

**On toxic urine in relation to certain surgical operations on the urinary organs / by Reginald Harrison.**

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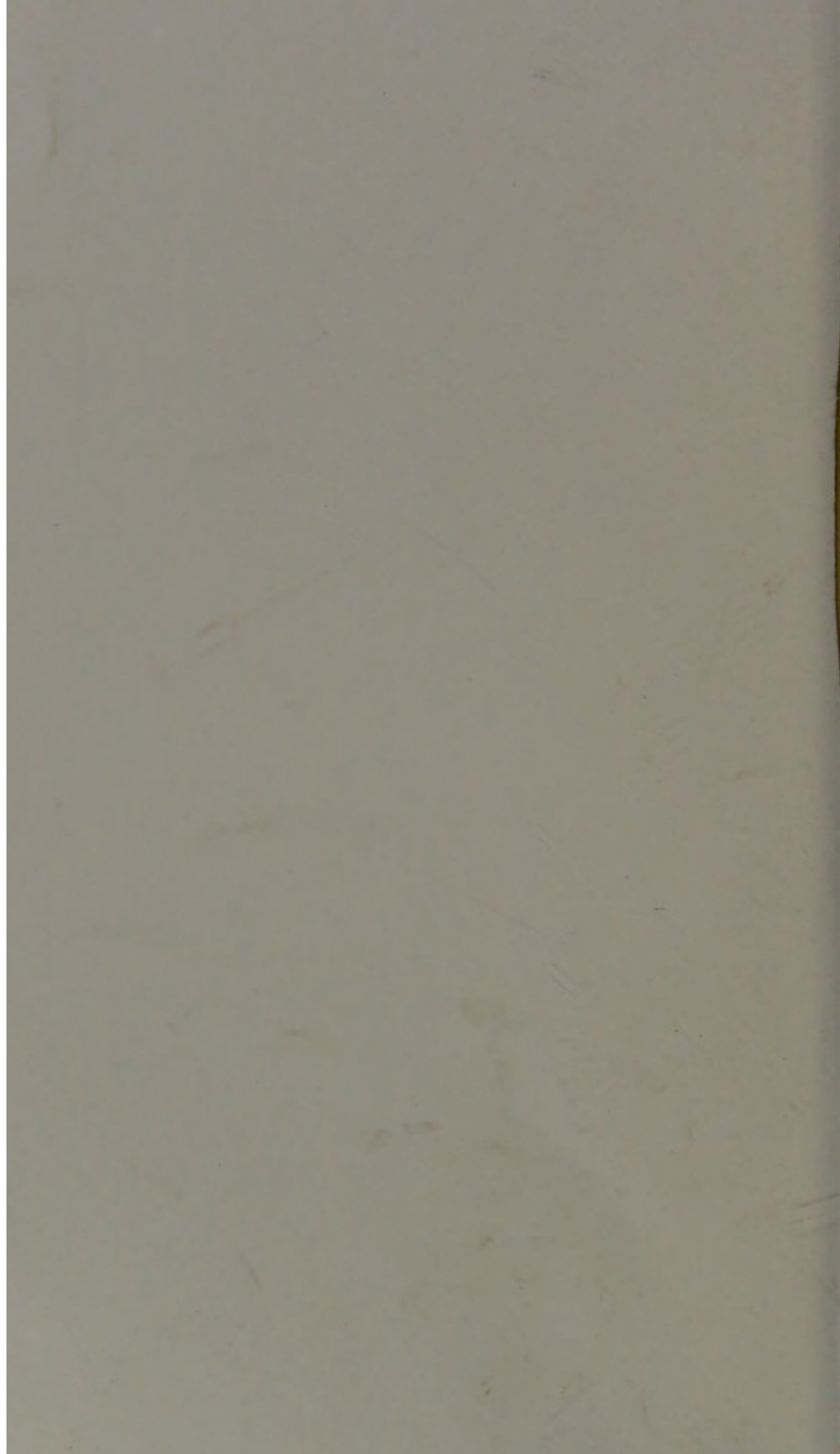
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ON TOXIC URINE IN RELATION TO CERTAIN  
SURGICAL OPERATIONS ON THE URINARY  
ORGANS. By REGINALD HARRISON, F.R.C.S., *Surgeon  
to the Liverpool Royal Infirmary, and Lecturer on  
Clinical Surgery in the Victoria University.*

It is impossible to study a series of cases of internal urethrotomy without recognising that, apart from their surgical interest, they may be regarded as extremely valuable physiological experiments in relation to some unworked-out problems connected with animal chemistry.

Until quite recently it may be said that certain events, following upon interference with the male urethra, proved little else than material for speculation, but little light being thrown upon what we have been accustomed to speak of somewhat vaguely as urinary fevers.

Some valuable communications have, however, from time to time been made in reference to this subject generally. Amongst these I would particularly mention one by my colleague, Mr Mitchell Banks.<sup>1</sup> A careful study of this paper led me to alter materially my practice relating to the treatment of certain strictures of the urethra, and eventually brought about some

<sup>1</sup> *Edinburgh Medical Journal*, June 1871



modifications in my proceedings, which I venture to believe have an important bearing upon the communication I am now making. Though the conclusions I have arrived at do not entirely correspond with those contained in the paper just referred to, I have no hesitation in expressing my indebtedness to the author for placing the matter before us in such a light as to furnish material for further elaboration and suggestion. It is now nearly fifteen years since, after practising the operation of internal urethrotomy on a tolerably large scale much as now employed, that I practically abandoned it. I have again resorted to it within the last two years, performing it, however, in a different manner, and under circumstances distinguishing it, I believe, widely from my previous custom. For the purposes of comparison and deduction I will briefly refer to the conclusions drawn from the two different methods of performing internal urethrotomy here referred to. The old practice of introducing some form of concealed knife within the urethra, and dividing the stricture by an incision, is almost invariably followed at an interval of somewhere about three hours with a rigor, and the subsequent development of more or less constitutional fever or pyrexia; these attacks may or may not be repeated at varying intervals; they differ widely in degree, in some instances being extremely mild, whilst in others they may prove severe or even fatal in a few hours. These phenomena have been explained in various ways, but none appeared to me to be satisfactory. That such symptoms have little or nothing to do directly with the pathological state of the kidney is clear, from the fact that they have been observed and have terminated fatally in individuals whose kidneys were *sans reproche*. That the state of these organs may, under certain circumstances, determine the degree or even direction of the pyrexial attack may not be improbable, but that it can cause it or even be responsible for it is obviously opposed to observation. That such effects are due to any form of direct nerve lesion or nerve traumatism of any kind seems to me to be equally improbable. Injuries to nerves are immediately followed by such anatomical or physiological signs as the nature of the lesion is capable of



affording. If a man's brain or spinal cord is damaged by a blow or a shock, he shows signs of concussion or nerve traumatism immediately upon the receipt of the injury, and not three or four hours afterwards. Again, if it is a nerve lesion of the urethra which is the primary cause of the phenomena following, why do we not see urethral fever after far more extensive nerve injuries, such as lithotomy and other equally great operations on the urinary apparatus? The improbability of urethral fever after internal urethrotomy, catheterism, and such like, being due directly to nerve shock, is indicated by other collateral considerations which may be noticed. In the first place, we should expect such symptoms to follow Holt's operation for stricture just as frequently and as severely as after section of the stricture from within. On the contrary, rigors and fever are far less commonly met with after dilatation with rupture than after internal urethrotomy—tearing or stretching is considerably less productive of urinary pyrexia than incision. In the next place, the position of the wound in internal urethrotomy, relatively to the circumference of any given part of the urethra, should hardly be expected to exercise a sort of determining influence in the production of rigors and fever, if the causation of these effects was a nerve lesion. Yet we find such symptoms more frequently follow when the section is made on the floor of the urethra in preference to the roof. A dependent position of the urethral wound is more likely to be associated with fever than one not so situated. Lastly, we should hardly expect the manifestation of these symptoms to be influenced by mechanical after-treatment if damage done to the local nerves was the cause of the symptoms that followed. Yet an analysis of cases seems to show that when a catheter is worn for a time immediately after the internal urethrotomy, and bladder drainage of urine is carefully carried out, that a considerable proportion of these instances escape attacks of urethral fever. As I have already remarked, If these effects are the result of nerve lesions, how is it we do not see them following lithotomy and properly performed perineal sections for urethral stricture? In reference to the latter operation, the earlier experience of Syme only



shows how easy it is to construct a perineal section which proves to be just as ready a cause for rigors and fever as any internal urethrotomy. In looking over the notes of my earlier cases of internal urethrotomy, it struck me, as being worthy of remark, that neither rigors nor fever showed themselves until after micturition had been naturally practised, or there was evidence that urine had found its way into the wounded urethra and was lodging there. This seemed to me to be opposed to the idea that nerve lesion had anything to do with the production of rigors and fever, inasmuch as these symptoms did not show themselves until urine had first been brought into contact with the wound. Such considerations as these led me to believe that the rigors and fever which I have referred to and illustrated by what follows internal urethrotomy were symptomatic of poisoning rather than shock. I therefore determined to test this point in practice, with the view at the same time of improving the condition of certain cases of stricture which proved unamenable to other means.

Adopting the view that rigors and fever, after internal urethrotomy and such-like operations, were illustrations of poisoning by material furnished directly from the urine, I resolved to perform a series of operations in suitable cases, where, though internal urethrotomy was practised, no urine was allowed to remain in contact with the freshly made wound. This involved an external perineal urethrotomy being done immediately after the stricture had been divided from within; in this way the urine was made to drain away just as rapidly as it was excreted. In the course of last year I published<sup>1</sup> a series of cases, since added to, with comments, where the double proceeding had been practised, my object being not only to prevent urine lodging from decomposing, and becoming absorbed by the wound, but at the same time to permanently improve the condition of the stricture. From these operations of external and internal urethrotomy combined, I soon learnt how it was possible to produce rigors and fever at will after operations on the urethra. So long as

<sup>1</sup> "On the Treatment of Urethral Stricture, by combining Internal and External Urethrotomy," *British Medical Journal*, July 18, 1885.



the bladder drainage of urine through the external perineal wound was free and uninterrupted, there was invariably a complete absence of rigors and fever; if these conditions were not fulfilled, either by reason of a flaw in the making of the drainage wound or in the apparatus used, I could see how such complications might arise. In carrying out these observations in regard to what I would speak of as the artificial production and prevention of rigors and urethral fever, I am particularly indebted to my house-surgeons in succession, viz., Messrs Pearson, Dawson, and Collins.

At this stage of the question it seems important that we should clearly recognise the different conditions under which the surgeon has to deal with wounds which are exposed to the action or influence of urine. Running healthy urine may be regarded as absolutely innocuous. When it can make its way over a fresh cut surface, or out of a cavity, just as fast and uninterruptedly as it flows over or in, it need cause no apprehension; on the other hand, when it is pent up, as in a wound or space, it is apt to be speedily converted into a most destructive, and, I believe, poisonous agent. How favourable are the conditions for the production of urine fever are those attending the operation by internal urethrotomy. The incision requisite for the division of the contraction necessarily paralyses the urethra to the extent, or rather more, of the wound that has been inflicted. Hence the process of repair has to be carried on with the wound soaked in the urine that is left behind to stagnate and to undergo change after each act of micturition. This is a very different condition from the incontinent flow of urine over the glazed and granulating open wound of a lithotomy or of a perineal section. In one case it is merely contact of urine with open spaces, in the other retention, and probably chemical rearrangement, within a space bounded by a freshly made wound. My direction and kind of work led me to believe some time ago that the urine could provide septic material of a kind which seemed to me to have been previously unappreciated in connection with the causation of urinary fever. It was with considerable interest that I perused the various communications bearing upon this



subject which have been recently made by Dr Bouchard of Paris. On a late visit I had the pleasure of seeing many of Dr Bouchard's experiments and tests, which he was good enough to show me at the Hospital Lariboisiere. These views relating to toxic urine, in conjunction with what I have stated as the result of my own observations in this department of practical surgery, seem to indicate tolerably clearly how poisonous normal urine may become, and how a grave complication may be added to a comparatively simple surgical procedure. I am much indebted to Dr A. Barron for kindly making me the following digest of Dr Bouchard's papers bearing upon this subject:—

In 1882, in a note<sup>1</sup> presented to the Société de Biologie, Bouchard showed that alkaloidal substances were constantly present in the urine in certain infective disorders, and that these alkaloids were of intestinal origin. That is to say, that they were substances produced in the intestinal canal by the growth of the vegetable organisms therein contained, also that they were analogous to the *ptomaines*. Subsequently these alkaloids were found to be present in normal urine. Bouchard found the same alkaloids present in the fæces, and he divided them into two groups—(a) those soluble in ether, and (b) those soluble in chloroform. He found that, when present in large quantities in the fæces, they were also present in proportionally large amount in the urine, and this applied to the ether and chloroform groups respectively. This first paper may be summarised as follows:—

1. In health alkaloids exist in the living subject.
2. These alkaloids arise in the intestinal canal through the action of putrefactive intestinal organisms.
3. The alkaloids of normal urine represent a fractional part of these intestinal alkaloids, absorbed by the intestinal mucous membrane, and excreted by the kidneys.
4. Diseases augmenting intestinal alkaloids augment *par consequence* the urinary.

<sup>1</sup> De l'origine intestinale de certains alkaloides normaux ou pathologiques, par Ch. Bouchard, *Rev. de Med.*, 1882, tom. ii. p. 825.



In his next paper<sup>1</sup> he determined the effects of normal urine on rabbits, and found that the same doses produced different effects according as the individual furnishing the urine was in health or not; also that the *toxicity* varied in different individuals, that the symptoms depended on several distinct substances. He proved by experiment that the symptoms were not due to the water of the urine, nor to the urea, uric acid, creatin, salts, or volatile matters. Further, that the alkaloids soluble in alcohol differed in their effects from those insoluble in alcohol, and that, although there might be five or six different substances present, they could symptomatically be arranged in two groups, a convulsive and a narcotic, and he concluded that the symptoms in different cases of uræmia might be explained by these groups being present in the blood in varying proportions.

Quite recently Bouchard has brought forward some further facts with regard to the urinary alkaloids and their properties.<sup>2</sup> He defines a *toxie* or a unit of poisonousness, as that amount of poison required to kill one kilogram of living matter, *e.g.*, of rabbit. The *urotoxie* is that quantity of urinary alkaloids capable of killing a rabbit weighing 1 kilogram. The symptoms of urinary toxæmia produced by introducing urine into the veins of a rabbit are, in the order of their occurrence—

1. Contraction of the pupil.
2. Acceleration and diminished amplitude of the respiratory movements.
3. Increase of urine.
4. Fall of temperature.
5. Diminution and finally abolition of reflexes.
6. Convulsions usually with coma, and
7. Death; the action of the heart and the electro-contractility of the muscles persisting for a time after death. The fall in

<sup>1</sup> "Recherches experimentales sur la toxicité des urines normales," *Comptes Rendus*, 6th Dec. 1884.

<sup>2</sup> "Sur les poisons qui existent normalement dans l'organisme et en particuliere sur la toxicité Urinaire," *Gazette Hebdomadaire*, Avril 1886; "Sur la variations de la toxicité urinaire pendent la veille et pendent la sommeil."

"Influence de l'abstinence, du travail musculaire, et de l'air comprimé sur la toxicité urinaire," *Gazette Hebdomadaire*, le 19 Mai 1886.



the temperature is due not to increase in the loss of heat but to a diminution in heat production. The urotoxic coefficient in man is .465; in other words, for each kilogram of body-weight enough poison is excreted in twenty-four hours to kill .465 grams of living matter, or in two days and four hours a man excretes enough to kill himself.

During eight hours, if asleep, only from one-quarter to one-half as much poison is excreted as during the same period when awake. If the whole day be divided into three periods of eight hours each, the proportional quantities of poison excreted are—sleep, 3; early waking period, 7; late waking period, 5. The urine of the sleeping and waking hours also differs qualitatively as well as quantitatively. The alkaloid of the urine of sleep is *convulsive*, that of the waking urine *narcotic*. The urinary poisons of the sleeping and waking hours are not only different, they are physiologically antagonistic.

Fasting increases the toxicity of the urine, probably because then the individual lives on his own tissues, and these are relatively more difficult of oxidation than the ordinary food, and are less completely oxidised. Labour greatly diminishes the toxicity of the urine, as does also the breathing of compressed air.

Opposed to the views I have advocated, that toxic urine is the cause of the rigors, and pyrexia, which constitute what we are accustomed to speak of as urine fever, may be urged the following considerations. How is it that such symptoms are not produced when urine, often ammoniacal, is subcutaneously forced amongst the tissues sometimes in large quantities as in cases of stricture and sudden urinary extravasation? and secondly, how does it happen that the same symptoms have been produced in sufficient intensity to cause death within a few hours, where there is no evidence to show that the urethral walls have been actually lacerated by the catheter or bougie, which is the assigned cause of the phenomena following? The latter considerations cannot fail to strike those who have perused Mr Banks' paper, to which I have already referred. To each of these points I will briefly address myself.

The conditions attending subcutaneous urine extravasation



are essentially different to those associated with the continuing contact of urine with a wound in the urethra, as in internal urethrotomy. A mixture of blood and urine seems to me to be capable of producing very different compounds from those that extravasated urine alone is likely to yield. Nor are we entirely to lay aside the consideration, that whatever *materies morbi* may be found at the seat of the wound by the conjoined decomposition of stagnant blood and urine, its entrance into the circulation must be favoured by the contractile power of the bladder from behind.

Again, when urine is extravasated amongst the tissues, its action is that of a virulent local poison, under the influence of which the contiguous tissues are killed outright, probably before they can exercise any power of absorption. Such a conclusion seems likely from some of Menzel's experiments, where putrid and normal urines were subcutaneously injected into various parts of the body.

In reference to the second objection which may be urged, namely, that cases are recorded which have proved rapidly fatal from urinary fever, where there is no evidence that the urethra has sustained any appreciable lesion. With all deference to those who think otherwise, I submit that this is a statement which should be received with considerable reservation. Though the operator is not conscious of having inflicted a lesion on the urinary passage with an instrument he has been using, nor the patient show evidence of it immediately, this by no means implies that a structural lesion on the urethra has not been inflicted. I have frequently drawn attention to this point, and demonstrated how readily false conclusions may be drawn in reference to it.

Curiously enough, it is not as a rule the most difficult cases of catheterism which are most liable to urinary fever; in those where structural damage is inflicted, or false passages made, they are generally on the distal side of the stricture, and consequently well protected from urine infiltration or contact.

I have seen a few cases where it has been found necessary to tap the bladder with the aspirator needle above the pubes. In



some of these I have ascertained that this proceeding was not resorted to until after prolonged attempts to get in an instrument by the natural passage had been made, such efforts probably meaning that a considerable amount of damage, in a legitimate way, had been done to the urethra but in front of the stricture. In none of those cases where puncture of the bladder had to be subsequently performed, could I discover that the patients suffered from urinary fever. Surely in these instances the amount of shock must be greater than that caused by the slight wound of a urethrotomy knife, where rigors and fever almost invariably follow.

As in connection with the whole subject of urinary pyrexia, I cannot deny that there are causes other than those proceeding from toxic urine and clinically distinguishable from them, I would take the opportunity of briefly referring to them, as I have met with them in practice.

In addition to the ordinary forms of fever, which may in some degree follow upon the infliction of any wound as in other parts of the body, as well as the extraordinary fever of the half-emptied septic-made bladder, about which we have recently heard so much in connection with catheter fever, there are two other forms of pyrexia which will in practice be met with. The one is essentially malarial, the other I would speak of as "irritative," for want of a better designation. The malarial variety is common enough in seaports. It is never seen except in persons who have had malaria, possibly at some very remote period of their lives, and is provoked by the passing of a bougie or a catheter. It comes on, as a rule, very shortly after the operation, sometimes within a few minutes; it bears no relation to the passing of urine; it is amenable to ordinary treatment by quinine, and can, as a rule, be prevented by giving the patient a third of a grain of morphia subcutaneously an hour before the instrument is passed.

Similarly, I have seen these attacks caused by the introduction of the finger up the rectum for the purpose of making a prostatic examination. I have never known febrile attacks of this description occasion any anxiety. The variety of febricula,



to which I have applied the term "irritative" for want of a better description, is hardly worth speaking of as a fever. It follows immediately upon the passing of an instrument; the patient is conscious of chilliness, and there is some elevation in temperature, which speedily declines. Precisely the same occurs sometimes when a patient passes water along the whole length of the urethra for the first time after lithotomy; this happened once to a patient of mine upon whom I had performed a prostatotomy on the first occasion he micturated naturally. In this latter instance it was more than a rigor; it was a convulsive movement, which lasted for several minutes, and was followed by a rise in temperature. The patient subsequently told me that he believed all this was due to what he described as "the consciousness of a new sensation,"—he should rather have said that it was the revival of an old one after six weeks' absence.

In making this communication I have endeavoured to apply my practical experience in the operative surgery of the urinary organs in the direction of throwing some further light on certain complications, which, though hitherto grouped under one name, permit, I believe, of further differentiation.

We know a good deal relating to the chronic forms of urine poisoning; of the acute much has yet to be learnt.

I desire to close this article with a paragraph taken from the address, entitled "Medicine of the Future," which was to have been delivered by Dr Austin Flint of New York, at the Annual Meeting of the British Medical Association in 1886, a copy of which I received just as this publication was going to press:—"Analytical Chemistry carries investigation beyond the limits of microscopical observation. The latter, at the present moment, both in pathology and physiology, seems to promise most; but is it not a rational anticipation to look for future results from chemical analysis of the components of the body, in health and disease, which in brilliancy and practical utility may surpass those of the labours in this field of investigation during the past half century? The medical semi-centenarian can recall the enthusiasm aroused by the labours of Liebig. Histology is now in the ascendent, but is it safe to predict that before the



lapse of another half century there will be another era in organic chemistry, and that light will penetrate dark recesses which histology cannot reach? . . . . . The supreme objects of study in pathology at the present time are the discovery of micro-organisms and their natural history. But these agents it is probable are pathogenetic, not directly, but indirectly, by means of the toxical products of their activity. What are these products, and how do they give rise to the phenomena of disease? We may ask the same question of certain of the poisons introduced from without the body. How is it that fractional quantities of morphia, hyoscyamin, strychnia, aconitia, atropia, and other alkaloids produce their lethal effects? It conveys no adequate information to say that they act upon the nervous system. This is merely the statement of a fact, not an explanation. For the latter we must look to the organic chemistry of the future." Such is an anticipation by one who has been appropriately spoken of as "America's greatest physician," and whose loss to science and society is so sincerely deplored.





