syringe. By suddenly squeezing $\frac{1}{2}$ oz. of the saline solution through the hole into the cell, an appearance is produced which, when represented on the screen, is exactly similar to what is seen when a urinary shoot occurs into the living bladder. The image at the back of the cell (Fig. 1) represents the orifice of the healthy ureter, when the bladder is distended with 7 oz. of solution. The mucous membrane is of a pale colour, and has only a few vessels ramifying on its surface. The lips of the orifice are rounded and slightly elevated. The ridge is moderately marked, and the opening is sharply defined, and the space between the lips is of a darker hue. The upper and lower angles are rounded and smooth. When the fluid is injected from the syringe the clear definition of the orifice is lost for a second or two, until the dense fluid mixes with the cell contents.

The mingling of the saline solution with the water produces the same appearance as the mixing of urine with the sterilized water in the bladder. You have now seen the appearance of shoots of healthy urine. Later on, by substituting coloured fluids and semi-fluids, I shall demonstrate to you the escape of pus, blood, and blood clots.

[Some of the more easily recognized diseases were then demonstrated, as will be explained in the next part.]

REFERENCE.

¹ *Glasgow Medical Journal*, 1883, vol. xx, p. 132.

(To be continued.)

THE SCIENCE COMMITTEE

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REPORT XCIV.

ANAESTHETICS AND RENAL ACTIVITY:

AN EXPERIMENTAL INVESTIGATION INTO THE EFFECTS OF $\frac{1}{2}$ PROLONGED CHLOROFORM AND ETHER NARCOSIS.

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(Concluded from page 614.)

PART II.—ETHER NARCOSIS.

EXPERIMENTS with ether were carried out in the same way as with chloroform. In the earlier series the urine was collected from the ureters, in the later from the bladder.

EFFECTS ON THE QUANTITY OF URINE.

Of previous observers, Kemp³³ found that the secretion of urine was early diminished, and finally stopped under free and continuous inhalation of ether. In the experiments of Buxton and Levy³⁴ the secretion of urine was slowed, but a complete suppression from the effects of ether was never witnessed. A temporary suppression, which did occur in certain cases was attributed to accidental traction on the ureter. My own earlier conclusions³⁵ (drawn solely from "ureter" experiments) were, that during its administration, ether causes an increased secretion of urine, followed after removal by a still greater outflow. One case of marked depression was treated as an exception. Further inquiry, however, has made it quite clear that both effects are usual—the increase representing an earlier and lighter influence, the decrease a later and more profound action.

Table IX gives the detailed effects upon urine secretion in both "ureter" and "catheter" series of experiments.

A glance at the table will show that the increased effect on urinary secretion is practically confined to the ureter group. In Experiments 2, 3, and 4 of this series both effects are demonstrated, the "decrease" being obtained by a fuller degree of anaesthesia. The latter are amongst the most recently performed of the ether experiments, and were undertaken to ascertain if both effects could be obtained in one and the same animal by varying the

degree of anaesthesia. Blood-pressure tracings of 3 and 4 are given later.

TABLE IX.—ETHER: EFFECTS ON THE QUANTITY OF URINE.

Experiment.	I.	II.	III.	IV.	V.
<i>Ureter Series.</i>					
1 ...	6.7	31.70	31.7	21.10	8.3
2 ...	11.4	(a) 14.65 (b) 8.30	63.0	17.65	—
3 ...	35.2	29.35 17.00	15.1	—	—
4 ...	10.6	27.90 4.35	9.4	9.70	—
<i>Catheter Series.</i>					
1 ...	7.7	18.90	7.7	4.00	4.5
2 ...	8.5	4.00	51.0	45.00	—
3 ...	278.0	23.50	130.0	66.00	—
4 ...	16.5	2.25	29.5	144.00	—
5 ...	12.0	2.00	55.0	55.00	—
6 ...	10.5	3.50	16.5	33.00	—
7 ...	14.5	8.00	11.0	20.50	26.0
8 ...	38.0	1.00	13.5	48.50	30.0
9 ...	15.5	10.00	32.0	79.00	44.0
10 ...	9.5	1.00	14.5	25.00	16.0

The periods are of two hours' duration, except in Experiment 1 of each series, where they are one hour each.

N.B.—In Ureter Experiments 2, 3, 4, the double columns during the anaesthetic period represent (a) the early; (b) the pronounced effect.

The averages per period, drawn from the four "ureter" experiments are:

I.	II.	III.	IV.	V.
15.99	(a) 24.4 (b) 7.6	29.8	12.11	8.3

The increase during the first stage of Period II amounted to 152.6 per cent.; the fall during the second stage brought the rate down to 46.65 per cent. of the normal.

In the "catheter" series, with the exception of the first experiment, all show during the anaesthetic period a very marked decrease of secretion. The drop in one case—namely, Experiment 3, was unusually great, as was also the rate of secretion during the normal period. In this case the animal had inadvertently got access to slops in which meat had been boiled, and drank freely a short time before the experiment was begun. This only transpired when the normal sample of urine was drawn off and found to be unusually great. It was decided, however, to proceed with the observations, in order to test the effect of ether under such conditions. The experiment, however, is treated as exceptional, and is not included in the following averages, which are drawn from the remaining eight "decrease" experiments in the series:

I.	II.	III.	IV.	V.
15.62	4.0	24.25	56.25	29.0

During Period II the rate of secretion dropped to 25.4 per cent. of the normal, and rose again in Period IV to 360 per cent. of that amount. The depression and reaction effects of ether are therefore more pronounced than those of chloroform. In several of the experiments the secretion of urine was stopped, or practically so, for considerable periods of time. In these it did not appear that the degree of anaesthesia was greater, though more prolonged, than that required as a rule for surgical operations on the human body. Observations in the later ureter experiments confirmed this. At a degree of anaesthesia just beyond the loss of conjunctival reflex, the urine frequently ceased to flow from the cannulae, and remained suppressed as long as the anaesthesia was kept up. The matter will be referred to again when the vascular effects are considered.

A preliminary note upon this effect in dogs was published by me last year.³⁶ Corresponding observations have also been carried out at my suggestion on the human subject by Dr. Harold Pringle, Mr. C. B. Maunsell, and Dr. Seton Pringle,³⁷ which fully bear out the results obtained on animals in the laboratory. This effect of ether—in suppressing urinary secretion—appears also to have been known to the late Mr. Lawson Tait, who refers to it in a short letter to the *Lancet*, vol. i, p. 988, 1897. It was likewise seen by Kemp, in his experiments on dogs. It is, I believe, less liable to occur when morphine has been previously given.

EFFECTS ON THE EXCRETION OF NITROGEN.

Leppmann³⁸ found the excretion of nitrogen to be slightly increased by ether narcosis. The results of my own earlier observations³⁹ agreed with this, except in the one instance in which the quantity of urine was diminished. In the following series it will be seen that the output of nitrogen per period corresponds on the whole with the effect on the quantity of urine.

In the "ureter" group during the early stage of increased urine secretion, the quantity of nitrogen also increased, while during the later stage of diminished flow, the excretion of nitrogen also fell. After removal of the anaesthetic a rebound occurred, which reached its maximum in Period III, and thereafter receded to a rate of excretion below the normal level.

TABLE X.—ETHER: EFFECTS ON THE EXCRETION OF NITROGEN.

Experiment.	I.	II.	III.	IV.
1 ...	0.1169	<i>Ureter Series.</i> 0.2618	0.2530	0.1772
2 ...	0.1401	(a) 0.1349 (b) 0.0552	0.3523	0.1270
3 ...	0.2523	0.2219 0.1490	0.1296	—
4 ...	0.1941	0.2091 —	0.1126	0.1162
3 ...	0.3892	<i>Catheter Series.</i> 0.1020	0.3749	0.2365
4 ...	0.1650	0.0227	0.1776	0.2217
5 ...	0.1747	0.0204	0.2787	0.2849
8 ...	0.3362	Negligible	0.1640	0.2838
9 ...	0.2040	0.2243	0.2939	0.3163
10 ...	0.2370	0.0235	0.1705	0.2723

Including the output of the anaesthetic period of Experiment I amongst the early effects the averages for the ureter series in the above table per period are:

I.	II.	III.	IV.	V.
0.1759	(a) 0.2070 (b) 0.1021	0.2119	0.1401	0.1240

During the first stage of Period II the increase rose to 118.25 per cent., and during the second stage fell to 58 per cent. of the normal, with a subsequent rebound to 120.5 per cent. The corresponding effects on the outflow of urine, as shown above, were in the same direction, but somewhat more marked.

For the experiments in which nitrogen determinations were made in the "catheter" series, the averages—excluding the special Experiment 3, where the rate of outflow was very unusual—are:

I.	II.	III.	IV.
0.2232	0.0581	0.2169	0.2758

That is to say, during the anaesthetic period the excretion of nitrogen dropped to 26.03 per cent. of the normal, returning in Period III, as shown by the averages, to somewhat below the latter amount. In most of the individual experiments the rebound was continued into Period IV, and the output did not always come down to normal level within the period of observation.

It is of interest to recall that during Period II the outflow of urine in the same series dropped to 25.4 per cent. of the normal, which corresponds closely with the effect on the excretion of nitrogen. Further, in the exceptional experiment, No. 3, the drop in the output of nitrogen was also to about the same figure—namely, 26.23 per cent. of the normal, although the secretion of urine fell to 8.45 per cent. These facts are, I think, of importance in showing that the ether influence on the excretion of nitrogen is in the main to be ascribed to its effect on the outflow of urine, and hence to vascular influence, while with chloroform this is not so. With ether also, in the later stages, the effect is not wholly vascular. The output of nitrogen in some cases suffers a greater depression than can be accounted for by the decrease in urine.

EFFECT ON THE CONCENTRATION OF THE URINE.

It is of interest to contrast the effects produced by ether on the concentration of the urine with those of chloroform. It will be remembered that under the influence of chloroform the concentration of the urine was nearly always reduced even when the volume was diminished.

With ether the rule is reversed. The diminished urine is for the most part more concentrated than the normal. The following table gives the percentage concentration of the urine for each period:

TABLE XI.—ETHER: EFFECTS ON THE PERCENTAGE EXCRETION OF NITROGEN.

Experiment.	I.	II.	III.	IV.	V.
1 ...	1.694	<i>Ureter Series.</i> 0.826	0.798	0.840	1.9096
2 ...	1.2292	(a) 0.9212 (b) 0.7560	0.5592	0.7196	—
3 ...	0.7680	0.7560 0.8764	0.8582	—	—
4 ...	1.8312	0.9548 —	1.1984	1.1984	—
3 ...	0.1400	<i>Catheter Series.</i> 0.4340	0.2884	0.3584	—
4 ...	0.9940	1.0080	0.6020	0.1540	—
5 ...	1.4560	1.0080	0.5068	0.5180	—
7 ...	0.8820	—	1.2152	0.5852	0.7588
9 ...	1.3160	2.2428	0.9184	—	—
10 ...	2.4948	2.3520	1.1760	—	—

N.B.—In Period II, columns (a) and (b) represent early and late effects respectively.

The difference between ether and chloroform in this respect is probably in the main a relative one. There are exceptions in the above table to the diminished urine being more concentrated, chiefly where the influence of the anaesthetic has been more marked than usual. Further, the increase in the percentage of nitrogenous solids was not, in the inverse sense, fully proportionate, as a rule, to the diminution in the volume of urine.

EFFECT ON THE CHLORIDES OF URINE.

An analysis of the chlorides was made in five of the "catheter" experiments. It was found that, as with chloroform, ether produces an increase which continues to augment for some hours after removal of the anaesthetic. The increase, however, is very small in comparison with that after chloroform.

The following table gives the results:

TABLE XII.—ETHER: EFFECT ON THE CHLORIDES OF URINE.

Experiment.	I.	II.	III.	IV.	V.
6 ...	0.0189	<i>Catheter Series.</i> trace	0.0660	0.1320	—
7 ...	0.0087	0.0704	0.0154	0.0041	0.0806
8 ...	nil	not done	0.0405	0.0145	0.0150
9 ...	0.0062	0.0270	0.0256	0.1027	0.0484
10 ...	0.0541	not done	0.0261	0.0300	0.0352

The averages per period for the above experiments are:

I.	II.	III.	IV.	V.
0.0176	0.0325	0.0347	0.0566	0.0448

In Period IV the output was three times that of the normal. A search in the literature for previous observations on the output of chlorides under ether narcosis gave negative results.

It will be remembered that normal animals placed in the same conditions without anaesthesia showed an increase of chlorides during Periods II and III. The increase was, however, much less than that with ether. The fact that ether causes an increase makes it very probable that the whole of the augmentation seen under chloroform cannot be derived from the chlorine of the anaesthetic itself.

VASCULAR EFFECTS.

Kemp⁴⁰ compared blood pressure with renal secretion during ether anaesthesia. The former (as recorded from the carotid artery) showed a rise from the beginning, which continued, or even slightly increased, when the ether was pushed. The secretion of urine was early diminished and finally stopped. The kidney volume increased at first, but rapidly fell under full anaesthesia. This shrinkage, which was not reflected in the blood-pressure tracing, was considered by Kemp to be evidence of a specific ether effect on the renal circulation. Buxton and Levy⁴¹ repeated the work of Kemp, but found that after an early increase the blood pressure frequently fell,

ETHER.

Fig. 5.—Effects of ether on carotid blood pressure and urine outflow.

and did so markedly when the ether was increased. The secretion of urine was slowed but not entirely stopped. The specific ether effect of Kemp was only obtained after prolonged administration of ether, or after repeated large doses, and was usually accompanied by a fall of blood pressure. The oncometer showed diminution in volume but not the extreme contraction observed by Kemp.

In the present series, owing to differences in the methods and length of observations, it was considered necessary as a starting point to compare urinary secretion with blood pressure throughout the different periods.

(a) Comparison of Blood Pressure and Urine Secretion.

The accompanying Fig. 5 gives a tracing of blood pressure from Experiment 4 (Ureter Series) upon which the outflow of urine is superimposed in curve form. In the above experiment morphine had been given before collecting the normal sample, but no other means of anaesthesia till the ether administration. The ether was given for two consecutive hours, to a light degree in the first, to a pronounced degree in the second. During the first hour, the curve of secretion shows a great increase in the rate of outflow which gave place to a rapid fall when the anaesthesia was increased. For a period of fifteen minutes in the middle of the second hour the secretion was suppressed, and during this time the fall in blood pressure was not of itself sufficient to account for the suppression. After the ether was completely removed the rate of secretion recovered and rose for a time above the normal.

ETHER.

Fig. 6.—Chart showing ether effect on blood pressure and urine secretion.

what anterior to the urinary increase. The same effect had been several times observed, but only when ether or chloroform or a mixture of these had previously been given. In the experiment in question a light ether-chloroform anaesthesia was used to supplement the morphine narcosis during the preliminary operations. This increase is, I believe, always liable to occur under similar circumstances, and can only be guarded against by a wait of several hours after removing the anaesthetic

The end of the tracing shows the characteristic decline in urine secretion seen at this stage, in all the experiments in which morphine had been given at the outset. Fig. 6 is a chart constructed from the results of Experiment 3 (Ureter Series), and represents a somewhat different type of ether effect.

It will be observed, on examining the above, that the rate of urinary secretion rapidly increased towards the end of the normal period. Blood pressure also rose somewhat

before collecting the normal sample of urine. When ether was subsequently given to observe its effect on the urine, the secretion rapidly fell, but not to complete suppression. The flow also remained low throughout the second hour, notwithstanding a high blood pressure. In the after-period, the feeble character of the reaction, which I have attributed to morphine influence, is shown.

(b) *Kidney Volume and Urine Secretion.*

Four experiments were performed with ether, in which kidney volume, blood pressure, and urine secretion were recorded. The same precautions were observed, and the same difficulties met, to which reference is made under "chloroform." The left kidney was placed in the oncometer.

The following table gives the urinary secretion per period for each kidney separately:

TABLE XIII.—ETHER: EFFECTS ON URINE VOLUME IN ONCOMETER EXPERIMENTS.

Experiment.	I.		II.		III.	
	L.	R.	L.	R.	L.	R.
1 ...	13.45	27.60	9.00	22.40	2.80	11.20
2 ...	2.00	2.90	2.90	2.70	2.50	2.45
3 ...	22.00	18.30	41.20	5.400	10.30	13.30
4 ...	3.90	4.50	4.50	6.60	6.10	7.50
			1.30	1.80		

In all the above experiments the periods are calculated for one hour duration. The anaesthetic period of Experiment 4 is subdivided into two half-hours.

In Experiment 1 the rates of secretion from the oncometer and normal kidneys were markedly different, and in consequence the experiment is excluded from the following averages. The averages taken for the different periods from the remaining three are:

L. Kidney (onc.) ...	9.3	16.6	6.3
R. Kidney ...	8.6	21.7	7.5

The rate of secretion was little affected by ether in Experiment 2. In Experiment 3 the "increase" effect is well shown, while in Experiment 4 the "increase" effect, which is shown in the first half of the anaesthetic period, is followed by a converse influence in the second half. Tracings from Experiments 3 and 4 of this group are given subsequently.

The output of nitrogen in Experiments 2, 3, and 4 of the above series was also determined, and is given in the following table:

TABLE XIV.—EFFECTS OF ETHER ON OUTPUT OF NITROGEN IN ONCOMETER EXPERIMENTS.

Total Output per Period.

Experiment.	I.		II.		III.	
	L.	R.	L.	R.	L.	R.
2 ...	0.0348	0.0483	0.0299	0.0545	0.0113	0.0439
3 ...	0.0739	0.0845	0.0713	0.0977	0.0374	0.0517
4 ...	0.0711	0.0805	a 0.1094 β 0.0246	0.1375 0.0312	0.0891	0.0688

Percentage Output, to show Concentration of Urine.

2 ...	0.3108	0.2100	0.3332	0.2436	0.4030	0.3920
3 ...	0.3360	0.4620	0.1708	0.1792	0.3640	0.3892
4 ...	1.8228	1.7304	a 2.4304 β 1.8830	2.1832 1.8690	1.4616	1.1844

N.B.—a and β represent early and late effects.

The output of nitrogen and concentration of urine are little affected during the anaesthetic period of Experiment 2. The same may be said of the output in Experiment 3, notwithstanding the great increase in urine volume—namely, to double the normal amount. In Experiment 4 the output of nitrogen is raised during the first part of the anaesthesia, partly owing to increase in the urine volume, partly also to a slight increase in the concentration. During the second part of the anaesthetic

ETHER.

Fig. 7.—Effects of ether on kidney volume, carotid blood pressure, and urine secretion.

period the total output of nitrogen is very greatly reduced, as is also the concentration, when compared with that of the previous half. The reduction in concentration did not, however, proceed lower than that of the normal sample.

In Period III the total output of nitrogen is subnormal, except in Experiment 4; the concentration of the urine is the reverse. These effects agree in the main with the influence on urine volume. Fig. 7 gives the results of Experiment 3 in graphic form, the curve of urine secretion being imposed on the tracing of blood pressure and kidney volume.

The normal period was forty minutes, during the latter half of which the secretion of urine increased rapidly. This is another instance which shows the effect of using ether-chloroform mixture to assist in the preliminary anaesthesia. A period of three-quarters of an hour had elapsed in this case after removal of the ether-chloroform before the urine collection was begun. Notwithstanding the increased rate of flow, the ether when subsequently given produced its usual effects. During the early part of the inhalation an increase in kidney volume occurred, with augmentation of the outflow of urine. During the fuller effect the outflow of urine rapidly fell, as did also, though to a less extent, the volume of the kidney. The effect on blood pressure was a slight fall. During the after-period the fall in kidney volume brought its size gradually down to a point below normal level with a slight rebound at the end. These conditions were reflected in the urine curve, but not in that of blood pressure. This distinctly rose in the later stages of the experiment.

ETHER.

Fig. 8.—Chart showing effects of ether in Oncometer Experiment 4.

No ether-chloroform anaesthesia was used to supplement the preliminary morphine narcosis and the normal rate of urine secretion is consequently uniform. During the anaesthetic period of seventy minutes both phases of the ether effect are shown on the urine volume. The early increase is accompanied by a rise in blood pressure, with augmentation of kidney volume. During the later part of the same period, and still more so in the after-period, a want of correspondence at different parts of the curve is very obvious. The divergence is, however, on the whole, much less between the curves of kidney volume and urine outflow than between the latter and blood pressure. The condition of the kidney volume during a state of almost complete arrest of urine outflow is shown towards the end of the anaesthetic period, and is by no means extremely small. It is difficult to guard against leakage in the volume-recording apparatus, and it is possible that the diminution shown in Kemp's results may have been exaggerated in this way. In the present experiments the apparatus were always carefully tested beforehand against leakage.

Reviewing the matter as a whole, it would seem that with ether there is a greater approximation to parallelism between the urine outflow and the changes due to vascular effects than was seen with chloroform. This conclusion is also supported by comparisons between urine volume and urine concentration.

These latter tend to show that the depressing effects of ether on renal activity are primarily vascular, in contrast to those of chloroform, which are primarily parenchymatous or protoplasmic.

Under extreme or prolonged effects the degree of vascular stasis caused by ether seems also to be more pronounced than is the corresponding condition referred to under chloroform. Flocculi in the glass tubes conducting away the urine from the ureters after great diminution or arrest of secretion are even more frequent than with chloroform. They are mainly composed of collections of leucocytes.

Similar results in the same or other vascular districts have been frequently observed after ether. Da Costa¹² found contraction of the pulmonary capillaries with irregular changes in the leucocytes of the blood. Lindemann,¹³ on the other hand, found great dilatation of the lung capillaries, with more or less oedema. Increase in the leucocytes of the circulating blood was observed by Lerher¹⁴ on the day following ether narcosis. The same condition was found immediately after the anaesthesia by Chadbourne,¹⁵ amounting in some cases to an increase of over 70 per cent. During the narcosis, on the other hand, the leucocytes were diminished. Eisendrath¹⁶ describes the occurrence of casts with or without albuminuria, both after ether and chloroform. They disappeared sooner after the former. Ogden¹⁷ also found casts in the majority of cases after ether.

ALBUMINURIA AFTER ETHER NARCOSIS.

Observations were made in eight of the "catheter" experiments, namely, 2, 3, 4, 5, 7, 8, 9, and 10. The reagent used for the detection of "albumen" was Spiegler's. Of the eight normal samples, six were free from albumen, one (Experiment 5) gave a distinct positive reaction, and one a doubtful result. In all of the experiments the urine at one or other of the later periods contained albumen. In that of Experiment 5, in which it was present at first, the quantity was increased by the anaesthetic.

In Experiment 3 the albumen reaction after ether was never more than faint, and was only obtained in the urine of two periods, namely, II and III. In five of the experiments the albumen had disappeared before the observations were concluded.

These results as a whole confirm the conclusions of numerous other observers, namely, that ether narcosis is more fruitful in producing temporary albuminuria than that of chloroform.

REDUCING SUBSTANCES IN THE URINE AFTER ETHER NARCOSIS.

Seelig¹⁸ finds that ether inhalation always produces glycosuria, sometimes to the extent of 10 per cent.

An examination for osazone-yielding substances was made after ether inhalation in ten of the foregoing experiments—one "ureter" and nine "catheter." Morphine had been administered in two of the cases, and both gave abundant crystals, one in the normal sample. Of the remaining eight, none gave crystals in the normal period, but four gave them in one or other of the succeeding periods. In none of these were crystals obtained in two periods of the same experiment. In two of the experiments the crystals occurred in the urine of the anaesthetic period, in another in that of Period III, in the fourth in that of Period IV. In all cases the crystals differed in appearance from those of glucosazone, and resembled those seen after chloroform. The quantity judged roughly was, however, much less, and the frequency of occurrence also less in the case of ether. The substance yielding the crystals was probably the same in both.

MIXTURES CONTAINING CHLOROFORM AND ETHER.

Observations were made on the effects of two more or less commonly employed anaesthetic mixtures, containing ether and chloroform. These were the so-called A.C.E. mixture and a mixture of ether and chloroform in the proportions of two parts of the former to one of the latter.

A.C.E. MIXTURE.

Effects on the Quantity of Urine.

The following table gives the results of six experiments:

TABLE XV.—A.C.E.: EFFECT ON THE QUANTITY OF URINE.

Experiment	I.	II.	III.	IV.	V.
1	11.00	10.00	16.80	16.80	—
		<i>Ureter Series.</i>			
1	20.50	2.00	20.00	57.00	—
2	20.50	7.50	45.00	117.00	21.00
3	27.50	16.50	31.00	36.00	36.00
4	6.50	1.00	12.50	9.50	7.50
5	13.00	8.25	14.50	15.50	12.50
		<i>Catheter Series.</i>			

A slight decrease in urine outflow is seen during the anaesthetic period in the ureter experiment; in all others there is a marked diminution. The averages from the latter in cubic centimetres per period are:

I.	II.	III.	IV.	V.
17.6	7.05	24.6	47.0	15.4

The quantity in Period II fell to 40 per cent. of the normal, and during Period IV the rebound reached to 267 per cent. of that amount. Compared with the effects of chloroform and ether singly, the A.C.E. mixture caused less diminution during Period II, but is followed by a more pronounced reaction in Period IV. The latter result is not reflected in the output of nitrogen.

Effect on the Output of Nitrogen.

Analyses of nitrogen were made in all of the foregoing experiments. In the "catheter" series, and also in the single "ureter" experiment, the output rose and fell with effect upon the quantity of water, but not in a proportionate degree. The following table gives the particulars:

TABLE XVI.—A.C.E.: EXCRETION OF NITROGEN PER PERIOD.

Experiment	I.	II.	III.	IV.	V.
1	0.1430	0.1440	0.1740	0.1650	—
		<i>Ureter Series.</i>			
1	0.1607	0.0311	0.2352	0.4309	—
2	0.2210	0.1277	0.2898	0.3341	0.1670
3	0.3158	0.2264	0.4409	0.5735	0.4999
4	0.1824	0.0963	0.2828	0.2346	0.1884
5	0.2439	0.0963	0.2728	0.3090	0.2905
		<i>Catheter Series.</i>			

The averages per period for the catheter experiments are as follows:

I.	II.	III.	IV.	V.
0.2038	0.1204	0.2962	0.3232	0.2138

The decrease in the anaesthetic period represented 58.77 per cent., and the increase in Period IV 1.5858 per cent. of the normal output. The fluctuations in nitrogen were therefore considerably less than in the escape of water. Compared with the effects of ether and chloroform singly, those of A.C.E. were less marked. During chloroform narcosis the average excretion of nitrogen fell to 18 per cent. of the normal, and in the case of ether to 26.05 per cent.

Effect on the Concentration of the Urine.

In half the "catheter" experiments the concentration of the urine fell during the anaesthetic period notwithstanding diminution in urine volume; in the remainder an increase occurred.

The following table gives the percentage excretion of nitrogen:

TABLE XVII.—A.C.E.: EFFECT ON THE CONCENTRATION OF URINE.

Experiment	I.	II.	III.	IV.	V.
1	1.3020	1.4140	1.0360	0.9800	—
		<i>Ureter Series.</i>			
1	0.7340	1.5540	1.1760	0.7560	—
2	1.0780	1.7024	0.6440	0.2836	0.7952
3	1.5120	1.3720	1.4224	1.5932	1.3888
4	2.8066	1.3720	2.2624	2.4696	2.5116
5	1.6760	1.1676	1.8816	1.9936	2.3240
		<i>Catheter Series.</i>			

The averages from the catheter series are:

I.	II.	III.	IV.	V.
1.6111	1.4490	1.4773	1.4204	1.4039

Effect on the Excretion of Chlorides.

An estimation of chlorides was made for each of the catheter experiments in the above table. The average output per period is as follows:

I.	II.	III.	IV.	V.
0.0179	0.0505	0.0990	0.1375	0.0611

A very considerable increase was caused by the narcosis, which reached its maximum in second period after removal of the anaesthetic. The output was then eight times the normal. The results as a whole are intermediate between the effects of chloroform and ether singly, a less augmentation than the former, a greater than the latter. In duration they resemble those of ether, that is to say, the decline towards normal sets in within the time limits of the experiments.

ETHER-CHLOROFORM MIXTURE.

As already stated, the research originated in the necessity (for control purposes) of ascertaining the effect of ether-chloroform mixture (2 to 1) upon the work of the kidney.¹⁹ This mixture is frequently employed in physiological experiments owing to its greater safety with lower animals than chloroform alone. The following results may, therefore, be of some interest:

Effect on the Quantity of Urine.

The results of six experiments not previously published are as follows:

TABLE XVIII.—ETHER-CHLOROFORM MIXTURE: EFFECT ON THE QUANTITY OF URINE.

Experiment	I.	II.	III.	IV.	V.
1	8.7	8.7	11.9	8.5	—
		<i>Ureter Series.</i>			
1	8.5	4.25	6.25	6.25	—
2	23.0	6.0	11.5	26.0	20.0
3	43.0	8.5	35.0	71.0	36.5
4	98.0	11.5	25.0	28.5	26.5
5	20.5	8.5	9.5	30.0	25.0
		<i>Catheter Series.</i>			

The averages per period from the catheter experiments (excluding No. 4, in which the normal rate of secretion was unusually high) are:

I.	II.	III.	IV.	V.
28.8	7.66	12.66	42.33	27.2

During the anaesthetic period the secretion fell therefore to 26.6 per cent. of the normal rate, and rose in Period IV to 147 per cent. of that amount. It would thus seem that the immediate effect in this class of experiment is more pronounced than with chloroform but somewhat less than with ether. The after-effect is considerably less than with either constituent when given singly. In the special case, Experiment 4 (Catheter Series), the secretion during Period II dropped to 11.73 per cent. of the normal rate.

The foregoing results differ from those previously published, to which reference has been made, and in which a less-marked influence on urine flow was observed. The two sets of experiments are, however, hardly comparable; the earlier were all "ureter" experiments, in which morphine was used, and the ether-chloroform influence kept as light as possible, the latter chiefly "catheter" experiments in which a full effect was produced. I am also inclined to believe that too little influence was at that time attributed to the after effects of the anaesthetic mixture used during the preliminary operations.

Effects on the Excretion of Nitrogen.

In its effects on the output of nitrogen per period, the ether-chloroform mixture resembled that of ether alone rather than that of chloroform. The effects were, however, less pronounced than with ether. The following table gives the results:

TABLE XIX.—ETHER-CHLOROFORM MIXTURE: EFFECTS ON THE EXCRETION OF NITROGEN.

Experiment.	I.	II.	III.	IV.	V.
1	0.3780	<i>Ureter Series.</i>		0.3237	—
		0.1156	0.3915		
2	0.1835	<i>Catheter Series.</i>		0.2120	0.2201
3	0.3130	0.0961	0.2019	0.2266	0.3015
4	0.4719	0.1323	0.2646	0.4365	0.3710
5	0.1538	0.1874	0.3500	0.2243	0.1652
		0.0878	0.1987		

The averages from the above (excluding Catheter Experiment 4 which is treated separately) are:

I.	II.	III.	IV.	V.
0.2168	0.1054	0.2217	0.2209	0.2289

During the anaesthetic period the nitrogen output fell to 48.6 per cent. of the normal. There was little or no after-effect. In the special case (Catheter Experiment 4) the nitrogen excretion fell to 28.65 per cent., a much less fall than that which occurred in the watery constituent.

Effect on the Concentration of the Urine.

Without exception, the urine of the anaesthetic period was more concentrated than normal. This again is a deviation from the effects of chloroform singly and a resemblance to those of ether. The following table gives the particulars:

TABLE XX.—ETHER-CHLOROFORM MIXTURE: EFFECT ON THE CONCENTRATION OF THE URINE.

Experiment.	I.	II.	III.	IV.	V.
1	4.578	<i>Ureter Series.</i>		3.8080	—
		4.7768	3.2900		
2	0.7980	<i>Catheter Series.</i>		0.8156	1.1004
3	0.7280	1.6018	1.7556	0.3192	0.8260
4	0.4816	1.5568	0.7560	1.5316	1.4000
5	0.7504	1.1760	1.4000	0.7476	0.6608
		1.0332	2.0916		

The averages from the catheter series are:

I.	II.	III.	IV.	V.
0.7588	1.3972	1.5344	0.6275	0.8624

It is remarkable that the percentage content of nitrogen was greatest in Period III, although the quantity of urine was considerably greater than in Period II. It would seem to indicate a retention of nitrogen constituents in the blood during the period of anaesthesia rather than an inhibition of their formation.

Effect on the Excretion of Chlorides.

The chlorides were estimated in three of the "catheter" experiments, two of which showed an increase, and one a decrease. The averages from the three are:

I.	II.	III.	IV.	V.
0.0497	0.0661	0.0371	0.0959	0.1188

The augmentation continued to the end of the periods of observation when it reached its highest level, the output being about two and a half times that of the normal. In the period at which the maximum occurred, the effect resembled that of chloroform, but the total influence of the mixture in augmenting the chlorides was less than that of any of the previous anaesthetics used in this research.

RÉSUMÉ OF THE PRONOUNCED EFFECTS OF THE FOREGOING ANAESTHETICS ON RENAL ACTIVITY.

In the following table are given the effects of the different anaesthetics already considered on urine volume, nitrogen per period, and nitrogen per cent. during the stage of anaesthesia. In each case the normal standard is taken as 100.

TABLE XXI.—RENAL ACTIVITY UNDER DIFFERENT ANAESTHETICS (EFFECT DURING ANAESTHESIA COMPARED WITH THE NORMAL).

	Urine Vol.	Nitrogen per period.	Nitrogen per cent.
Chloroform	35.0	18.00	70.20
Ether	25.4	26.03	110.00
A.C.E.	40.0	58.77	89.94
Ether-chloroform	26.6	48.60	184.13

The similarities between the effects of chloroform and those of A.C.E. are seen at a glance, likewise those between ether and the ether-chloroform mixture.

SUMMARY.

Ether.

1. During ether narcosis the volume of urine secreted, as in the case of chloroform, is affected in two ways. In the majority of experiments there is a decrease, in a few an increase. The latter is probably an early or light effect, the former a pronounced effect. The depressing effect is, however, more marked than with chloroform, and complete arrest more readily occurs.

2. The after-effect is also similar to that of chloroform, but, as a rule, less marked. The maximum outflow of urine occurs about three hours after removal of the anaesthetic.

3. The effect of ether on the output of nitrogen corresponds more closely with its influence on the outflow of urine than is the case with chloroform. In the later stages of the anaesthesia, where the urine volume is decreased, the excretion of nitrogen is diminished almost exactly to the same degree as the urine volume. In the group of catheter experiments the excretion of nitrogen fell to 26.03 per cent., the quantity of urine to 25.4 per cent. of the normal amount.

4. The effect of ether narcosis on the concentration of the urine differs also from that of chloroform. With the former, the urine when diminished in volume is, as a rule, more concentrated (contains more nitrogen). The converse was the case with chloroform. The effect of ether is, therefore, primarily vascular.

5. In ether narcosis, when the curves of urine outflow, kidney volume, and blood-pressure are compared, although there is not complete parallelism there is, on the whole, a closer correspondence than is the case with chloroform. This statement does not apply to the arrest of urinary secretion, which occurs more readily, and with a relatively higher blood-pressure, in ether than in chloroform narcosis.

6. The escape of leucocytes into the urine after full ether narcosis is more marked than with chloroform, probably indicating a higher degree of stasis in the glomerular capillaries. Dilatation of capillaries and escape of leucocytes have been seen by previous investigators after ether inhalation in the case of other vascular districts than renal.

7. An increased excretion of chlorides is seen after ether inhalation, but much less and of shorter duration than in the case of chloroform.

8. Temporary albuminuria appears in dogs in a much larger proportion of experiments with ether than with chloroform.

9. Reducing substances, not sugar, which were not present in the normal urine, appeared in a small number of the experiments after ether narcosis.

A.C.E. Mixture.

1. During full narcosis from the above the outflow of urine is diminished, but to a less degree than with either chloroform or ether. The after-effect is usually greater than with either.

2. The excretion of nitrogen is less depressed than the volume of urine. The average in the two cases are 58.8 per cent. and 40 per cent. respectively.

3. The effect on the concentration of urine is variable. In half the experiments with diminished volume there was also diminished percentage of nitrogen. In the remaining half the percentage of nitrogen was increased. The results, therefore, alternate between those of chloroform and ether.

4. The chlorides are increased to a less degree than with chloroform, but to a greater degree than with ether. In its short duration the effect resembles that of ether.

Ether-Chloroform Mixture.

1. The full influence of the mixture produces a diminution of urine less than that of ether, but more than that of chloroform. The after-effect is considerably less than with either chloroform or ether.

2. The excretion of nitrogen is less influenced than that of urine—a fall to 48.6 per cent. in the former case as contrasted with one to 26.6 per cent. in the latter. The effect resembles that of ether more than that of either chloroform or A.C.E. mixture. The after-effect was inappreciable.

3. The urine of the anaesthetic period was in all cases more concentrated than normal, in this respect also resembling the influence of ether.

4. The chlorides were increased, but to a less degree than with any of the previous anaesthetics. The effect closely resembled that of ether.

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TREATMENT OF CICATRICAL STRICTURES OF THE URETHRA WITH THE ELECTROLYTIC NEEDLE.

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THE far from satisfactory results obtained by me, during several years of my special practice, from the methods usually followed in the treatment of cicatricial strictures induced me to try another process that might lead to a complete recovery. In the Chirurgico-Urological Section of the Thirteenth International Medical Congress, held in Paris in 1900, Dr. Albarran declared, in the discussions on non-complicated inflammatory constrictions, that no treatment had hitherto led to a perfect cure. He stated that resection and the plastic method were still those that gave comparatively the best results. Internal urethrotomy gave less favourable results, relapses occurring not less frequently than after progressive dilatation. The most frequent cases of relapse had been met with by him in cases of circular and linear electrolysis.

Tripier and Mallez are of opinion that these operations are by no means free from danger, as they have often seen undoubted evidence of attendant complications; nor have I myself been able to obtain any better results, and the repeated relapses would compel the patients to have recourse to the bougie for years, followed, after a time, by deviations of the vesical passage, with all its injurious consequences. The same favourable effects obtained by Professor Oberländer from the treatment of the different degrees of infiltrations and constrictions of the urethra with his two-branched and afterwards a four-branched dilator, have also been verified by me in soft and in hard infiltrations of a slight and moderate degree; but in cases of the densest infiltrations and longest cicatricial strictures this method did not afford the desired results, and relapses always occurred.

In his book treating of strictures of the urethra, Hamonic gives the following definition:

The name of stricture of the urethra is given to any fibrous neo-formation of an inflammatory or cicatricial nature, deposited either in the form of a ferule or a ring on the inner circumference of the urethra, or in the form of a valvule or of a callosity on one of the wall coats, the direct consequence of which is to diminish gradually the calibre of the passage, thus giving rise to a number of different troubles, to produce secondary injuries to the genito-urinary organs, and finally to render various surgical operations imperative according to the nature of the case.

Looking upon the constriction as a new fibrous formation, I thought I might obliterate it by means of an electrolysis needle, a method sometimes used to destroy small cicatrices and glands in the skin, and one which Professor Oberländer recommends to remove the marks left by his treatment with a dilator.

The following is my method of procedure: After the dilatation of the constriction up to No. 23 of the Charrière gauge, either with Béniqué bougies or by internal urethrotomy, if the induration of the cicatrized tissue be very strong and the bore of the passage too small, I commence

the treatment with the electrolytic needle. I first make a thorough and minute irrigation of the urethra with a solution of oxycyanate of mercury; I then insert Oberländer's urethroscope tube, corresponding with No. 23-30 of the Charrière gauge, passing along the whole length of the stricture. In examining the urethra I slowly withdraw the tube until the surface of the constriction is shown in the opening. The needle, ending in a strong platinum point from 1½ cm. to 2 cm. in length, isolated almost quite close to its point, is forced to a depth of ½ cm. to 1 cm. into the fibrous tissue according to the dimension, thickness, and hardness of the tissue. The needle is the negative pole of a galvanic battery, the positive pole of which, a large moistened, wetted disc, is placed on the thigh or on the belly. I allow the electric current of from 4 to 6 milliamperes to work for three minutes. Before withdrawing the needle I interrupt the current, and drive the needle into another part. This operation may be repeated four or five times during a sitting, and, if executed by an expert hand, is not very painful.

In cases in which the constrictions are extensive and thick, the operation may be practised in the beginning at least twice a week. Later, one sitting a week will suffice. After each sitting the urethra is duly irrigated with a solution of oxycyanate of mercury or of nitrate of silver 1 in 4,000. These irrigations before and subsequent to each sitting are indispensable for the prevention of complications.

During the six years that I have treated cicatricial constrictions in this manner, I have never met with such complications as epididymitis, cystitis, or "bacteriuria," etc.

During the whole period of treatment a bougie is introduced once a week, followed by an irrigation with a nitrate of silver solution to promote reabsorption, and to maintain the passage of the urethra at the size required. The number of the sittings will depend on the extent of the stricture as well as on its thickness and hardness. Sometimes three or four sittings will prove sufficient; sometimes, however, it does happen that the treatment has to be continued for several months.

With the help of the urethroscope the process of the cure may be verified by observing the progressive change in the aspect of the surface of the constriction, the greyish colour of which gradually changes to a pale red. The surfaces again become supple and level, and, later on, shiny.

Owing to the fact that the lacunae and the glands only partly show themselves, and the longitudinal folds and the longitudinal streaks but faintly, the place in the urethra where the stricture was situated will easily be found. When the whole surface of the mucous membrane has come to be of a reddish colour, I insert every fortnight a Béniqué bougie corresponding with No. 25-26 of the Charrière gauge, and from time to time I again use the needle to destroy the remaining traces of the cicatricial tissue.

The treatment here described has been productive of the best results during the six years I have applied it. In several cases in which I have had the advantage of again seeing my patients two years after the treatment, I have been able to verify and confirm the fact of the permanence of the cure by introducing with facility into the urethra a Béniqué probe corresponding with No. 26 and 27 of the Charrière gauge.

With the aid of the urethroscope the side of the urethra is seen to be quite flexible, limp and shiny at the site of the stricture, whilst the longitudinal folds and striae and the lacunae have not been quite restored, and are even almost completely wanting.

The results thus obtained have induced Dr. Schoemaker, chief of the surgical section of the Hague Municipal Hospital, and myself to try to reduce or obliterate hypertrophied prostates by way of the urethra, in accordance with the aforesaid method.

I insert, if possible, the largest tube of Oberländer's urethroscope right into the bladder, withdrawing it again until the tissue of the prostate is seen, which is easily verified with the aid of the urethroscope, and is further indicated by the suppression of the flow of urine. At the same time, with my finger in the anus, I determine the position of the tube. By these means the right place may exactly be chosen at which to force the needle