Chemical reactions with Millon's reagent, a white precipitate soluble in excess.

Boiled with KOH, no reaction.

Crystals fused with KOH gave smell of ammonia, and the resulting solid had a rancid smell; the solid dissolved in water gave a slight brown colour with Nessler's reagent.

These chemical and physical reactions afforded adequate evidence that the crystals were veronal.

Portions of the brain and a mixed portion of viscera were examined by the following processes respectively: Treated with about 75 c.cm. of 90 per cent. alcohol acidified with a few drops of acetic acid, macerated and allowed to remain for twenty-four hours at 30° C.; the liquid decanted and the residue treated with feebly acid alcohol four times; the alcoholic extracts mixed, filtered, and evaporated to a syrupy consistency at about 35° C.; 200 c.cm. of absolute alcohol added and allowed to stand, filtered, and again evaporated to a syrup at 35° C.; taken up with water and turbid liquid filtered, concentrated by evaporation at 35° C. to 15 c.cm.; treated with blood charcoal and filtered; extracted with two volumes of ether four times; ether extract filtered and evaporated to dryness at low temperature. A crystalline residue showing similar physical characters to the crystals from the urine was obtained in each of these cases.

Amount of crystals from viscera, 0.0235 gram.

Amount of crystals from brain, 0.0385 gram.

On purifying these crystals a melting point of 184° C., somewhat lower than the melting point of the crystals from the urine, was obtained.

Regarding this evidence as sufficient to show the presence of veronal in the body as well as in the urine, and in view of the fact that the visceral organs were not weighed, it seemed best to construct the probable dose from the urine only. The amount of urine received was 225 c.cm.; it was taken from the bladder seventeen hours after the onset of coma; it does not, therefore, represent the total output of urine in twenty-four hours, in which time 50 per cent. of the veronal is excreted; it is not unreasonable to assume that at least twice this amount of urine was excreted, and that the deceased person took a dose between the fatal dose of 50 grains and the minimum recorded fatal dose of 15 grains.

We are indebted to Mr. F. E. Need, F.C.S., for his assistance with the analytical part of the work.

VERONAL POISONING: CASE OF RECOVERY FROM 125 GRAINS.*

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I WAS recently called between 8 and 9 one Monday morning to see a healthy young lady of 20, who had not appeared at breakfast at the usual hour, and could not be roused by those who entered her room. She had gone to bed quite as usual the night before, and about 11 a member of the household visited her in bed and kissed her "good-night." The patient remarked as her friend left the room, "I am glad you came to wish me 'good-night,'" and this was her last speech for four days.

I found her quite unconscious; shouting, shaking, slapping, and pin-pricks elicited no response whatever. The eyes were open, eyeballs fixed and staring, pupils semi-dilated, light and corneal reflexes abolished. The cheeks wore what seemed a natural flush, the breathing was perfectly quiet and natural and the pulse full and regular (72). There had been no incontinence of urine or faeces. The patient had been the subject of depression and of baseless misapprehensions regarding her health, which a doctor who had been consulted had tried without success to reason away; two days before a bottle of veronal tablets had been taken from her and had since disappeared; neither this bottle nor any other clue to the drug taken could be found on looking round the bedroom.

The patient was held up in a sitting position, a cork placed between the jaws, and a stomach tube passed without much difficulty. The stomach was nearly empty, only a little colourless fluid and mucus being withdrawn. After washing out the stomach, half a cup of black coffee was introduced; about 16 oz. of urine, of normal colour, were withdrawn by a catheter. An attempt was made to administer a soap-and-water enema, but the sphincter was not acting. After hypodermic injection of $\frac{1}{10}$ gr. of strychnine, a second attempt was made, and a good evacuation of the bowel followed, after which half a pint of normal saline was injected and retained. I thought it useless to try stimulation by the galvanic or faradic current, but as some time had now elapsed since the dose of coffee, I passed a stomach tube again and gave a second half cup. This was a

mistake, for it produced retching, and a little of the half-vomited material found its way into the glottis, threatening suffocation. Cyanosis remained after the choking fit was over, and oxygen was then administered; it was found most useful, not only at this stage, but in the recurring attacks of cyanosis which interrupted the progress of the case. From this point Dr. Walsh was good enough to watch the case with me, and to him I am also indebted for references to some of the other cases cited. We decided to adhere to the treatment already commenced—namely, periodical rectal injections of saline and withdrawals of urine by catheter, with oxygen inhalation for cyanosis, and strychnine hypodermically as the pulse weakened.

These measures were fortunately successful, but not without a period during which the patient appeared to be slipping downhill. It appears from the notes that the catheter was passed six times and 85 oz. of urine in all withdrawn; five saline injections were given, in all 3½ pints, and, in addition, three nutrient enemata, each consisting of 5 oz. milk and white of one egg. The pulse and temperature observations are summarized in the following table:

	Pulse.	Temperature.	Remarks.
Monday:			
Morning ...	72	—	
11.15 p.m. ...	114	99.8°	
Tuesday:			
5.15 a.m. ...	—	—	Cyanosis; oxygen ten minutes.
7 a.m. ...	120	102.4°	Resp. 40; strychnine $\frac{3}{10}$ gr.
10 a.m. ...	—	—	Rigor; strychnine.
1.30 p.m. ...	130	103°	Rales right and left bases.
3.30 p.m. ...	—	—	First return of corneal reflex.
6 p.m. ...	88	100.1°	Catheter specimen kept for analysis.
9.30 p.m. ...	92	100.6°	
11.30 p.m. ...	—	—	A few drops of water were swallowed automatically. Restless.
Wednesday:			
12.50 a.m. ...	—	—	Turns herself about.
2 a.m. ...	92	100°	Resp. 26.
6 a.m. ...	96	99.8°	Resp. 28.
6.45 a.m. ...	—	—	Opened her eyes.
7 a.m. ...	—	—	Wept for half an hour.
Noon ...	—	—	Few drops of water swallowed.
2 p.m. ...	84	99°	
3 p.m. ...	64 (!)	100°	Pulse feeble and intermittent; strychnine $\frac{1}{10}$ gr.
4.30 p.m. ...	—	—	Swallowed a spoonful of milk.
5.30 p.m. ...	—	—	Swallowed a spoonful of coffee and brandy.
6.30 p.m. ...	66	99°	
7 p.m. ...	—	—	Strychnine $\frac{1}{10}$ gr.; milk and brandy in spoonfuls. Bowels opened twice.
9.45 p.m. ...	—	—	Drank a glass of water.
10 p.m. ...	68	99°	
11 p.m. ...	—	—	Opened her eyes and cried a good deal.
Thursday:			
1.45 a.m. ...	68	98.8°	Resp. 26.
6 a.m. ...	82	98°	
8.30 a.m. ...	—	—	Swallowed half a cup of milky tea.
9 a.m. ...	70	98.2°	Catheter passed for last time.
11.30 a.m. ...	—	—	Has talked rationally.

She slept most of the time, with occasional restless fits, and did not talk any more until Friday morning, when she awoke full of her old misapprehensions and wept a good deal. She was now able to tell us that she had taken a whole bottleful of veronal, twenty-five tablets five at a time, before getting into bed the night before. She could not remember what she had done with the bottle, but later recalled that she had put it into her sponge bag, where we found it empty. In a day or two she was none the worse for her experience, excepting that a transient erythematous rash appeared on trunk and thighs, and she was in places bruised from attempts to rouse her.

The period of total or partial unconsciousness lasted three and a half days, although the corneal reflex returned in about forty hours. Several fits of weeping preceded her return to speaking consciousness, the mind evidently picking up the emotional attitude which preceded the

*Paper read at the meeting of the Bath and Bristol Branch of the British Medical Association, at Bath, November, 1913.

sleep. The idea of taking veronal occurred to her from reading the newspaper account of the notorious Hove case. Several cases of veronal poisoning have been published since this case, and in more than one instance it is stated that the suggestion arose from it.

In the Hove¹ case 150 grains were supposed to have been taken; the patient was seen within two hours, but died in thirty-two hours. I was at first under the impression that my patient's recovery from 125 grains was a "record," but, as far back as 1904, Hald² recorded a recovery from 135 grains in a young woman; the symptoms were deep stupor, dilated pupils, clonic spasms with retraction of head; pemphigus-like eruption with symmetrical erythematous patches, especially on hands. An eruption appeared rather late in my case also, and Vernet³ has lately drawn attention to cases of bullous and erythematous veronal rashes.

Shortly after my case Dr. Alexander⁴ recorded a recovery from the same amount—125 grains—in a man of 45 whose stomach was washed out within five hours; and Dr. Chitty⁵ a similar case of recovery from 125 grains in a man of 40. Unconsciousness in the first case lasted four days; the pupils were contracted. Laing⁶ records a case of recovery from 92½ grains in a prize-fighter, who had taken also 150 drops of chlorodyne an hour before the

after noting that veronal is two to four times more toxic than was commonly supposed, states that it has a marked action on the abdominal vessels, causing periodic rise and fall in blood pressure; in cases of overdose, he says, the abdominal vessels should be compressed, the patient kept warm, and oxygen inhalations administered. Veronal appears rarely to cause vomiting, but a case is recorded in which nausea, persisting vomiting, and vertigo, ending in recovery, ensued after a dose of 70 grains. A dose of veronal is reported as having caused hemiplegia in an aged person.¹⁷

Backus¹² points out that, to be of any use, the stomach must be washed out early, since even after large doses only a small portion is found there some hours later; 90 per cent. of that given subcutaneously appears in the urine if only small doses are given; with larger doses 40 to 50 per cent. only. As the faeces only contain small amounts, about half a large dose must be destroyed in the body.

An important distinction to keep in mind is that between veronal and its congeners (of which Willcox¹³ cites nine or ten) which are ureides, or derivatives of urea, and sulphonal, trional, and tetronal, which are of totally different constitution, being sulphones or ketone derivatives, containing a characteristic sulphur group. A crude

Fig. 1.—Veronal crystals recovered from the urine of the patient.

veronal; he was seen within four hours of finishing the veronal, and recovered consciousness under treatment in two hours. Several other cases of recovery from fairly large doses are on record. Death from 60 grains,¹⁴ 100 grains,¹⁵ 125 grains¹⁶ are recorded, and quite recently one from 90 grains. The largest quantity I have seen recorded as having been swallowed is 232 grains (Ehrlich⁷); this was by a lunatic, who died in twenty hours; the symptoms were respiratory paralysis, cyanosis, contracted reactionless pupils, scarcely perceptible pulse; 360 milligrams were recovered from the urine. Fraser⁸ records the case of a woman who took 120 grains in ten days, was comatose when seen, and died eighty-six hours after; 24 grains were recovered from the urine. Willcox,⁹ in opening a discussion on hypnotics at the Brighton Meeting of the British Medical Association, remarks that as small a dose as 15 grains has been fatal, and describes the symptoms accompanying the coma as high temperature, rapid breathing, and the clinical signs of acute pneumonia. This is interesting in connexion with my case, in which on the second day occurred a temperature of 103°, pulse-rate of 130, and respirations 40, with râles at both bases. In moderate doses veronal is stated by Carl Roemer, who has written fully on its pharmacology,¹⁰ to lower somewhat the body temperature, retard the rate of breathing whilst increasing the depth, and lower the blood pressure by dilating the peripheral vessels. He also states that in consequence of its specific paralytic action on the vascular walls it is contra-indicated in cases where dilatation of the vessels should be avoided—for example, in diseases of the kidneys associated with venous congestion. Grober,¹¹ writing in 1911,

Fig. 2.—Veronal from alcoholic solution.

distinction is that the former group contains no sulphur and the latter no nitrogen.

Veronal is sometimes named "diethyl-malonyl-urea" and sometimes "diethyl-barbituric acid," and its graphic formula is:

whilst sulphonal is dimethyl-methane diethyl sulphone, and its formula is:

One observer of a case of veronal poisoning notes the absence of haematoporphyrinuria. This is not surprising in view of the difference of constitution between sulphonal and veronal.

The chemical tests for veronal are unsatisfactory. It is easily recovered from the urine by slightly acidifying if necessary, evaporating to dryness, extracting with alcohol, evaporating the alcoholic extract to dryness, and extracting with ether, as in Stas's process for the detection of alkaloids. The first quantity of urine withdrawn from my patient's bladder was, contrary to my order, thrown away, but I extracted from 1 oz. of the urine (specific gravity 1026, acid, free from sugar and albumin), obtained forty-eight hours after taking the drug, 25 mg. of purified crystalline ethereal extract, whereas 1 oz. of normal urine

tested as control by the Stas process yielded only 4 mg. of non-crystalline ether extract.

The crystals were dissolved in alcohol and a drop allowed to evaporate on a microscope slide. (Fig. 1.) A rough quarter of a tabloid was then dissolved in 1 oz. of normal urine, which was put through the same process; 53 mg. were recovered and crystallized from alcohol. (Fig. 2.) A single large crystal of veronal was also photographed. Fig. 3 shows sulphonal crystals from

Fig. 3.—Sulphonal from alcoholic solution.

alcohol; the distinction between it and veronal is easy, as they belong to different crystalline systems, and, whether in single crystals or arborescent forms, could not be confounded together. Sulphonal appears to crystallize in the rhombic and veronal in the monoclinic system. Dr. L. C. Davis, Lecturer in Chemistry in the University of Bristol, has been kind enough to point out to me his ingenious method of identifying even small quantities of veronal and other crystals by taking advantage of the fact that when two bodies of similar melting point are mixed the melting point of the mixture is lowered; thus veronal melts at 191° C. and aconitine at about the same temperature, whilst a mixture of equal quantities of the two melts at 160° to 175° C. He also tells me that veronal was synthesized as far back as 1882.

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A CASE OF VERONAL POISONING.

BY

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IN view of the ease with which veronal has been procured in the past by the general public, the following notes may be of interest.

Miss B., aged 40, had been suffering for some weeks with severe facial neuralgia accompanied by headache, and had been unable to sleep. For this she had on her own initiative taken at times 5 or 7 grains of veronal. On the night in question, her face and head being very bad, and having tried to sleep without avail, she got up and took the box, which contained five capsules containing each 7 grains of veronal, down to the kitchen, and sat down by the fire. She has a confused memory of taking the first capsule, and later on finding the empty box in her hand and throwing it in the fire.

It can therefore be reasonably assumed, in view of the effects to be described, that she took all five capsules—a dose of 35 grains altogether, taken on an empty stomach, and almost immediately absorbed. She does not remember returning to bed.

Her father, on hearing her snoring, which was not her usual habit, got up and found that she could not be roused.

When I saw her she was breathing quietly, the pulse rate was

normal, and she looked like a person in a natural but very profound sleep. The pupils were normal, and reacted to light. On pricking her hands or her feet with a pin she drew them away. She could be sufficiently roused by flicking her face with a wet handkerchief to turn her head away and screw up her face. Further efforts resulted in no conscious response, and on leaving the patient alone she relapsed almost immediately into the same profound sleep. She continued in this state for fully fifty hours, when the nurse succeeded in rousing her sufficiently to drink some tea, but she seemed thoroughly dazed, saying nothing, and at once dropping off to sleep again. After seventy-two hours she roused herself, but was able to speak only in a very hesitating and incoherent manner; she complained that everything "looked funny," some of us having three eyes, others four heads, etc. At this time she was quite unable to stand or walk, but could use her arms naturally.

From this time onwards she gradually improved, though she slept more or less thirty-six hours more, and it was not till then that her brain seemed to clear.

In this case there was neither burning nor itching of the skin, nor swelling, such as has been reported in similar cases, and there was no erythema and no vomiting.

THE RESULTS OF NEPHROPEXY.

BY

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SOME years ago I published a description of a method of performing nephropexy,¹ which subsequent experience has proved to be simple, safe, and efficient. This was followed by a second paper upon the indications for the operation;² both appeared in the BRITISH MEDICAL JOURNAL. Having now operated upon upwards of 500 patients and fixed in position more than 800 kidneys, the operations being spread over a period of nearly nine years, a review of the results obtained is interesting and instructive.

The results of nephropexy must be considered from two standpoints, mechanical and therapeutic. This is important, for only when operative success has been obtained is it fair to estimate therapeutic effects. Many failures as regards general benefit are really due to failure to secure successful mechanical results—that is, they must be classed as surgical failures. No one expects a man with a recurrent hernia to have benefited by the operation; and equally, benefit from nephropexy cannot be hoped for unless the kidney has been successfully and permanently restored to its normal position.

Surgical success in operations upon movable kidneys means (1) permanent restoration of the kidney to a position as nearly normal as possible, and (2) absence of unpleasant sequelae such as pain, sinus, and weakness of scar.

Judged from this standpoint, the surgical results in my series of 515 cases have been most satisfactory. There have been 4 deaths, 2 of which were due to pulmonary embolism, 1 to acute dilatation of the stomach and 1 to exhaustion from mania. This gives a mortality of less than 0.8 per cent., which must be considered low in view of the facts that the condition of many of the patients was very unsatisfactory at the time of operation, and that in about two-thirds of them both kidneys were dealt with at the same time.

To my knowledge, in only one instance has the kidney acquired fresh mobility after having been anchored, though almost all the patients have been repeatedly examined by myself and other competent observers. In a few instances there has been pain in the loin due to implication of a nerve in the scar. The pain comes on some weeks after operation, and when severe has been relieved by excision of a length of the affected nerve. In one case a small hernia developed in the scar as the result of a severe strain within a few weeks of the operation, and necessitated a slight further operation. In no case has a sinus resulted, and in no case has any subsequent trouble arisen in the kidney itself. The following extract from the report of a practitioner who performed a *post-mortem* examination upon one of my patients (death being due to a cause unconnected with the operation) seven months after nephropexy indicates how firmly the kidney becomes anchored: "The right kidney was very firmly attached to its moorings, and I could not separate it at all, so did not disturb it." These results compare very favourably with those obtainable in any other branch of surgery, and the operation described in 1907 has proved so satisfactory