May 31st 450 cc urine excreted containing albumen 1.5 per mille; few granular casts in deposit.

Urine fell to 40 cc on June 1st, albumen amounted to 4 per mille. Deposit - granular tube casts.

June 2nd - 120 cc of urine, albumen 5 per mille, deposit same.

The albumen gradually disappeared from the urine. June 16th albumen nil; weight 1790. June 18th injection repeated (.05 gm. Pot. Chrom. in 10 cc of water) subsequent nephritis was slight. Albumen .5 per mille in the next 5 days.

June 25th - .05 gm. Pot. Chrom. injected. No urine excreted on the following day but on second day rose to 240 cc. There was a heavy precipitate of albumen.

Rabbit died July 8. Weight 1010 grms.

Changes in the Blood

Before injection

Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
7,530,000	10,600	53	45	2

After injection

	Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
31.5.06	7,200,000	9200	44	52	4
2.6.06	7,500,000	16000	60	40	2
4.6.06	8,220,000	10600	45	45	10
7.6.06	7,300,000	12500	54	40	6
16.6.06	7,900,000	10500	48	44	8
18.6.06	7,000,000	13300	54	40	6
20.6.06	6,000,000	10500	-	-	-
28.6.06	6,000,000	13000	-	-	-

Histological changes in the Organs

Spleen

Is congested. Malpighian Bodies are small and comparatively inactive. Endothelial cells in sinuses are very prominent and in the sinuses there are large cells which contain a dark brown pigment.

Marrow

Is congested. Fat cells are shrunken and diminished. Erythroblastic action is diminished, total number of red cells greatly reduced and very few nucleated red blood corpuscles visible. There is marked evidence of red cell destruction.

Scattered through the marrow, but tending to collect in areas, are large cells (as seen in the spleen) which have engulfed red blood corpuscles; these may be seen lying in the cells in all stages of disintegration.

Leucoblastic tissue is unusually active, the number of eosinophiles and pseudo-eosinophiles seen in all stages of mitosis being very great.

Kidneys.

Show marked congestion of blood vessels and glomeruli, in a few instances haemorrhagic effusion between the glomeruli and capsul~~e~~ and into the surrounding tissue is present.

Epithelium of convoluted tubules is swollen, nuclei stain indistinctly; lumen very much narrowed and filled with desquamated cells.

Descending, ascending, and loop tubules of Henle show desquamation of cells to a very much slighter degree.

Collecting tubules practically unaffected.

Early interstitial changes seen throughout the kidneys.

Liver.

Shows slight congestion. A few granules of pigment in cells at periphery of lobules.

In the hepatic capillaries, here and there throughout the liver are granular leucocytes in all stages of mitosis.

Table of Experiment VI.

	Daily urine in cc	Albumen per mille	Weight in grms.
Average before injection	210		1845
May 31st	450	1.5	
June 1st	40	4	
2nd	120	5	
3rd & 4th	145	3	
5th	115	1	
6th	185	.5	
7th	165	Trace	1790
June 19th	50	.5	1740
20th	240	.5	
21st	320	.5	
22nd	160	.5	
23rd & 24th	360	.5	
25th	380	Trace	
26th	no urine	-	
27th	240	<i>heavy</i> Many ppt.	
28th	200	"	
29th	no urine		1010

Experiment VII.

Rabbit - 1750 grms.

2nd Oct. 0.05 grms of Pot. Chromate was injected.

The induced nephritis was slight, albumen small, never above .5 per mille.

Oct. 12th - Injection (0.05 grm. Pot. Chrom.) repeated. On Oct. 15th albumen amounted to 4 per mille, deposit-granular and hyaline casts in abundance.

Oct. 16th albumen equalled 10 per mille, deposit similar as on 15th.

Rabbit killed 16th Oct. Weight - 1450.

Changes in the Blood.

	Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
Before injection	6,660,000	8500	48	47	4
After injection	6,000,000	10500	53	43	4

Histological changes in the OrgansSpleen

Is congested. Malpighian Bodies are not prominent. In the sinuses there are many large cells which have ingested red blood corpuscles. A golden brown pigment present chiefly intracellular.

Liver

Is congested. Cells show considerable amount of/

of fatty degeneration.

Very few granules of pigment to be seen.

Kidney

Malpighian Bodies are swollen and congested.

Many of the convoluted tubules have undergone a hyaline change, so that they appear homogeneous..

In many of the ascending, loop and collecting tubules casts are seen.

Marrow

Fat cells show absorption. Erythroblastic action is diminished. Very few nucleated red cells to be seen.

Leucoblastic activity is considerable, mitotic figures seen in several of the large leucocytes.

Giant cells normal.

Table of Experiment VII.

	Daily urine in cc	Albumen per mille	Weight in grms.
Average before injection	350	-	1750
Oct. 4th	410	.5	
5th	360	.5	
6th	320	.1	
7th & 8th	220	Trace	
9th	190	"	
10th	200	"	
11th	400	Nil	
12th	350	Nil	
Injection repeated			
13th	240	.5	
14th	205	.1	
15th	220	4	
16th	120	10	1050

Experiment VIII.

Rabbit - 1560 grms.

Aug. 20th injected 0.05 grms Pot. Chromate.
Nephritis lasted for six days, albumen never above .5 per mille.

25th Sept. injection repeated (0.05 grms).

Again reaction was poor. On the day following injection there was a slight diminution of urine but no albumen was present. On the following three days the albumen never rose above .5 per mille.

Oct. 2nd weight 1400 grms. 0.05 gram of Pot. Chromate in 10 cc of water was injected.

Oct 4th., albumen -.5 per mille. Oct. 5th, 3.5 per mille.

No urine was excreted on Oct 6th and 7th.

Rabbit found dead on Oct. 8th.

Changes in the Blood.

	Red cells	White cells	Poly-morphs	Lymphocytes	Basophiles
Before injection	7,250,000	7000	46	48	6
After injection 24.8.06	6,900,000	8000	47	47	6
27.8.06	7,500,000	7000	39	56	5
29.8.06	6,800,000	8800	41	52	7
6.9.06	6,000,000	10000	60	32	8

Table of Experiment VIII.

	Daily urine in cc	Albumen per mille	Weight in grms.
Average before injection	220		1560
Aug. 21st	200	.1	
22nd	200	.55	
23rd	205	.5	
24th	210	.1	
25th	190	trace	
26th	250	nil	1450
Injection repeat- ed Sept 25th			
Sept. 26th	75	nil	
27th	110	.5	
28th	220	.4	
29th	185	.1	
30th	160	trace	1400
Injection repeated			
Oct. 2nd			
3rd & 4th	210	.5	
5th	240	3.5	
6th No urine		-	
7th No urine		-	1230

Experiment IX.

Female dog. .1 grm of Pot. chromate in 20 cc of water was injected on 2nd July 1906.

3rd July - The urine was lost as the dog suffered from diarrhoea.

4th July - 560 cc, slight amount of albumen, deposit nothing to note.

5th July - 610 cc. Trace of albumen, deposit few granular casts and epithelium.

6th July - 555 cc. Trace of albumen. 0.05 grm. Pot. Chrom. injected.

7th July - 730 cc., rise in amount of albumen

8th July - 710 cc. Fairly heavy precipitate with Nitric Acid and on boiling. Deposit granular tube casts.

9th July - 370 cc., albumen and deposit same as on 8th.

The total Nitrogen, Chlorides, Phosphates and Creatinin were estimated daily.

	<u>Daily urine in cc</u>	<u>Total Nitrogen in grm per diem</u>	<u>Chlorides in grm of NaCl</u>	<u>Phosphates in grm of P₂O₅</u>	<u>Creatinin in grm per diem</u>
Average before injection	550	4.6	1.6	1.05	.435
July 4th	560	3.7	.67	0.87	.392
5th	610	3.7	.88	1.22	.449
6th	555	3.3	.66	0.79	.320
Reinjected on 6th					
7th	730	4.8	1.04	1.43	.492
8th	710	2.71	.71	1.10	.383
9th	350	3.05	.49	0.84	.297

61

Experiment X

In this experiment the proteids in the urine were separated.

Dog - 14½ Kilos.

26th Nov. 1905. 1 grm of Pot. Chromate in 20 cc of water was injected.

	Proteid per cent	Serum Albumen	Serum Globulin
Nov. 27th	1.29	0.9	0.38
28th	.69	0.56	0.13
29th	no urine		
30th	.122		
Dec. 1st	.08		
2nd	.04		
3rd	.02		
4th	.018		
Injection repeated 9th Jan. 1906			
Jan. 18th	0.17	0.12	0.05
11th	0.21	0.16	0.05
12th	0.14	0.10	0.04

Changes in the Blood

	Red cells	White cells	Poly-morphs	Lymphocytes	^{Baso.} Basophiles
Before injection	8,160,000	10,100	69	30	1
After injection					
28.11.05	5,350,000	17,000	75	20	5
30.11.05	5,370,000	16,400	66	25	10
5.12.05	7,040,000	11,600	70	20	10
10. 1.06	6,470,000	23,200	75	20	5
15. 1.06	7,870,000	16,800	63	26	9

Effect of Nephritis on Amount of Urine

The results in this connection can perhaps be best compared by expressing the daily quantity of urine passed after injection as a percentage of the urine before injection.

<u>Experiment</u>	<u>Days</u> -	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>
I.		80	85				
II.		82	182				
III.a.		43	53	48	37	77	
b.		53	40	48	63	76	
c.		65	65	52	44	53	
d.		58	19	40	46		
IV.a.		70	50	90			
b.		50	0	101	41	45	
c.		54	0	35			
V.a.		56	21	44	64	120	
b.		48	32	44	40	98	98
c.		40	84	56	101		
VI.a.		19	57	69	56	88	
b.		23	101	150	76	85	
c.		100	0	101	95	85	
VII.a.		117	103	91	63	100	
b.		68	58	62	34		
VIII.a.		90	90	91	95		
b.		34	50	100			
c.		95	0	0			
		<u>1165</u>	<u>1040</u>	<u>1212</u>	<u>855</u>	<u>743</u>	<u>98</u>
		20	20	18	14	9	1
Averages		58	52	67	61	82	98

Studying the tables, we find there is a marked fall in the amount of urine passed after the onset of the nephritis. This change is most marked during the first two days, when the urine fell to an average figure of 50%; after this the amount gradually rises again and by the 7th day the normal amount may be reached.

Excretion of Solids (Exp. IX.)Total Nitrogen

The average Total Nitrogen for three days before induction of nephritis was 4.6 grms. per diem.

After the onset of Nephritis:-

July 4th 3.7 grms per diem

5th 3.7 " " "

6th 3.3 " " "

7th 4.8 " " "

8th 2.71 " " "

9th 3.05 " " "

average of the 6 days - 3.1 grm.

Chlorides

The average output of chlorides for three days before induction of nephritis - 1.6 grms NaCl per diem.

After onset of nephritis:-

July 4th 0.67 grms per diem

5th 0.88 " " "

6th 0.66 " " "

7th 1.04 " " "

8th 0.71 " " "

9th 0.49 " " "

Average for the six days - 0.74 " " "

Phosphates

Average for three days before induction of
nephritis - 1.05 grm P₂O₅

After the onset

July 4th	0.87	grms	per	diem
5th	1.22	"	"	"
6th	0.79	"	"	"
7th	1.43	"	"	"
8th	1.10	"	"	"
9th	0.84	"	"	"
Average for the six days -	1.04	"	"	"

Creatinin

Average for three days before induction of
nephritis - .435 grms.

After the onset

July 4th	.392	grms	per	diem
5th	.449	"	"	"
6th	.320	"	"	"
7th	.492	"	"	"
8th	.383	"	"	"
9th	.297	"	"	"
Average for the six days -	.388	"	"	"

The total nitrogen was reduced on the onset of nephritis from 4.6 grms per diem to 3.7 grms per diem and still further when the albumenuria was more marked, viz - 2.71 grms per diem.

The chlorides were excreted in less amount during the nephritis; falling from 1.6 grms per diem to 0.67 grms. The amount rose as the albumen diminished, then there was another marked fall as the albumen increased again, viz - to 0.71 and 0.49 grms per diem.

The phosphates and creatinin showed less variation. The creatinin follows the curve of the chlorides but to a less extent. The phosphates show practically no reduction.

Summary Table

	Nitrogen (grms p. diem)	Chlorides (grms per diem)	Phosphates (grms per diem)	Creatinin (grms per diem)
Average before Nephritis	4.6	1.6	1.05	.435
Average during Nephritis	3.1	0.74	1.04	.388

Studying the results, as regards the total nitrogen, the chlorides, the phosphates and creatinin, we find the most distinct alteration in a reduction of total nitrogen and chlorides. To a

less extent there is a diminution of the creatinin and there is practically no alteration in the phosphates.

The total nitrogen is reduced by 25% and the chlorides ^{by} over 50%

There has been a considerable amount of work done ^{clin}chemically by French observers. The chief work has been done by Widal and Javal, they state that in interstitial nephritis there is practically no reduction of chlorides, but in parenchymatous nephritis there is a marked retention of chlorides, leading to an increase of fluid in the tissues and this retention is proportional to the albumenuria.

Labbe contradicts this statement and says there is no evidence of excess of chlorides in the blood.

In experiment IX., the very marked fall of the chlorides and the proportional rise in the albumen tends to confirm the contention of Widal and Javal.

When we compare the results along with the microscopical appearances of the kidneys of rabbits similarly injected, the diminution of the chlorides and nitrogen is evidently due to the epithelial changes of the convoluted tubules, as the glomerular changes are not great unless the nephritis has been long continued.

Proteid per diem expressed in Milligrammes.

Days	1	2	3	4	5	6
Exp. I.	0	700				
II.	170	250				
IIIa	730	720	160	62	60	
b	60	50	60	70	60	
c	160	480	220	180	16	
d	60	400	320	190		
IVa	80	120	110			
b	120	0	730	220	100	
c	60					
Va	0	0	275	80	160	
b	0	200	50	260	20	20
c	300	420	70	130		
VIa	160	600	430	110	90	
b	25	120	160	80	70	
c						
VIIa	40	180	160	110	170	
b	120	20	880	1200		
VIIIa	2	10	10	10		
b	0	50	100			
c	100	84	0	0		
	<u>2187</u> 20	<u>4560</u> 20	<u>3535</u> 16	<u>2662</u> 14	<u>746</u> 9	
Average	109	228	220	190	82	20

Proteid present in the Urine.

The table shows that the urine excreted the day after injection of Potassium Chromate, contains Albumen and that the albumen is present in largest quantities during the second day. From the second day the albumen gradually subsides, till by the seventh the urine contains practically none.

When we compare the tables of daily excretion of urine and the total output of proteid in the urine in 24 hours, it will be noticed that as the proteid rises the quantity of urine falls and as the albumen disappears the urine tends to return to the normal level.

In three experiments (I., II., and X.) the proteids were separated.

	Total Pro- teid	Serum Al- bumen %	Ser. Glo- bulin	Per cent of Total	
				S.A.	S.G.
Exp. I	0.35	0.27	0.07	75	25
II	0.078	0.05	0.028	66	34
	0.07	0.06	0.01	85	15
Xa	1.29	0.9	0.38	64	36
	0.69	0.56	0.13	81	19
b	0.17	0.12	0.05	73	27
	0.21	0.16	0.05	75	25
	0.14	0.10	0.04	71	29

The ratio of Serum Albumen to Serum Globulin
is/

is never constant. Serum albumen is present as a higher percentage of the total proteid and when the total proteid is high the globulin is present in greater amount.

Summary of Changes in Urine.Amount

I. The total urine per diem falls at the onset of nephritis, gradually rising again as the pathological condition subsides.

II. The amount of urine varies in inverse ratio with the actual amount of proteid it contains.

Excretions of Solids

Coinciding with the onset of nephritis there is a fall in the excretion of nitrogen, also marked retention of chlorides. To a less extent the creatinin output is diminished and practically no alteration in the output of phosphates occurs.

Proteid

I. In view of its relationship to the output of total nitrogen and other constituents, the amount of proteid present in the urine may be taken as an indication of the severity of the kidney lesion.

II. That Serum Albumen and Serum Globulin are always present,- Serum Albumen always being in excess.

In the presence of a high albumenuria, Serum Globulin is in greater proportion than in a low albumenuria.

Clinical Observations on NephritisCase 1 - Acute Parenchymatous Nephritis

	Daily urine in cc	Sp. gr.	Reaction	Proteid
Feb. 5th	275	1017	Acid	7.%
6th	1230	1016	"	6.5%
7th	1300	1015	"	7.%
8th	1360	1013	"	6.%

	Total Nitrogen grms per diem	Urea Nitrogen grms per diem	Ammonia grms per diem	Creatinin grms per diem
Feb. 5th	1.56	1.35	.084	.3
6th	7.65	5.8	.270	1.0
7th	4.81	4.03	.416	.74
8th	4.0	3.06	.340	.94

Note

The diet in Cases 1 and 2 was similar - milk and milk foods. In case 3 the patient was on convalescent diet - Fish, fowl, etc.

Case 2 - Subacute Parenchymatous Nephritis

	Daily urine in cc	Sp. gr.	Reaction	Proteid
Feb. 5th	900	1022	Acid	.1%
6th	1440	1016	"	.05%
7th	2520	1013	"	.05%
8th	2350	1014	"	.05%

	Total Nitrogen grms per diem	Urea Nitrogen grms per diem	Ammonia grms per diem	Creatinin grms per diem
Feb. 5th	10.26	8.73	.45	.9
6th	8.8	8.00	.32	1.4
7th	10.5	8.10	.2	1.5
8th	8.4	7.40	.8	1.6

Case 3 - Chronic Interstitial Nephritis

	Daily urine in cc	Sp. gr.	Reaction	Proteid
Nov. 15th	1740	1015	Acid	.018%
16th	1420	1020	"	.016%
17th	1820	1018	"	.05%
18th	1200	1022	"	.074%

	Total Nitrogen grms per diem	Urea Nitrogen grms per diem	Ammonia grms per diem	Creatinin grms per diem
Nov. 15th	10.3	9.5	.278	.93
16th	15.	12.6	.36	1.4
17th	16.8	15.4	.56	1.2
18th	13.4	12.4	.48	1.62

Separation of Proteids

	Total Proteid	Serum Albumen	%	Serum Globulin	%
Nov. 15th	.018%	.01	55	.008	45
16th	.016%	.01	63	.006	37
17th	.05 %	.035	66	.015	34
18th	.074%	.05	66	.024	34

Comparison of CasesTotal Nitrogen

	Case 1. grms per diem	Case 2. grms per diem	Case 3 grms per diem
	1.56	10.2	10.3
	7.65	8.8	15.
	4.81	10.	16.8
	4.	8.4	13.8
Average	4.5	9.3	13.8

Taking the daily excretion, we find there is a great variation from day to day.

This is most noticeable in the case of acute parenchymatous nephritis, whereas, in the case of subacute nephritis the daily amount shows comparatively slight alterations.

The amount excreted in all three cases is reduced, 13.8, 9.3 and 4.5 grms per diem.

The kidney lesions in the case of acute parenchymatous nephritis causes a marked reduction of the excretion of nitrogen, the amount rising as the pathological changes pass off.

In the case of chronic interstitial forms the reduction is slight

Nitrogen excreted in the form of Ammonia

Expressed as percentage of the Total Nitrogen

Case 1.	Case 2.	Case 3
5.4%	4.2%	2.7%
3.5%	4.8%	2.7%
8.4%	2.0%	3.5%
8.4%	2.0%	3.5%

The nitrogen excreted in the form of Ammonia is remarkably high in the acute parenchymatous type (as high as 8.4%), while in the subacute case the highest is 4.8% and in the interstitial case, only 3.5%

Creatinin

Creatinin is excreted in a fairly steady amount in Case 2 and Case 3 and only slightly altered in Case 1.

Summary of Results

I. Total Nitrogen

In the case of acute parenchymatous nephritis there was a marked reduction and irregular excretion, whereas, in the subacute case the amount rises and is more regular.

In the interstitial form the total nitrogen is not much below normal.

II. Urea Nitrogen

The urea nitrogen follows the same course as the total nitrogen.

III. Ammonia Nitrogen

In the case of acute parenchymatous nephritis the percentage of nitrogen excreted as ammonia is comparatively high.

IV. Creatinin

The Creatinin excretion is only slightly interfered with in Acute Parenchymatous Nephritis and in the other two cases the excretion is fairly regular and high.

Changes in the Blood in Nephritis

The following tables show the changes expressed as a percentage of the blood before the induction of nephritis.

Table I.

Showing changes in percentage of red and white blood corpuscles also day of experiment when observation was made.

	Red Blood Corps.	White Blood Corps.	Day of Experiment
Exp. II.	93	125	2nd
Exp. III.	114	100	7th
	96	96	4th
Exp. IV.	96	110	4th
	96	108	4th
	93	105	10th
Exp. V.	93	230	3rd
	89	128	1st
	89	103	3rd
	94	100	12th
	80	171	2nd
	91	92	8th
Exp. VI.	95	87	1st
	100	150	3rd
	109	100	5th
	96	118	7th
	104	99	12th
	94	125	1st
	79	100	4th
Exp. VII.	79	125	3rd
Exp. VIII.	90	117	4th

Table I. (Con.)

	Red Blood Corps.	White Blood Corps.	Day of Experiment
Exp. VIII. (Con.)	95	114	4th
	103	100	1st
	93	125	3rd
	82	142	4th
Exp. X.	65	168	2nd
	66	162	4th
	86	129	9th
	79	229	1st
	96	166	6th

Table II.

Changes in Red blood corpuscles arranged according to the days of experiment.

1st to 3rd Day	4th to 6th Day	7th to 9th Day	10th to 12th Day
93	96	114	93
93	96	91	94
89	96	96	104
89	109	89	<hr/>
80	79	<hr/>	<u>291</u>
95	90	<u>390</u>	<u>3</u>
100	95	4	
94	82		
79	66		
103	96		
93	<hr/>		
65	<u>905</u>		
79	<u>10</u>		
<hr/>			
<u>1122</u>			
<u>13</u>			
Average			
86	90.5	97.5	97

Table III.

Changes in White Blood corpuscles arranged according to days of experiment.

1st to 3rd day	4th to 6th day	7th to 9th day	10th to 12th day
125	96	100	105
230	110	92	99
128	108	118	100
103	100	129	—
171	100	—	<u>304</u>
87	117	<u>439</u>	<u>3</u>
		4	
150	114		
125	142		
125	162		
100	166		
125	—		
168	<u>1215</u>		
	10		
229			
—			
<u>1866</u>			
13			
Average			
143	121	109	101

These tables show the following changes in the blood:

(1) The red cells during the first three days of the nephritis fall to an average figure of 86%, gradually rising again during the next ten days to the normal percentage.

(2) The white blood corpuscles show a marked increase during the first three days to an average figure of 143%, falling during the fourth to the sixth day to 121% and by the 12th day they have practically reached the normal number.

The increase in the leucocytes is accompanied by a rise in the number of polymorphs as seen by the differential counts.

In the dog experiment the resolution of the nephritis was accompanied by a marked increase in the eosinophiles.

The results accord with the common statement (Bezançon and Labbé) that there is generally a fall in the number of the red cells, with an increase in the leucocytes on the onset of nephritis.

The leucocytosis of nephritis seems to be fairly constant even though associated with other pathological conditions. Gulland has pointed out that in several cases of pernicious anaemia the onset of nephritis was accompanied by a leucocytosis, while a pneumonia occurring in such cases does not usually produce any leucocytosis.

In scarlet fever, Bowie has shown that the onset of nephritis is accompanied, or even preceded by a distinct increase in the white cells.

Cabot says there is a slight diminution of the red cells in acute nephritis, but a leucocytosis is only present when there is some complication, such as, uraemia or loss of blood by the kidney.

The results of my experiments are not in accordance with the latter part of this observation.

In Experiment X. there was a great rise in the eosinophiles as the albumenuria passed off. This change has been recorded by Pieraccini,- he says that in the early acute stages the eosinophiles may be greatly reduced, but, as the case resolves they reappear and may be in great excess. This has also been confirmed by Lessow.

Summary of Chief Results.

I. In acute experimental nephritis caused by Potassium Chromate in rabbits, there is a diminution in the quantity of the urine excreted to the extent of nearly 50 per cent on the first two days. After this the quantity gradually returns to normal.

II. The daily output of albumen is small on the first day of the induced nephritis. It rises to a maximum on the second day, after which it gradually disappears. The quantity of urine varies in inverse ratio with the output of albumen.

III. In three experiments the proteids were separated. Serum albumen and serum globulin were always found to be present. Serum albumen was always in the higher percentage of the total proteid. In the case of a high albumenuria serum globulin was present in greater proportions than in a low one.

IV. During experimental nephritis in a dog the total nitrogen was reduced by 20 per cent., the chlorides by 50 per cent. while the creatinin was also to a comparatively slight extent reduced. The phosphates showed practically no alteration.

V. In three contrasted cases of nephritis in the human subject the results were as follows:-

Acute Parenchymatous Nephritis	Sub-acute Par. Nephritis	Interstitial Neph. Chronic
(1) <u>Total Nitrogen.</u> Reduced with great daily var- iations.	Reduced and practically constant.	Slightly reduc- ed with tri- vial varia- tions.
(2) <u>Ammonia % of Total Nitrogen.</u> High with daily variations.	Low	Low
(3) <u>Creatinin.</u> Slightly reduc- ed.	Slightly re- duced	Practically normal.

The urea nitrogen follows the total nitrogen in each case.

VI. In seven rabbits and a dog, (1) the red blood corpuscles showed an average fall of 14% on the onset of the nephritis and gradually rose again to normal; (2) the white blood corpuscles rose to the extent of 43%, gradually returning to the normal as the albumen disappeared.

The curve of the white blood corpuscles followed the curve of the proteid in the urine.

The differential counts showed an increase in the polymorphs and these also showed a return to normal, *pari passu* as the nephritis subsided.

VII. The histological changes in the organs, induced by Potassium Chromate, in the rabbit were acute nephritis, chiefly affecting the tubules and to a slightly less extent the glomeruli.

A remarkable congestion and phagocytosis of red blood corpuscles in the spleen. Slight pig-mentary changes in the liver and a marked leuco-blastic hyperplasia in the bone marrow followed by degeneration.

These changes were remarkably constant and the description of one might equally apply to any of the others.

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