

Sir Robert Christison (1797–1882): the man, his times, and his contributions to nephrology

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ABSTRACT Sir Robert Christison was a professor of Medicine in Edinburgh for 50 years, and twice President of the Royal College of Physicians there. Despite this, few modern descriptions and assessments of either him or his work have been published. In particular, his major work in the field of renal disease, which allows him to be considered one of the fathers of nephrology, has been almost completely forgotten, even in Scotland. In this paper, Christison and his work in renal disease are described, trying to place his sometimes apparently paradoxical views and actions as a physician in the context of a man who lived across major changes in medicine.

KEYWORDS Acute renal failure, glomerulonephritis, history of renal disease, history of pharmacology, history of jurisprudence, nephrotic syndrome

LIST OF ABBREVIATIONS British Medical Association (BMA)

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INTRODUCTION

In a previous paper, Christison's work on renal disease was described in brief.¹ Here, the man behind the books and papers is presented in detail, and his output assessed more thoroughly, placing it within the ideas of his time. We explore further why Christison's work, fundamental to the beginnings of nephrology, may have been neglected for so long. It seems surprising that such an important figure in nineteenth century Scottish medicine has failed to attract the attention of scholars even within that country. Other than our previous paper, only one undergraduate thesis² and a short paper on a single limited event³ have dealt with Christison in recent times, and neither mentions his work on renal disease; the *Dictionary of National Biography* mentions his book on granular kidney only in passing.⁴

Although work in the area of renal medicine formed only a small part of Christison's formidably broad output over more than 60 years of professional life, he was the first author to deal with the subject of renal disease following the publication of *Bright's Reports of Medical Cases of 1827*.⁵ First, he confirmed and then extended Bright's work on albuminuria and dropsy, showed that it might be reversible, and finally established its relationship to acute nephritis and granular kidney. In addition, he discovered the basis for understanding uremia whilst applying chemistry to the study of blood and urine in patients with renal disease, described and quantitated the anemia of renal failure for the first time, made early microscopic examinations of the kidney and the urine, and finally

described the syndrome of acute renal failure from renal disease, and not as the result of obstruction.

CHRISTISON – THE MAN AND HIS CAREER

To better understand Christison's work, it is necessary to contextualise him in time and place. He was a major late figure of the early and mid nineteenth century, in the medical school in Edinburgh, Scotland – a medical school by then undergoing a slow decline from its monumental peak at the commencement of the nineteenth century. He was brought up in the classical traditions of the predominantly humoral medicine of the eighteenth century, but also had the benefit of a training in the burgeoning science of the day. Thus he presents a complex mixture of the old and new, as some of his colleagues later observed:

'Sir Robert Christison was not only a great physician, but a physician of a type of which he was almost, if not altogether the last representative ... It has so happened that the sixty years which may be taken as era of his professional life have embraced a transition in medical science ... It was this combination of Hippocratic and the modern scientific method which distinguished Sir Robert Christison, and which, so to speak, made him the physician of two ages...'

Thus wrote an anonymous obituarist in 1882.⁶ Another wrote in the *Lancet*:

'... there was in truth in him a strange mixture of the old and the new, the conservative and the progressive elements'.⁷

MILESTONES^{4, 6-11}: THE EDINBURGH SCHOOL¹²

Christison was born in Edinburgh on 18 July 1797. As the name suggests, the Christison family were originally of Norwegian stock from Forfar (Angus), on the East coast of Scotland, probably near Edzell. His great-grandfather's parents moved from there to a farm in Redpath in West Berwickshire, near Melrose, about the end of the seventeenth century. Robert Christison's father, Alexander Christison (1753–1822) broke free from the life of farming at Longformacus, through study and learning, to become a schoolmaster. To begin with, he taught at the local school, but then he was appointed to Edinburgh High School, where he then became Professor of Humanity (*Literae Humaniores*) in Edinburgh, occupying this post from 1806 to 1816. Robert's mother Margaret (1759–1831) was a member of the border family, the Johnstons, who had by that time long resided in Edinburgh. In his autobiography, Christison remarks:

'... with a pirate at the end of one line and a robber at the other, one may fairly pretend to a decent ancestry.'¹¹

Alexander and Margaret were married in November 1784, and their firstborn John (1788–1862) became an advocate and Sherriff of Ayrshire. Alexander and Margaret's twin girls both died of whooping cough in childhood, but then twin boys were born, the elder called Alexander (1797–1873). He became a minister in Foulden just over the border from Berwick-upon-Tweed. He lost three sons, one by drowning in a river in Queensland, Australia, a second at sea, and the last killed by pirates – but his fourth son became a millionaire sheep farmer in Queensland. The younger twin to Alexander, by a few minutes, is the subject of the present work.

Robert Christison was educated at Dr Milne's Academy, Drummond Street in Edinburgh, then at the city's High School, under Doctors Irving and Pillans, and then on to the town's University in 1811, aged only 14, to take the general arts course.

In Christison's time, as a result of the Scottish enlightenment powered by stellar intellects such as David Hume and Adam Smith, Edinburgh was truly 'the Athens of the North'.^{13, 14} It is beyond the scope of this article to explore just how unlikely this apogee must have seemed as recently as the middle of the eighteenth century; Scotland had been absorbed into an unequal political and economic union with England in 1707, losing status, monarchy, government and trade, most of the country was still backward and had been ravaged by the aftermath of the abortive 1745 rebellion, and Edinburgh itself was a:

'byword for violence, filth, squalor, drunkenness, disease, conspiracy and religious mania ... [with]

much of the Council's affairs and advocate's legal matters conducted in taverns ...'¹⁵

Nevertheless, over the next 30 years, an amazing transformation took place. The list of individuals whose work is still known and influential today is extraordinary, and does justify the comparison with classical Athens.^{13, 14} The 1790s saw Edinburgh peak as perhaps the major European centre of intellectual innovation, but it was to be replaced by Paris within a decade or two. By 1820, the major figures of the Scottish enlightenment were either dead or retired, and local conflicts in religion began to dominate thinking, with innovation gradually waning. In Christison's time as a student, one of the many important figures of the enlightenment, Dugald Stewart, had just stopped teaching moral philosophy, but his influence on the university had been immense. Intellectual life in every field had been buzzing with new ideas for some thirty years, and medicine and related sciences were no exception.

This eminence in medicine was fuelled by the continuing close relationship between Edinburgh and the important Dutch school in Leiden, where Sir Archibald Pitcairne (1652–1713) of Edinburgh took on an already great seventeenth century tradition and led on to the teachings of Hermann Boerhaave (1668–1738). This liaison was continued by his successors throughout the eighteenth century. Boerhaave taught in turn the army surgeon John Munro (date of birth unknown–1737), who was responsible along with a group of physicians – all pupils in Leiden – for the founding of the Edinburgh School in 1719–1740, his son Alexander (1697–1767) (*Monro primus*) becoming the first professor of anatomy as well as physician.

A major figure in shaping the medicine taught to Christison was the physician and chemist William Cullen (1710–1790), second only to Boerhaave as a teacher in seventeenth century medicine, who himself taught most of Christison's medical mentors. He both lectured and taught in English (not Latin, a precocious innovation which persisted) in the new clinical teaching wards established in the Royal Infirmary in the 1740s by John Rutherford (1695–1779). Edinburgh was then the only British medical school which required of its pupils a broad grounding in philosophy and science. Moreover, unusually for the time, the students were encouraged to meet, observe and work with patients, particularly by the physician Andrew Duncan (1744–1828). In 1807, Duncan had also pressed for the foundation of a unique school of medical jurisprudence. He occupied the first chair, and Christison later filled it. The students selected their courses themselves, and only paid for those they attended, keeping their lecturers in the theatre and on their toes!

Students flocked from outside Scotland to Edinburgh to study medicine, not only because of its high reputation, but also because they were driven from studying in

England or Ireland for being Catholic or dissenters. This latter group included such names as Thomas Hodgkin (1798–1866) and Richard Bright (1789–1858). At that time, to enter either Oxford or Cambridge (the only two universities in England) a profession of faith in the Church of England was required. From 57 students in 1720, by 1780 some 200 students attended courses in Edinburgh, and more than twice that number by 1820, to make the city the biggest medical school in Europe.

Christison began his study of clinical medicine in 1816, having amongst his many teachers, Alexander Monro *tertius* who taught him anatomy. He, however, barely continued the distinguished work of his forbears, so that Christison turned to one of the many ‘private lecturers’, the famous John Barclay (1758–1826). Others amongst his teachers were the charismatic John Playfair in natural philosophy, Andrew Duncan, James Home (both hopeless lecturers in Christison’s opinion) but, more importantly, John Abercrombie (1781–1844), William Hope and, above all, James Gregory (1753–1821) in medicine, a member of the famous family which, like the Munros, spanned four generations. Surgery was taught by Mr Syme. Important for his later general research interests, he voluntarily attended Robert Jameson’s courses in natural history – meteorology, mineralogy, hydrography. After a period of clinical training under the modest and rather obscure Dr William Spens, he graduated as MD in 1819 with a thesis on the epidemic fever in Edinburgh,¹⁶ a topic to which he was to return again on several occasions, and which left its mark on him in that he suffered recurrent fevers for the rest of his life. It is interesting to see that the oral part of his final clinical examination (by Gregory and others) was still, despite Cullen, conducted entirely in (dog) Latin!¹¹

Bright was briefly a contemporary of Christison’s in Edinburgh, from October 1812 to September 1813, but Christison was then only studying general subjects such as moral and natural philosophy, and did not even decide to read medicine until 1815 (he toyed with the idea of becoming an engineer but was dissuaded by his father), whilst Bright was pursuing mainly clinical studies, including those for a graduation thesis on erysipelas. So it is unlikely that they met in class, although social contact was of course possible. The students in fact had few mutual contacts outside their lectures, and several student societies were set up to relieve this need. No mention of Christison is to be found in Bright’s letters of the period either,¹⁷ and sadly no personal correspondence of Christison from this, or any other, period has survived, apart from that included by his sons in Volume II of his autobiography.¹¹ Nor has his journal survived, which was available to his sons in 1886. Neither during his visit to London in 1821 does he mention Bright, even though he visited Guy’s hospital to see the famous surgeon Sir Astley Cooper operating. This is perhaps not surprising, since Bright had only just been appointed assistant physician,

and had as yet published nothing on renal disease. There is no evidence either that Christison, despite his adulation of Bright and his work during the late 1820s and 1830s, ever went to London to meet him then, although much later they were in contact.

The medicine taught to young Christison would be unrecognisable to a student of today, although the vocabulary to some extent remains familiar. The most striking differences are in the classifications of disease, as well as the notable absence of diseases. Despite the work of Morgagni in Italy, and of Baillie in London, organ pathology was still unrecognised. The nosology of Cullen was widely used and, naturally enough, dominant in Edinburgh. Cullen himself did not attach particular importance to them, and was flexible on the topic though some of his followers were not. What we would regard as symptoms such as fever, inflammation and swellings appear as ‘diseases’, or at least as conditions worthy of separate consideration. This was a world with anatomy, but without any notion of tissues or cells. Affections localised to a single site were considered as a separate order. Therapy relied principally on ideas of humoral pathology from Galen, and used the many plants and few minerals known more than a thousand years earlier to Dioscorides, with a few important additions (opium, mercury, digitalis). Above all, there is no system at all of pathogenesis or of explanation, although antecedent events are noted.

The short period Christison spent in London in 1821 was spent at St Bartholomew’s hospital studying anatomy under Abernethy, during which he formed a very poor opinion of the physicians at that hospital, which had only three students! Then he went to Paris for an extended visit in 1821–1822, a most important journey which shaped his future interests and work profoundly. It also suggests that he was aware that Edinburgh was no longer capable of satisfying all his educational needs. At first, he attended a number of ward rounds, including those of the famous Broussais (whom he regarded as little better than a charlatan), and also attended operations, forming a low opinion also of Parisian surgery with the exception of Dupuytren, whose skill and sensitivity he admired. Through his old fellow student in Edinburgh, Pierre Coindet of Geneva, he was able to spend the bulk of his time in the laboratory of analytical chemistry run by Pierre-Jean Robiquet (1780–1840) (who discovered codeine in 1832). Christison’s practical work was mainly to analyse the proportions of elements in organic materials such as opium. Thus he was too busy to accompany Coindet to learn the use of Laennec’s stethoscope at the Necker Hospital, which he later regretted.¹¹ He also attended lectures by Gay-Lussac in physics, and by Vauquelin in chemistry, but most important of all, in toxicology, by the brilliant Catalan, Mathieu Orfila (1787–1853).



FIGURE 1 Christison as a young man in 1821. GB, after F Grant, Courtesy of the Library of the Royal College of Physicians of Edinburgh.

This training determined the future course of his career, and taught him that chemical analysis of body fluids and tissues was a major route to increased understanding of disease as well as the study of poisons and poisoning. Paris was the centre of this new knowledge.¹⁸ Christison's meticulous laboratory skills were encouraged by Robiquet, whilst Orfila was the leading figure in the new field of medical jurisprudence and the study of poisons, publishing profusely. Christison's own first paper published in 1823 with Coindet concerned experiments on oxalate poisoning.¹⁹

Whilst still in Paris he heard of the death of the great James Gregory in April 1821, which brought about a reshuffling of the professorial chairs in Edinburgh, and meant that his friend and supporter William Alison vacated the sole chair of medical jurisprudence in the UK, which was in the patronage of the Crown. Christison was nominated for the chair in his absence, and was, despite his youth, the obvious candidate for this because of his experience and an excellent reference from Robiquet. However, his appointment as Professor at the age of only 25 appears to have required considerable application of political pressure within the university and at court by Sir George Warrender and Lord Melville. He was awarded the FRSE and the FRCP Edin only in the following year (1823), and was then appointed Physician to the Royal Infirmary in 1827, an important step as this secured a practice income for him, necessary only because lecture fees were falling as the student body decreased in size; he had hoped to concentrate only on his departmental

university work. His private practice remained modest at first, but expanded greatly after the retirement of Abercrombie, the premier clinician of the period. From about this time comes the first portrait we have of him.

Christison held one chair or another in Edinburgh from then until 1877, 55 years in all. He held his first chair for 10 years until 1832, during which time the number of students paying for this course rose from 12 to over 90. He was an expert witness, almost for the first time in his life, in the notorious trial of the grave robbers and murderers Burke and Hare in 1829. Famously, he testified as to the cause of death of the subjects murdered for autopsy in the anatomy school of Dr Knox, establishing that bruising could not take place after death. In all, there were some 16 victims murdered. He describes the 'resurrectionists' (bodysnatchers) in his autobiography¹¹ (at pp. 175–180) in a curiously neutral fashion, being 'well acquainted' with many of them, although of course he condemns the later murders as another matter. The trade in bodies was finally overcome by Warburton's Anatomy Act of 1834, but the memories of this grisly period are still strong. In that same year of 1829, his *Treatise on poisons*³⁵ was published, and this established his reputation outside Edinburgh. In 1832, he transferred to the Chair in *Materia Medica*, and in 1855, he was nominated for the principal University Chair, that of Physic, but turned down the offer, for complex reasons, and so remained in the former Chair for a total of 45 years. One of his many pupils was Arthur Conan Doyle, and one wonders whether some of Christison's forensic approach found its way into the character of Sherlock Holmes, although the main contender for this role in most people's estimate remains the superb diagnostician, Christison's colleague Dr Joseph Bell.

By 1832, Christison already had a large hospital practice, and by 1839, he was elected President of the Edinburgh college of Physicians, serving again in this office from 1848; In that same year, he was appointed Physician-in-Ordinary to Queen Victoria in Scotland, and was made a baronet by Queen Victoria in 1871 at the suggestion of Gladstone, after he attended Princess Louise whilst the royal family were in Scotland on holiday (he had long been Physician-in-Ordinary to the Royal Family in Scotland). He was Dean of the University faculty of medicine from 1832 to 1840. In 1875 to 1878, he served as President of the BMA, and was honoured by both Cambridge and Oxford, as well as by foreign Academies. Although nominated as Rector of the University in 1880, he was not elected, Lord Rosebery being preferred.

A particularly severe episode of his recurrent fevers in 1877 was complicated by a deep vein thrombosis and resulted in his resignation from his Chair at the age of 80. Although his health improved in 1879–1880 and he was fully active, he became sick again in late 1881 with carcinoma of the stomach, and died on 27 January 1882.

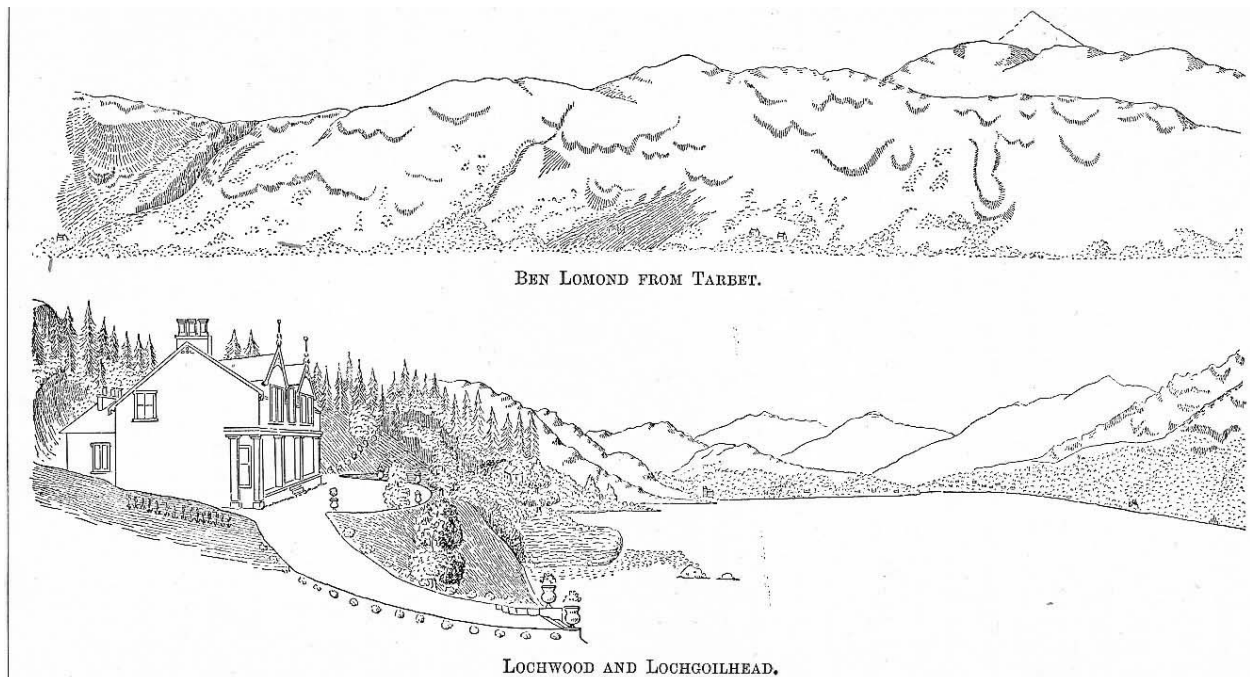


FIGURE 3 One of Christison's drawings of the Highlands, of which he did a number mostly following his retirement. From: Bright R. *Reports of medical cases* Vol I. London: Longman, Orme, Rees; 1827.

After a service in St George's Church on 1 February 1882, he was given a funeral by the city, being buried in the New Calton Cemetery in Edinburgh, not far from the ancient palace of Holyrood. The ceremony clearly had a major impact, with many mourners.

In his will, the material success of his long practice was shown by the fact that, apart from his fine house at 40 Moray Place in the New Town and its rich contents listed in the inventory, Christison bequeathed £20,000 to each of his three sons, the residue of the estate to go to Alexander as eldest and now baronet. It is difficult to translate this into contemporary value, but would probably now well exceed a million pounds all told: for comparison, Sir William Withering, said to be the richest physician ever in England, left an estate of over £300,000 in 1892.²¹

CHARACTER AND FAMILY

Christison was clearly an impressive man, both physically and intellectually, with an amazingly retentive memory as his autobiography testifies again and again. He was tall (a shade under six feet), lean and good-looking, with enormous energy which persisted into his 80s, hill-walking being one of his passions. He thought nothing of covering 15, 20 or even 25 miles, usually averaging four miles an hour or even more over all terrain, and considered a prospect of the Highlands his favourite view. His autobiography is full of accounts of days spent tramping the hills. We know he spoke and also sang well in a rich bass voice and sang solo, in groups and in choirs:

'he had, if ever any man, a rare power of speech, with a music in his voice ... being also a musician. His fine mellowed and modulated song can never be forgotten by those who heard him, nor can the memory be lost of his stentorian declamation when angry...'¹¹

For many years he kept a journal or diary, upon which presumably he based his autobiography.¹¹ It is written in an almost impossibly regular and beautiful hand, and this is reflected in his meticulous drawings, which became numerous after his illness of 1877 (see Figure 2) made him less physically active and he spent much time at Onich, near Ballachulish and Glencoe on the West coast of Scotland – although it has to be said that even then at over 80 years of age, he could still out-walk most of his younger friends and colleagues on the hills. Thus, he remarks in a letter of October 1879, aged 82:

'I walked 9 miles without a stop but soon I found my right pace was no longer 4 ½ but 3 ½ per hour.'¹¹

He climbed a favourite mountain, Beinn Vorlich (985 m) in Perthshire in 1876, perhaps to celebrate his 80th birthday. He was near-sighted (although no portrait with spectacles exists) and used quill pens he made himself; he also made use of the indelible ink invented by his old friend (Sir) Thomas Traill of Liverpool.²⁰ This activity ceased only when his eyesight failed in his penultimate year.

Like most notable physicians of the nineteenth century, Christison was an able linguist, speaking fluent French from his schooldays, which he improved in Paris, and

having taught himself German from 1823. In his autobiography, he quite frequently quotes Italian in the original. Thus, he could easily gain access to information available in the European literature.

Unfortunately for us, although his lost journal continued until his death, his written autobiography ceases prematurely in 1830, and confines itself almost completely to his professional career: we learn little from him directly of his feelings – he devotes just one paragraph to his wedding in 1827, and immediately discusses the subsequent careers of those present and the details of his travels to Glasgow for what would now be called a honeymoon. Perhaps the memories of his wife were still too painful for him when this was written in 1871? His sons remarked, however:

‘Reserved and somewhat unbending as Sir Robert was, he had a tender and affectionate heart... and long afterwards occasionally showed, almost inadvertently, the loving recollections of his wife’.¹¹

She displayed a type of personality and acquired restraint well known in Scotland. Volume II of his autobiography includes a number of letters and journal extracts referring to his family.

His beloved wife was Henrietta Sophia Brown (1805–1849), daughter of David Brown of Greenknowe, Stirlingshire. He had fallen in love with her as early as 1820 when she was barely fifteen, although as he wrote much later ‘but three years beyond it in point of mind and conduct’. Thereafter, in 1822, they became estranged for two years ‘without any clear or sufficient reason’, and he took the opportunity to plunge himself into the work of his new professorship. Finally, in 1827, they married on a November day ‘in weather suitable to the season’ and then had three sons, the eldest of whom, Alexander (1828–1915) later became second baronet in 1882. Alexander took service with the East India company in Oudh and participated in the Burma war of 1852, finally becoming Surgeon-general to the Bengal Army, also serving in the Indian ‘mutiny’ of 1857. The second son David (b. 1830) also qualified in medicine at Edinburgh, being a house surgeon alongside Lister in 1854, and practiced in the city. A third son, John (b. 1832) worked in the University, becoming Writer to the Signet and secretary of the University Court.

Sadly, Henrietta died in 1849 at the age of only 44, after what her sons described as a ‘long and painful illness’; Christison did not remarry, as was common at the time. We know that he cared for her during her illness with a remarkable tenderness.¹¹ Certainly, the affectionate letters to his grandchildren (through his son David) in India betray a more sensitive and loving character than his public reputation suggests, as in this letter to his granddaughter Edith, aged 7. Bob and May

were her brother and sister, Henriette their cousin, another grandchild:

‘what a day that will be when you all turn up here! You will be a shy puss. Bob will rush from room to room till he finds some new thing to play with. May will be struck dumb for a while. H.(enriette) will be like to leap out of her skin for joy, and to crush Bob and you to him for love. And we old folks at home will be glad – glad, though we may not show it so much as you young folk will.’¹¹

In the second volume of his autobiography, published by his sons three years after his death, is a detailed appreciation of Christison’s character by Sir Henry Acland, Sir William Gull’s son-in-law. Another commentator, also cited above, was Professor Thomas Gairdner, who wrote of him as a physician.

‘His training in research ... had left upon his manner the impress of a certain reserve, or as some considered it, hauteur, which was perhaps not quite favourable to a rapid or extreme success in private practice ... this was not from any lack of sympathy, but from a kind of shyness, which interfered with the freedom of his communication with the sick, especially when they were of a kind likely to cause distress ... on the other hand, no man was more entirely straightforward ... and he was trusted accordingly’.¹¹

The anonymous obituarist in the *British Medical Journal*⁸ wrote that he ‘had at times a manner which could be considered cold and imperious’. However, just as to his family, also to his students, the other side of his personality was revealed. He seemed to them ‘the oldest young man they ever knew’ (*Lancet* 1882⁹) and ‘his influence and popularity with the students were probably unequalled’.⁶

In politics, he supported the Conservative party, and although he favoured and initiated general reform of the University over the years and brought in many new practices, in the 1870s he opposed strongly the admission of women as medical students²². A battle went on during several years in the many University committees of which he was a member, with his opposition as leader and principal spokesperson of the contrary faction implacable. He wrote:

‘There is no evidence of any adequate demand amongst females to be educated in medicine’.

He even reported in a University meeting that Queen Victoria herself was opposed to such ideas^{22,23}. It is said also that he even threatened to resign if women were admitted; they were, but he did not. His major opponent, the indefatigable Sophia Jex-Blake (who referred to him

on one occasion as 'the Ogre') finally qualified from Edinburgh University as its first woman graduate in medicine in 1877.²² This antipathy to women in medicine was shared by his son Alexander, the second baronet and himself a military surgeon, so that his daughter Irene Christison was only able to become a doctor against her father's wishes by going to America.²⁴

Christison's position on the cusp of classical and modern scientific medicine has been noted already.^{6, 7} One example of his medical conservatism was his retention of bleeding as a favoured form of treatment, long after this practice was shown to be useless by Pierre Louis in Paris in 1835.²⁵ He even had himself bled on a number of occasions during his intermittent lifelong fevers, whose nature is difficult to discern after so many years; brucellosis is one possibility. On the other hand, in contrast to his strategies for 'depletion' in 1851 outlined above, by the 1870s, he realised the importance of the work of François Magendie, Claude Bernard and others in physiology in relation to therapeutics and poisoning:

'therapeutic physiology is a splendid and still little-trodden field, without which we shall never make any material advances in the knowledge of the actions of remedies and their real uses in disease'.¹¹

Thus it seems he never fully resolved the conflict of these new ideas with those derived from his traditional training, both of which continued to occupy his attention.

CHRISTISON'S PAPERS AND BOOK ON RENAL DISEASE

The early papers

In 1827, the remarkable year in which Richard Bright published his epic *Reports of Medical Cases*,⁵ the young Christison immediately realised the immense importance of this work, especially that on the connection between dropsy and kidney diseases, and published an unsigned but extensive multi-part appraisal and summary of the book the following year in the *Edinburgh Medical and Surgical Journal*²⁶ – the first written comments on Bright's work to appear anywhere.

Not only did he make this analysis, but he realised also that he was himself seeing such patients at the Infirmary. His friend and longterm mentor Dr William Alison (1790–1859), whom Rayer suggested later had made similar observations to those of Bright as early as 1823,²⁷ pointed to their frequency:

'Very soon after the publication of Dr Bright's *Hospital Reports* in 1827, my attention was riveted on that portion of the work which announced his great discovery of the relation between dropsy and a previously unknown organic disease of the kidneys. I

had written an analysis of that investigation for the *Medical and Surgical Journal* for July 1828; and at the same time I began to observe cases of the disease under my charge in the hospital'.¹¹

Christison noted that others denied they saw any such cases:

'It was said that such cases as he described had been seen only at Guy's hospital, and in the scum alone of the London population'.¹¹

This resistance to ideas which Christison heartily endorsed made him quickly assemble his own experience of the condition, which was published without delay in the *Edinburgh Medical and Surgical Journal* of 1829²⁸. This was the first paper on Bright's disease (although this term was employed first in 1834²⁸) to appear anywhere in the world after Bright's initial description:

'in the course of the twelvemonth prior to May last [1828] no fewer than about twenty cases have occurred in the different wards of our Hospital; and at the present moment five cases of the kind are under treatment'.²⁸

Given the relatively small population of Edinburgh at that time (162,000 for Edinburgh and its suburbs in the 1831 census, up from 40,000 a century earlier) this statement backs up that of Bright a few years later, and suggests that the nephrotic syndrome was much more common in their day than today, 175 years later.²⁹ This work of Christison's contained several major advances: first, that he was able to establish without doubt – as Prout and Bostock had tried unsuccessfully – 'the occasional presence of urea in the blood of persons labouring under the disease in question'. At that time, the methodology was too insensitive to detect the small amounts of urea in normal plasma. Detailed analyses of blood and urine were reported in several patients as never before. Second, Christison also pointed to recovery from dropsical Bright's disease, which at that time Bright had not observed and which remained a contentious point for a further decade.³⁰ Finally, he related the acute forms of Bright's disease, which the master himself had barely touched on, with the dropsical cases, although William Charles Wells (1757–1817) had described these clearly – but without any observations on the state of the kidneys – twenty years previously.³¹

Christison's 1829 paper gives details of seven patients with dropsy and coagulable urine, and the immediacy and personal detail of the accounts mirror those of Bright. Robert Irving was a 58-year-old veteran of the battle of Walcheren in 1809, followed by a year's fever, after which 'about four pounds of matter were withdrawn by a puncture' from his abdomen '... his liver at that time believed to be affected'. Christison did detailed chemical

analyses of his urine and 'contained only half the natural proportion of urea' and was markedly coagulable. Irvine remained in hospital for six months under observation and treatment, mainly with squills³² and supertartrate of potass, but developed dimming of vision and a firm pulse for which he was venesected; he then developed a cough, and was bilaterally dull at the lung bases. His outlook seemed bleak, but in November 1828 he improved, lost his coagulable urine and his dropsy, and discharged himself the day after New Year's Day 1829, only to relapse a month later with severe oedema and ascites, and more neurological symptoms. He died in March. At post mortem examination there was evidence of an old intracerebral bleed and the liver was healthy, but the kidneys were 'small, hard, pale and scabrous'.

Francis Magee, a 57-year-old weaver, was admitted with similar complaints including headache and drowsiness and a contracted pupil. He deteriorated rapidly despite bleeding, purging and digitalis, and died. His kidneys 'were both much diseased' being small, with diminished cortex and fatty infiltrated medulla, which matter Christison identified as 'cholesterine'. Christison analysed his blood with care. The blood was concentrated by evaporation 'during which a fetid odour was exhaled, exactly the same as the patient's breath during life ... the extract had the same fetor' ... which then after treatment with nitric acid 'immediately fine, grayish-red, flaky crystals of a pearly lustre were formed in abundance ... these were evidently scales of nitrate of urea'.

Christison next compared the blood of another patient, a middle-aged dropsical travelling salesman James Thomson, with that of a young woman 'feigning sickness': her blood was negative for urea, but his was loaded with it. Post mortem was refused in this case. Murdoch Campbell, a 27-year-old labourer from Skye, recovered after a severe dropsical illness with coagulable urine.

Marion Clinksales, aged 27 years, was admitted under Christison's brilliant young colleague James Crawford Gregory, who was the son of James Gregory and died aged only 32, three years later. She also lost her coagulable urine and dropsy, and was discharged after only three weeks' illness. Later she relapsed, and eventually died of the disease or its complications.

Christison comments on these cases, mainly seeking to reinforce Bright's conclusions, but remarks in addition:

'The specific gravity of the serum has always been lowest where the urine has been most loaded with albumen. It is hence probable that the albuminous secretion of the urine is nothing more than a transudation of serum from the blood'.²⁸

He then goes on to discuss his finding of urea in the blood of several patients, something which he points out that

'Dr Bostock sought for ... in the serosity of several of Dr Bright's patients', but could detect only 'a matter possessing peculiar properties, which seemed to approach those of urea'.

Christison had also studied other patients in whom blood and urine could be examined simultaneously, and his results showed that:

'it may be regarded as proved, therefore, that in the dropsy arising from diseased kidney, urea exists in considerable quantity in the blood when it is missing from the urine. The preceding results confirm the conclusion drawn not long ago by MM Prévost and Dumas from their ingenious experiments on the extirpation of kidneys in animals – that urea is not generated by the kidneys but exists ready-formed in the blood, and is merely eliminated by these organs'.²⁸

Christison discusses symptoms outcome and treatment. The usual armamentarium of the period was employed: bleeding, tartrate of potass, squill,³² on one occasion leeches, digitalis, various purgatives. It is of interest that he discussed no general theories of disease or causation, or rationale for treatment, in this paper.

At that time, bleeding was standard treatment for any disorder regarded as inflammatory in nature, and so up until the practice was discredited in the 1840s and 1850s,²⁵ physicians had ample access to their patients' blood for chemical analysis. This was reflected in an abundance of papers describing the chemical nature of this fluid at that time, even though analyses required very large volumes. The humoral theories as espoused especially by the Paris school of François Joseph Victor Broussais (1772–1838) regarded almost every disease as inflammatory in origin and to be treated by depletion using bleeding or the application of leeches; Broussais personally used more than 100,000 per year. The humoralists, constructing a nineteenth century extension of the traditional Greek humoral theories, pictured that all changes in organs and in tissues (a relatively new concept arising from the work of the brilliant young Xavier Bichat in 1805) arose as the consequence of alterations in the blood. These ideas retreated only when Rudolph Virchow (1821–1902) introduced the idea of cellularpathologie in the 1850s, driven of course by the first descriptions of cells as the unit of tissue, by Henri Dutrochet in 1824, and then by Jakob Schleiden and Theodor Schwann in 1839. Christison in his time in Paris¹¹ had formed a very poor opinion of Broussais as a physician.

Christison noted the presence of oily matter in the blood of his patients with milky serum, and the following year drew again upon his chemical and forensic expertise in a paper again published in the *Edinburgh Medical and Surgical Journal*³³ entitled 'On the cause of the milky and whey-like

appearances sometimes observed in the blood'. Christison noted that milky serum had been observed by many previous clinician-chemists in those blood-hungry days, including by William Hewson (1739–1774) in London, who supposed that, following the Galenic tradition, a portion of the chyle was not being converted to blood.³⁴ Hewson had made the additional important observation that on evaporation such serum to dryness, the residuum made a greasy stain upon the paper. Christison reviewed also the work in 1821–1823 of his friend Sir Thomas Traill (1781–1862) of Liverpool (an intimate of Bright's associate John Bostock) finding as much as 2.5 to 4.5% parts of the serum to be an oily substance in three such samples.

Christison studied also blood drawn from a patient with a fever and muscle pain, which 'were quite undistinguishable from new milk'. He first extracted the oily matter with 'sulphuric ether', then showed that after evaporation it was in part fluid at the temperature of hot water, flammable and colourless. Thus it resembled the 'oleine' and 'stearine' recently described by Chevreul. He then examined serum from three dropsical patient with 'whey-like serum', obtaining similar results, and some perfectly clear sera in which he again found traces of a fat-like material, shrewdly observing:

'it is hence extremely probable that in the natural state of the blood there is ... a greater or lesser proportion of fatty matter exactly corresponding with the fat of adipose cells'.³³

The book of 1839 on granular kidney

Christison was then distracted by the third of many editions of his major work *A treatise on poisons in relation to medical jurisprudence, physiology, and the practice of physic* which first appeared in 1829.³⁵ His interest in renal diseases persisted, however, and this period culminated in his principal contribution to nephrology, his book of 1839 with its eccentrically spelled title, *On granular degeneration of the kidneys and its connexion to dropsy, inflammations and other diseases*.³⁶ This book had only a single edition, but was translated in 1841 into German by Johann Meyer and Carl Rokitsansky (1804–1878).³⁷ In addition, several of his papers were published simultaneously on the continent of Europe¹¹ so that not only was Christison aware of work in Europe, but also his publications were well known there.

The first 164 pages of this short book are devoted to a general discussion of the subject, followed by another 124 pages devoted to the histories of 'illustrative cases'; pages 242–288 cover a section boldly entitled 'Cases with recovery'. The general discussion is divided into sections on the pathogenesis and morbid appearances of the kidney, then the symptoms and clinical history, followed by consideration of kidney disease in relation to dropsy, catarrh, dyspnoea and diseases of the heart. The causes

of granular kidney are then explored, the prognosis discussed with particular attention to answering the question whether the disease is curable, and then a section on treatment.

Much of this text, particularly that pertaining to dropsy, confirms and little extends Bright's observations. However, in addition, Christison made a number of original observations of great importance, particularly in relation to the acute and chronic phases of the disease, scarcely treated by Bright in his book of 1827 (although discussed in more detail in his papers of 1836³⁸). First, Christison knitted into the spectrum of Bright's disease (this term was used in France from 1834 and in Britain at least from 1843) the acute phase of congestion, drawing also on the observations of John Hamilton³⁹ and James Crawford Gregory and their students of epidemics of scarlatina in Edinburgh in 1831.⁴⁰

Next, Christison presented new observations on the nature of the disease in the chronic phase. As is well known, Bright observed copiously but speculated little, except for his (later) inspired connection of left ventricular hypertrophy to chronic renal disease in 1836.³⁸ However, Christison was interested in the possible humoral basis of what became called the 'uraemic state' from 1847.⁴¹ As someone trained, like William Prout, Alexander Marcet and John Bostock, in both chemistry and clinical medicine, he notes with approval in 'the state of the blood' (at pages 58 and following) the: '... recent improvements in chemistry, and more especially in the department of analysis' but regrets the general neglect of this area '... but the pathology of the fluids and more especially the blood is little else than an untrodden region'.

He noted that in these patients the specific gravity of the serum was generally low, and confirmed that this is the result of a lowered serum albumin. So much was known already from Bostock, but then, at p.62, Christison adds:

'[a]nother not less remarkable departure from the healthy constitution of the serum is the presence of a large quantity of urea ... [which] is invariably found in the serum at all stages of the disease, when the daily discharge of it by the urine is diminished materially ... but if the urine approach the healthy standard in point of quality ... urea cannot be detected satisfactorily, although still traces of it may be elicited'.

At that time, and for another century, until the studies of Volhard, clinicians were most impressed with the neurological consequences of granular disease of the kidney, some of which, following Volhard, we would today attribute to hypertension. Christison (at p. 2) reached the important conclusion that in the state of uraemia:

'ultimately its intrinsic result is to overwhelm the functions of the brain, probably the consequence of

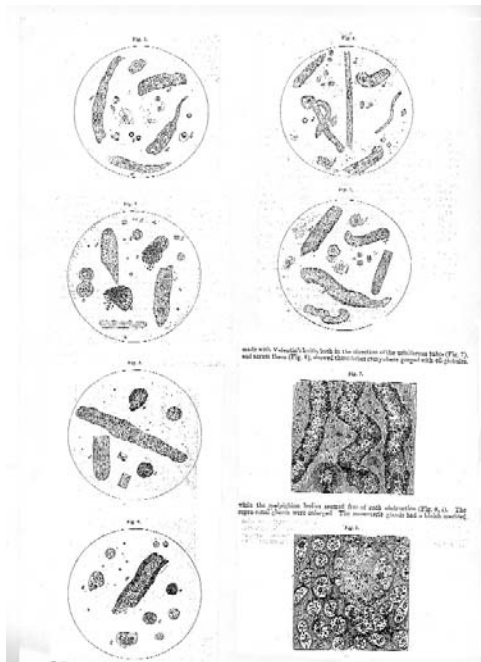


FIGURE 8 Illustrations from the paper based on the 1851 lectures (see Christison R. Bright's disease of the kidneys (delivered 11 and 18 March 1851). *Edin Monthly J Med Sci* 1851; 12:551–73.) Showing appearances of urine in dropsical patients with the inflammatory type of disease: red cells (Figures 2a, 3a), degenerated epithelial cells (Figures 1b, 3b), and epithelial cell casts (Figures 1d, 3d) are shown.

the blood ... being (on the one hand) poisoned by the accumulation of urea, and deprived on the other hand of its colouring matter (haematosine)'.³⁷

However, Fourcroy and Vauquelin had speculated as early as 1808 that this might be so, in an extraordinary leap of imagination;⁴² and famously in their landmark paper on nephrectomy in dogs of 1821 Prévost and Dumas⁴³ had shown the mounting levels of urea in the blood after the operation. What was completely new, however, were Christison's observations on the anaemia of chronic renal failure.

Chevreul in Paris had described 'Hematosine' (haemoglobin) in 1814 as the colouring matter of the blood, and it had been noted by Bright that in patients with chronic disease: 'after a time, the healthy colour of the countenance fades'.³⁸

Christison however gave the matter detailed consideration, making quantitative observations using a gravimetric method on blood defibrinated by agitation with lead pellets, then separated into fibrin, serum and coloured matter, based on that used in Paris by Lecanu. He noted that in the early stages of granular kidneys there were no major changes, but that:

'by far the most remarkable character of the blood in the advanced stage of the [Bright's] disease is a gradual and rapid reduction of its colouring matter

or haematosin. At the commencement ... this ingredient undergoes little or no diminution. But in the progress of time its proportion sinks; and at length it is reduced so much as to form less than a third of average ... the reduction which takes place in granular disorganization of the kidneys [sic] is far beyond what can be accounted for by the extent to which blood letting is usually carried'.

and concludes:

'thus then, in the advanced stage of granular disorganization the proportion of haematosin in the blood is invariably and greatly reduced ... I am acquainted with no natural disease, at least of a chronic nature, which so closely approaches haemorrhage in its power of impoverishing the red particles of the blood'.

Following this, he also gives a much more complete description than Bright, over a full page, of the appearance and complexion in advanced renal failure:

'sometimes a pale transparent waxy hue is gradually induced ... at other times a peculiar dingy brownish tint is communicated'.

Christison's quantitative observations are presented in a table on page 73. In a 'healthy young woman', he found 1,207 parts per thousand and 1,535 parts per ten thousand in a 'stout seaman' noting that these figures agreed with previous observations in healthy individuals (by Lecanu), but in seven patients with chronic nephritis he found reduced quantities: 427–955 parts per ten thousand whilst in the acute phase the figures were substantially normal: 1,111, 1,339 and 1,046 parts per ten thousand. Today's standards differ little from his figures, and that he noted the difference in haemoglobin concentrations between men and women.

Christison's observations were much quoted by Pierre Rayer (1793–1867), the French founder of nephrology in his great treatise of 1840²⁶ discussed further below. Rayer had been influenced by Donné to study urine using microscopy from 1837 onwards, and looked at blood as well in chronic Bright's disease, writing:

'lorsqu'on examine au microscope le sang provenant d'individus hydropiques, atteints depuis longtemps de néphrite albumineuse chronique, les globules rouges paraissent moins nombreux que dans le sang sain'.

However, he made no quantitative observations on this, since the techniques for counting cells would not become available for more than another decade.⁴⁴ George Owen Rees (1770–1846) one of Bright's many associates, who conducted the clinico-chemico-pathological observations on dropsical patients at Guy's under Bright's supervision in

the famous Summer study of 1842, also measured the proportion of red cells in the blood in 1843 and noted:

‘the great diminution in the proportion of colouring matter observed in the blood of patients affected with the advanced stage of the Morbus Bright’.

and in the table of the accompanying paper, 24 of 37 patients were said to be ‘anaemiated’.⁴⁵

Christison himself had studied the reaction between blood and oxygen as early as 1831, noting that agitation of defibrinated venous blood with air made it lose its dark colour and become like arterial blood.⁴⁶ Haemoglobin was crystallised by Reichert in 1849, and the papers of Justus von Liebig (1803–1873) and Ernst Hoppe-Seyler (1825–1895) established that this molecule was the agent responsible for oxygen exchange during the 1850s. It must be judged surprising that the anemia of chronic renal failure was generally lost to view for another 80 years. Almost no mention of it was made in the major articles and papers in France, Germany and Britain up to 1900 and beyond, although Sir William Osler was an exception.⁴⁷ Only after the American papers of Brown *et al* as late as 1922⁴⁷ did it become usual to comment on this feature of uremia, but even so, many authorities, even in the modern period, made little or no mention of it.

Tweedie’s System of Medicine (1840)

Christison’s next publication on renal disease has received no attention or commentary in contemporary accounts. The 20-author six-volume text *A System of Practical Medicine Composed in a Series of Original Dissertations*,⁴⁸ was edited by his contemporary student in Edinburgh (but now working in London) Alexander Tweedie (1794–1884)⁴⁹, and was published in London in 1840.⁴⁹ Christison contributed the 84-page section *Diseases of the kidneys and urinary tract* in Volume 4, and also those entitled *Fever and Continued Fever* in Volume 1. It is notable that as well as his account of renal disease, Dr Thomas Watson of the Middlesex Hospital also contributed a separate chapter on the dropsies, which illustrates nicely the co-existence of older symptomatic classifications of disease with those following the modern ideas of Giovanni Battista Morgagni and Matthew Baillie, classified according to anatomical site.

Christison’s account of granular kidney naturally followed his account of the previous year closely, but he gives a long section on the urine, its normal and abnormal appearances and constituents. This is devoid of any mention of microscopy, perhaps surprising when one considers the time that Christison spent in the laboratory in his forensic work, and the popularity of urine microscopy in Paris from 1837 onwards in the schools of Donné and others.⁵⁰ However, he was first and foremost a chemist; only later in the 1840s did he exploit the microscope (see below).

To modern readers, the most interesting part of the rest of his section on urinary tract diseases is that on ‘ischuric’ anuria, that is anuria that is not the result of obstruction from, for example, stones. He writes:

‘When suppression of urine takes place suddenly from any cause ... the usual results are the following: at first little or no uneasiness of any kind is occasioned; but ere long there is languor, restlessness, vague general discomfort ... upon which the attention is probably called to an excessive diminution or total suspension of urine. The pulse then commonly becomes excited ... at length drowsiness comes on, generally in the course of the 3rd day; and about the same period or sooner puffiness of the features is observed ... the drowsiness gradually passes to coma, which is usually formed on the fourth day and death ensues either within 3 days more and without any additional symptom, or at an early period of the coma with a precursor stage of convulsions ... [if a catheter is passed in the early stages this shows] a few drachms of muddy urine ... often coagulable by heat as well as nitric acid. At a later period the bladder is quite empty’.

This excellent description of acute uraemic coma perhaps derives from the earlier account of one of his teachers, John Abercrombie (1781–1844), published in 1821⁵¹ with which it has similarities, although Christison’s description is more complete. Rather surprisingly, since Christison’s account is liberally referenced with colleagues’ names, Abercrombie is not cited here.

As to causes, Christison notes that apart from stones:

‘in some cases suppression appears to be commonly caused secondarily through the intervention of acute nephritis ... suppression occurs very seldom in the course of acute and chronic organic disease of the kidneys.. [it may arise also from] ... poisoning with large doses of foxglove, corrosive sublimate [mercuric chloride], cantharides [Spanish fly] ...’

Thus speaks the toxicologist. Although he does not mention trauma or childbirth, noted by his other Edinburgh colleagues Cumin in 1823⁵² and Simpson in 1843⁵³ respectively, these descriptions are one of the best accounts of acute renal failure from the early and mid-nineteenth century; only the brief 1892 description of William Osler⁵⁴ would improve and expand on it.

The lectures of 1851

Christison, although continuing a prolific output on other subjects, published only one further paper on renal disease, in 1851. This interesting long paper⁵⁵ on Bright’s disease again seems to have been forgotten completely and has never been, so far as I can ascertain, cited or

reviewed previously other than by Christison himself in his autobiography of 1871, which was not published until 1886. This is surprising since it contains some early histological insights and pictures of microscopy of the urine, as well as new clinical data. It was evidently based upon lectures given in Edinburgh, presumably at the Royal Infirmary, on 11 and 18 March 1851. These lectures predate not only George Johnson's textbook of renal disease⁵⁶ published the following year, but also Samuel Wilks' seminal papers in 1853–1856^{57, 58} and Theodor Frerichs' *Die Bright'sche Nierenkrankheit* published only in 1859.⁵⁹

Unfortunately for historians, Christison's oral introductory historical review of clinical work, which had reported since Bright's first papers, is noted as being excluded from the written record, by either the author or the editor, so the main body of the first lecture begins with a review of histology. Gabriel Valentin's (1810–1883) double-bladed knife, introduced in 1837,⁶⁰ plus the increasing availability of improved microscopes with apomorphic lenses from 1830 onwards, led to a surge in interest in the microscopy not only of urine, pioneered by Rayer in Paris,^{50, 61} but also of the kidney itself. The father of renal histopathology, Gottlieb Gluge (1812–1898) of Brussels, is given due credit by Christison, together with George Johnson, John Toynbee and James Simon in London, although several others not mentioned by Christison had also studied renal anatomy under the microscope by then,⁶² especially in Germany. Christison adds a hitherto unrecorded comment that his colleague in Edinburgh, William Gairdner, had made studies of renal histology in his (Christison's) patients in 1848. A search of Gairdner's papers reveals no additional publication on this subject, however.

Christison's section on clinical data includes a comment on urine microscopy which was evidently routine by 1851 in his practice in Edinburgh, as in other centres in the acute phase:

'the urine is at times bloody ... in which the microscope discovers blood-corpuscles ... and fibrinous casts of these tubes' and later 'various combinations of blood-globules, pus globules, oil-globules ... [and] fibrinous tube casts are seen'.⁶²

Then he recommends both heat and nitric acid as tests for coagulable urine, since 'heat alone may separate earthy salts ... but a coagulum which resists both heat and nitric acid can be nothing else than albumin'. He notes that 'pleurisy, pericarditis and peritonitis ... are a frequent cause of death' and also that 'established mainly from observations made in this city by my colleague Dr Simpson',⁵² Bright's disease with convulsions could occur in pregnancy. Commenting on the minority of cases who recover, he notes also that 'there is little doubt that many recover permanently in whom it originates in scarlatina ... [and in] those who are attacked in advanced pregnancy'.

He then gives a section on 'Morbid Anatomy and Pathology' which is the main and most important part of this work. He sets out his conclusions in a series of propositions, which are a synthesis of the work previously published, plus those since made in Edinburgh. He divides the fundamental processes into two: an inflammatory reaction, and an infiltration with 'oil-globules'. The features of the first affect principally:

'epithelial cells lining ... the minute uriniferous tubules ... considered by most physiologists to be the proper secreting tissue of the kidneys [with] a preternatural formation and the detachment or desquamation of these cells, so that by accumulating in the interior they obstruct the tubes and block them up'.

In contrast, 'the malpighian bodies – supposed by some good authorities to secrete rather the watery part of the urine – remain for along time little or not affected ... [but] several microscopical observers have said they have seen the malpighian [sic] bodies oppressed and by congestion within and pressure outside ... at an early period of the morbid process'.

Thus begins a debate which was not fully resolved until the introduction of electron microscopy during the late 1950s. Only in 1879 did Edwin Klebs (1834–1913) introduce the term 'glomerulonephritis' and emphasise involvement of the Malpighian corpuscle as a primary event.⁶³

Christison continues:

'The other morbid affection of the kidneys ... is a peculiar degeneration unconnected with any inflammatory action, and consisting in deposition of oil-globules within the urine-tubes, distending these cells, detaching them from the epithelium wall, distending consequently the tubes by their accumulation, bursting the tubes here and so escaping into the interstitium'.

Christison illustrated, as George Johnson had done five years previously,⁶⁴ these distended tubular cells engorged with fat in the urinary deposit. He noted also 'oleiferous casts' in such cases. He discussed the nomenclature, finding it – as everyone has for almost two centuries – to be unsatisfactory, finally suggesting 'inflammatory' and 'stearotic' desquamation. He notes that during his last period on the wards, he had seen seven patients with Bright's disease in this stage, of whom he judged on clinical and microscopic grounds one to be 'stearotic', four 'pure inflammatory' and two 'mixed'.

He then discussed individual cases, illuminated by drawings taken 'by Dr Sanders, then principal clerk on the wards'. The first person, William McMillan, aged 22, had clear urine on admission for diarrhoea, but when tested after he had become oedematous was found to be

coagulable; he went on to develop ascites, and these changes followed treatment with calomel 'until his mouth became slightly affected', amongst an array of other treatments: leeches, bismuth, opium, hydrocyanic acid, cupping of the loins, Dover's powder, gallic acid, and a blister over the liver which turned troublesome. Not surprisingly to us, he discharged himself home 'to the country', unhappy with his 'lack of progress'. Elizabeth McBirnie, aged 21, swelled five days after confinement, with a full abdomen. The urine was 'scanty, dusky and highly coagulable'; she had microscopic haematuria and epithelial casts without oil globules. She again was battered with diverse therapies, but after a two-week period during which her oedema became worse, affecting even the conjunctivae, she had a diuresis and the urine became free of albumin. Her recovery was attributed to the diaphoresis brought about by Dover's powder. She was considered by Christison to be a purely 'inflammatory' case. A third patient, James Wood, aged 55, was less lucky. He had a necrosed femur with a discharging sinus, recent oedema which became rapidly severe with genital swelling, coagulable urine with broad oily casts, and despite treatment with diuretics (digitalis, squill, tartate of potash) he died. His kidneys displayed 'appearances which Professor Gluge and Dr Johnson themselves could not desire to see surpassed'. The microscopical appearances were illustrated by pictures of two sections taken using Valentin's knife, showing:

'tubes everywhere engorged with oil-globules whilst the malpighian [sic] bodies seemed free of such obstruction' ... the spleen was enlarged and firm ... the left femur presented ... necrosis generally'.

We may easily – but perhaps erroneously – re-interpret these cases in modern terms as mercurial intoxication, puerperal nephrotic syndrome and amyloidosis. Christison does not appear to have been aware of Rokitansky's 1842 description of renal amyloid (Speckniere),^{65, 66} and its first appearance in the English literature was with Wilks' paper, not published until 1856, although hepatic amyloid had been noted by several British authors. Christison was aware that mercury might induce coagulable urine as Wells and Blackall had described half a century before, and mentions this amongst causes, but curiously he does not comment on this here.

Christison was an expert in pharmacy and helped assemble the first national formulary (see below). It seems almost as though he wanted to display the whole of this therapeutic repertoire in his treatment of Bright's disease:

'the main remedies for the fundamental disease are general depletion, topical depletion, local counter-irritation, diuretics and astringents. In acute cases general bloodletting is an essential measure'.⁶⁷

To achieve this somewhat eighteenth-century goal, already challenged by Graves, Todd and others, he used what appears to be a bewildering list of remedies: Dover's powder and warm baths to induce sweating, diuretics if the urine is scanty (digitalis, squill and bitartrate of potash taken together – he had little success with broom tops, nitrous ether, acetate of potash, or oil of juniper), acetate of lead or gallic acid may, he thought, have had some effect on the basic disease. Lead and opium pill was good for the frequent diarrhoea; or a fatty suppository of muriate of morphia. Vomiting – again common – could be treated using bismuth, morphia, hydrocyanic acid, creosote, naphtha, chloroform or, one notes with relief 'little fragments of ice' but 'a blister of the epigastrium has succeeded occasionally'. Thus, despite Christison's considerable innovation in the field of pharmaceuticals, he relies here on a mixture of eighteenth century anti-phlogistic remedies and newer, early nineteenth century chemical agents. Bleeding and cupping for general and local 'depletion' of inflammatory diseases are still to the fore, as was the case with a patient now described as a 'robust female-servant of 38' in whom both were used as primary treatment of an acute dropsy with coagulable urine; it is interesting that in the year 1846 when she presented for investigation and treatment, Christison was not yet microscoping the urine routinely, although this had begun in 1839 in France, and by 1842 was being done in Germany,⁶¹ as well as by Golding Bird at Guy's Hospital in London from 1844. This patient lost her 'strongly-coagulable' urine, but only after several months' illness, and four years later was in good health and had delivered a child without problems.

Christison's patients seem to have done much better than Bright's, even when they had a comparable clinical presentation with dropsy. Three further cases are described in the 1851 paper with long term follow-up and recovery. One was a doctor with haematuria and coagulable urine, but another had uraemic foetor when he presented, but nevertheless survived and remained well.

From this time until his retirement from his chair in *Materia Medica* in 1877, Christison appears to have published no more work on the kidney. No case books have survived, his autobiography (written in 1871) stops in 1831, his journal is lost and so we cannot tell whether he went on seeing and treating such patients during this period. It would be odd if he had not done so, given his great interest in the subject and his continued large clinical practice, but it seems that his major interests in these years lay elsewhere. During these 16 years, some modest advances were made in the field of renal disease, especially in the field of histology, but by 1877, the clinical and histological view of Bright's disease did not differ much from that outlined in his writings of 1829–1851, (exemplified by George Johnson's major monograph of 1873⁶⁸). Around at that time, however, the momentous advances in description and understanding of

hypertension were just entering clinical practice, too late for Christison to have exploited them. The clinical thermometer, introduced in 1862 by William Gull would certainly have intrigued him with his interest in fevers, and the sphygmograph would surely have had an impact; but one guesses that he might have opposed the idea of Akbar Mahomed's 'prealbuminuric', Bright's disease of the 1870s.

It would be interesting to know what Bright thought of Christison's work, apart from his brief comment in the 1836 papers in *Guy's Hospital Reports*.³⁸ However, the evidence that they were in contact is scanty and late. On 31 January 1850, he wrote to Bright about the illness and death of Bright's old Edinburgh friend Lord Jeffrey¹¹ [at p. 294], and a letter survives from Sir Benjamin Brodie to Bright, inviting him to dinner together with Christison, probably some time in the 1840s⁶⁹ (the year is not given); however Berry and Mackenzie⁶⁹ state that 'they ... became close friends', but no evidence is presented for this statement.

CHRISTISON'S WORK IN OTHER AREAS OF MEDICINE

Only the briefest summary of a vast and varied output can be given here, in chemistry, jurisprudence, pharmacology, general medicine, meteorology and botany, with occasional forays into medical education, actuarial matters and geology.

His first paper in 1822, as befitted a new professor of Medical Jurisprudence, dealt with poisoning from oxalate,¹⁹ and his hugely important book *Treatise on poisoning*³⁵ whose first edition appeared in 1829, and ran to four editions by 1845, is perhaps his most lasting monument. He continued to publish papers in toxicology and pharmacology for almost 60 years (1823–1882). He commonly tested out new and unknown substances on himself, and in 1876 (just before he turned 80!) assessed the effect of the newly discovered South American coca (or cuca as he called it) leaf on fatigue and hunger, by running up and down Ben Vorlich with and without the drug, finding it to be a powerful suppressant of both appetite and fatigue.⁷⁰ A less happy episode was when, in 1855, he took what turned out to be a near-fatal dose of the West African Calabar bean^{3,71}, and survived complete paralysis only by rapidly inducing vomiting by drinking his shaving water! The book, *A dispensatory or commentary on the pharmacopoeias of Great Britain*, appeared in 1842,⁶⁷ with a second edition in 1848, and this later formed the core of the first *British Pharmacopoeia* of 1864, on whose committee he served. He published many papers on medical evidence, and set the first standards for procedure in forensic science.

In 1860, he suggested, in response to an enquiry from a Leith whaling captain, that whales might be caught using a hydrocyanic acid capsule on the harpoon.⁷² Despite

successful trials, this was not adopted because the crews, having seen the effects of the poison on something as large as a whale, were understandably reluctant to dissect or even touch its massive body. At that time, whaling was still a major industry, practiced, mainly from ports on the East Coast of Scotland, from a need for lamp oil. Christison, with his work on the nature of paraffins,¹¹ himself helped to make whale oil obsolete.

He wrote a number of papers on medical topics besides those on renal disease,¹¹ including diabetes, alcohol, scurvy (which he erroneously attributed to a deficiency of nitrogenous substances), cholera (a new disease in the 1830s in the UK) and especially on fevers, having worked in the fever hospital in the early 1820s and subsequently suffered lifelong attacks himself. He kept meticulous medical records of these attacks and their treatment, whose source is difficult to identify today, although brucellosis is a plausible suggestion. He had also studied the chemical interaction of blood with oxygen in the air, in 1831,⁴⁶ but took these important observations no further.

As medical officer to the Standard Life Assurance Company, he kept a huge record of mortality over a number of decades, and although he published some papers on this topic in the 1850s, the final analysis was incomplete at his death and was published posthumously by his medical sons in 1882.⁷³ Finally, he published 15 papers on botanical subjects,¹¹ some of his last observations, published in 1882 when he was confined by illness to his house, being on the growth of trees and their measurement.

WHY WAS CHRISTISON'S WORK ON RENAL DISEASES SO NEGLECTED ?

One of the more surprising aspects of Christison's work is that despite his immense importance in medicine in Scotland and Edinburgh, there has been no evaluation of his role and work from his native country or city since his death. Whether an individual, and his or her work, be remembered and cited or not depends on many factors besides its intrinsic quality, interest and originality. Moreover, many who are quoted frequently and are well-known during and just after their lives then sink into oblivion. Longevity usually helps, and undoubtedly early deaths and lack of disciples helped obscure the reputations of (for example) Akbar Mahomed⁷⁴ and Senhouse Kirkes⁷⁵ who both practised during Christison's lifetime. However, survival to a ripe old age does not seem to have aided a prolonged appreciation of Christison's renal work. Despite his huge innovation in the techniques of forensic chemistry and poisoning,³⁵ no test or disease was named after him. In renal medicine, neglect of his important contribution to the study of uraemia and particularly renal anaemia is particularly puzzling today.

Christison's own enormous output in other fields to some extent 'buried' his work on renal disease. Almost all the accounts of his life (for example in the *Dictionary of National Biography*)⁴ as well as his obituary notices, either do not mention his work on renal disease at all, or do so only as a brief note or even footnote. He was known to the world in the main for his work on forensic medicine, poisoning, jurisprudence and pharmacology. Second, so far as we know he worked actively on renal disease for only a rather limited period of his career, from 1828 to 1851. He did not, like Sir George Johnson (1818–1896) in London, continue to publish into the 1870s and beyond on this subject.⁶⁸ A third factor was that, although he was famous in Scotland, he remained in Edinburgh all his working life, and the Edinburgh school undoubtedly continued to decline in reputation during his lifetime. It was already past its peak as an unparalleled world centre of learning by 1820, and certainly the medical student roll fell during the 1820s, and especially the 1830s, as new medical schools opened in London which would accept Catholics, Jews and dissenters (King's College, University College). This also happened in Ireland; these groups had formed a good proportion of the large medical student body in Edinburgh in the 1820s. As a result, the money available both to the University and those working in it, as Christison noted ruefully, fell; and he himself had to take up private practice, despite his wish to remain a full-time academic.

Finally, he travelled not at all outside the UK after his time in Paris, and appears not to have travelled much within Britain either. It is easy to forget that when he went first to London in 1821,¹¹ it was by fishing smack from Leith to St Katharine's Dock by the Tower, and the journey of 400 miles took nine days!⁷⁶ Then, when later he returned from Paris to London and learned of the terminal illness of his father in London, it took three-and-a-half days continuous journeying in express coaches to get to Edinburgh just in time to witness his passing. Few intellectuals of the period travelled far, using the pen and the scientific journal as their major point of contact. By the time he died, however, the railways had made almost all parts of the country accessible within a day at most, the wireless telegraph had been introduced, and the telephone was in its infancy. His brief Presidency of the British Medical Association in the 1870s must have meant trips to London, perhaps by train, and the generation of a wider circle of acquaintances. It is worth noting that despite his enormous reputation and influence in Scotland, and the knowledge on the continent of Europe of his work, no notice of his death was carried by the *London Times*,⁷⁷ suggesting that he was little known in London circles, at least at that time.

However, apart from all this, the major factor in neglect of Christison's work may have been the publication in 1840, the year after his own book on renal disease, of Pierre Rayer's *Traité des Maladies du Rein*.²⁶ This is despite

the fact that Rayer (1793–1862) frequently and admiringly quoted from Christison's work in his book and his lectures. Christison himself remarks rather ruefully in 1871 in his *Autobiography*, in the short section dealing with his renal work:¹¹

'It is odd that English writers in more recent times seem disposed to quoting the French enquiry for facts, which, with scarcely any exception, were previously established in my investigation. A professor seems doomed to see his oral precepts occasionally appear first in print under the authority of others, and he can scarcely reclaim them. But when he does publish, he may reasonably expect that what he enunciates shall not be assigned to others who merely repeat and confirm his observations. A refinement on this loose and careless procedure is when an author himself repeats the *ipsissima facta* of a prior inquiry, and quotes his own facts only as authority for his conclusions, of which trick in authorcraft I could quote an instance, were I maliciously inclined'.

Even though his close contemporaries Sir George Johnson and Sir William Gull (1816–1890)⁷⁹ do quote Christison, and his works must surely have been in the forefront of the mind of the young George Johnson when he published his work on fatty nephrotic kidneys in 1846⁶⁴ – a work in turn quoted by Christison in 1851⁵⁵ – his ideas seemingly had little currency in the journals of the day. A final important factor is that Christison, unlike both Bright and Rayer, rather surprisingly left behind him no body of students carrying on his work at the Royal Infirmary, perpetuating his memory and quoting his work.

Finally, his protagonists today admit that the later nineteenth and twentieth century worlds seemed to be not much impressed with the work of Christison on renal disease undertaken during the 1830s and 1840s. Today, we appreciate more his pioneering role, but must recognise that he apparently failed in making his contemporaries and successors move the study of renal diseases into new directions, or when he did, his own role in this was poorly recognised by the medical public. Perhaps this work will do something to redress this enduring imbalance.

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REFERENCES

- Cameron JS, Hicks JA. Sir Robert Christison (1797–1882). A neglected founder of nephrology. *J Nephrol* 2003; **16**:776–83.
- Watts EO. Poison, proof and a professor: Sir Robert Christison's work in medical jurisprudence in Edinburgh, 1822–55. BSc dissertation. Wellcome Institute for the History of Medicine; 1994.
- Dopson L. Pharmacology by ordeal. How a self-test of the Calabar bean one hundred years ago nearly ended the career of Sir Robert Christison. *Chem Drug* 1955; **163**:348 (see also ref. 46 below).
- Anon. GTB Robert Christison (Sir Robert, MD). *Dictionary of National Biography* Vol 2. London: Smith Elder; 1904; 290–2.
- Bright R. *Reports of medical cases* Vol I. London: Longman, Orme, Rees; 1827.
- Anon. TJK and JB (Brown J). Sir Robert Christison. *Edin Med Surg J* 1882; **27**:852–64.
- Anon. Obituary of Sir Robert Christison. *Lancet* 1882; **i**:193.
- Anon. Obituary. Sir Robert Christison. *BMJ* 1882; **i**:214–5.
- Sir Robert Christison. *Scotsman*. 28 January 1882.
- Anon. Report of Proceedings at the public dinner in honour of Sir Robert Christison, Bart. MD, DC, President of the Royal Society of Edinburgh, etc, etc, on Friday February 23rd 1872, being the Fiftieth anniversary of his induction as a professor in the University of Edinburgh. Edinburgh: printed for private circulation; 1872 (copies in library of the Royal College of Physicians, Edinburgh, and in the care of Brigadier Nicolas Ridley).
- Christison R. *The life of Sir Robert Christison, Bart.* Edited by his sons. In two volumes. Vol. I *Autobiography*; Vol. II *Memoirs*. Edinburgh: Blackwood; 1885. Volume I contains an autobiographical account of his life up to 1831, and volume II, appreciations by colleagues, and a more or less complete bibliography of his writings.
- Comrie JD. *History of Scottish medicine*, 2 vols. London: Balliere, Tindall and Cox; 1932.
- Buchan J. *Capital of the mind: how Edinburgh changed the world*. Edinburgh: John Murray; 2003.
- Herman A. *The Scottish Enlightenment. The Scots invention of the modern world*. London: Fourth Estate; 2003. For a more popular account, see also: Herman A. *How the Scots invented the modern world. The true story of how Western Europe's poorest nation created our world and everything in it*. New York: Three Rivers Press; 2001.
- Welsh I. *Flower of Scotland* (a review of Buchan J. *Capital of the mind: how Edinburgh changed the world*. Edinburgh: John Murray; 2003). *Guardian* (review section), 23 August 2003.
- Christison R. *De Febrae Continua quae nuper hac urbe epidemica fuit; et exemplis, apud nosocomium regium tactatis, deducta*. Edinburgh: J Pillians and Son; 1819. Christison included some of these observations and data in his later review of the subject: Christison R. On the changes in the constitution of fevers and inflammations in Edinburgh during the past forty years. Part I. *Edin Med J* 1858; **iii**:577–95; Part II, *ibid.* **iv**:38–48.
- Bright P. *Dr Richard Bright*. London: Bodley Head; 1983. The Bright archive of family papers is today held in the University of Melbourne library, courtesy of Mr Peter Bright.
- Richet G. The chemistry of urinary stones around 1800: a first in clinical chemistry. *Kidney Int* 1995; **48**:876–86.
- Christison R, Coindet P. An experimental inquiry on poisoning by oxalic acid. *Edin Med Surg J* 1823; **19**:163–9, 323–37 (also published in Magendie's *Journal de Physiologie* 1823; 274–300).
- College of Physicians Library, Edinburgh. File IYY: Letter from Christison to Dr Poole of East Broughton Place: under the signature is 'written in Dr Traill's indelible ink which no chemical agent whatever will remove ...'
- The subsequent history of the family can be summarised: Alexander's son Robert Alexander (1892–1945) became 3rd baronet, and in turn, Alexander's second son, General Sir (Alexander Frank) Philip (1893–1993) the 4th baronet (Anon.: General Sir AF Philip Christison. Kemp T, Dalkeith 1974, for the Burma Star Association – I am grateful to Brigadier Nicholas Ridley, Christison's great-great grandson, for the loan of this booklet). Although the latter studied medicine, he never qualified fully as a result of the First World War. He served with distinction in the Cameron highlanders, and was wounded and then decorated at Loos in 1915. Later in the Second World War as a Brigadier-General, he played a notable role in the Burma campaign of 1943–44. He outdid even his grandfather as a man of many parts: scholar, linguist (including Gaelic), singer musician, athlete, soldier, leader and diplomat, he lived exactly a century; there are many resemblances between grandfather and grandson. General Sir Alexander's only son, John Anthony Alexander Christison (1918–42) was killed in action elsewhere in Burma without issue, so the title became dormant, as a baronetcy is inherited only through the male line. Three sisters survived him: Heather, who was the eldest (1916–1975), Alison (b. 1924) who now lives in Australia, and Fiona (b. 1932).
- Todd M. *The life of Sophia Jex-Blake*. London: Macmillan; 1918.
- It is of course possible that Christison was telling the truth, as he had access to the Queen on her visits to Scotland through his position as physician-in-ordinary, and was made a baronet only the following year; even so, quoting the Queen in a public University meeting did not display his usual caution – perhaps because he felt so strongly about the topic.
- Personal communication to the author from Mrs Alison James, great-grand-daughter of Sir Robert (2003).
- Pierre Louis' great work (Louis PCA. *Recherches sur les effets de la saignée dans quelques maladies inflammatoires, et sur l'action de l'émétique et des vésicatoires dans la pneumonie*. Paris: JB Ballière) was published in Paris in 1835, but the use of bleeding persisted in some areas as far as the beginning of the twentieth century. It is curious that, with his contempt for Broussais, the great blood-letting and leech user, Christison still persisted with these treatments for so long.
- Anon. (Christison R.) Review of Bright's Reports of medical cases etc. *Edin Med Surg J* 1828; **96**:107–116; *ibid.* **97**:372–81.
- Rayer P. *Traité des maladies des reins*. Paris: JB Ballière; 1840. 3 Vols and Atlas. Vol II, 543 (reprinted in facsimile without the atlas by Elibron Classics, USA, 2005 (no town of publication given)).
- Christison R. Observations on the variety of dropsy which depends upon diseased kidney. *Edin Med Surg J* 1829; **32**:262–91. It is worth noting that 'Bright's disease' appears to be the first ever eponymous disease, certainly employed from 1834 onwards, especially in France (e.g. Constant: see ref.30). Many have remarked that a name attached to a disease indicates with near certainty that the person concerned was not the first to describe it, but (in some cases) the one who made it known, and the life of the medical eponym is only now drawing to its inglorious close. In Bright's case, this criticism is scarcely justified, since elegantly he achieved both.
- Statistics are available for deaths from renal disease in the UK from 1840 onwards, and although their value is diminished by serial changes in definitions, the changes are so dramatic as to remain useful. From 1840 until 1900, the death rate remained relatively stable, but from about 1900 to 1970, deaths from 'nephritis' declined from over 600million per year to 134 million

- per year (from about 70,000 to approximately 7,000 per year). Equally, in developing countries today, data for admission diagnosis of a nephrotic syndrome suggest an incidence up to 100 times higher than the 0.04 % in Western Europe and the US. Britain in 1840 was in a similar state to third world countries today, with life expectancy at birth of only 40 years. What drove, and still drives, these differences is open to speculation, but control of infections and ambient nephrotoxins such as lead, improved nutrition and immunity have all probably played a role. As a marker, amyloid secondary to infection shows similar patterns.
- 30 Only in 1833 were children whose dropsy remitted described, first by Dr T Constant in Paris (Maladie de Bright. *Gaz Méd Paris* 1834; **1**:105–7) and then by others in Paris. For details, see Cameron JS. The nephrotic syndrome: a historical review. In: Cameron JS, Glassock RJ. *The nephrotic syndrome*. New York: Marcel Dekker; 1988;3–56.
 - 31 Wells WC. Observations on the dropsy which succeeds scarlet fever. *Trans Soc Improve Med Chir Knowl* 1812; **3**:167–86 (paper given in 1806).
 - 32 At that time, only agents of vegetable origin such as squill, plus mercury in the form of calomel, were available as diuretics and were widely used. See Aliotta G, de Santo NG, Touwaide A. The diuretic use of scilla from Dioscorides to the end of the 18th century. *J Nephrol* 2004; **17**:342–7.
 - 33 Christison R. On the cause of the milky and whey-like appearances sometimes observed in the blood. *Edin Med Surg J* 1830; **33**:274–80.
 - 34 Hewson W. An experimental enquiry into the properties of the blood. With remarks on some of its morbid appearances, etc, etc. London: T Cadell; 1771; 141, 148, 149.
 - 35 Christison R. *A treatise on poisons in relation to medical jurisprudence, physiology, and the practice of physic*. Edinburgh: A Black; 1829 (subsequent editions 1832, 1835, and 1845).
 - 36 Christison R. *On granular degeneration of the kidneys [sic] and its connexion [sic] with dropsy, inflammations and other diseases*. Edinburgh: Adam and Charles Black; 1839.
 - 37 Mayer J, Rokitsansky C. *Ueber die Granular-Entartung der Nieren und ihre Verbindung mit Wassersucht, Entzündungen und anderen Krankheiten. Aus dem Englischen Uebersetzt von Johann Mayer, mit Anmerkungen versehen von Carl Rokitsansky*. Wien: C Gerold; 1841.
 - 38 Bright R. Cases and observations illustrative of renal disease accompanied by the secretion of albuminous urine. *Guy's Hosp Rep* 1836; **1**:338–79.
 - 39 Hamilton G. On the epidemic scarlatina and dropsical affection which prevailed in Edinburgh during the autumn of 1831. *Edin Med Surg J* 1833; **39**:140–64.
 - 40 Gregory JC. On the diseased states of the kidney connected in life with albuminous urine. Part I. *Edin Med Surg J* 1831; **36**:315–63. Part II *ibid*. 1832; **37**:54–94.
 - 41 The word 'uremia', derived from the 'urée' of Vauquelin and Foucroy was coined by Pierre Piorry (1794–1879) in 1847. (Piorry P. *Traité de Médecine pratique*, Vol II, Chapter XII, nos 4430–40). Would that he had rather named it 'urinemia' to emphasise that urea was not the only substance retained!
 - 42 Almost certainly Christison got the seeds of these ideas from his stay in, and continuing contact with, Paris in particular the lectures of Vauquelin. See: Fourcroy AF, Vauquelin N. Mémoire pour servir à l'histoire naturelle chimique et médicale de l'urine humaine. *Mémoires de l'Institut* 1797; **2**:431; Fourcroy AF, Vauquelin N. Premier mémoire pour servir à l'histoire naturelle, chimique et médicale, de l'urine humaine contenant quelques faits nouveaux sur son analyse et son altérations spontanée. *Ann Chimie* 1799; **31**: 48–71; (see also: 1799; **32**:150–5); Vauquelin suggested urea might be toxic from its retention (Fourcroy AF, Vauquelin N. Nouvelles expériences sur l'urée. *Annales du Museum d'Histoire Naturelle* 1808; **11**:226), but in: Ségalas d'Etchepare, Vauquelin N. Sur de nouvelles expériences relatives aux propriétés médicamenteuses de l'urée. Lettre à M Magendie. *Journal de Physiologie* 1821–2; **2**: 354, urea injection was shown to lead only to a diuresis. Nevertheless, they must have credit for first suggesting that retention of urinary solutes might be toxic, the idea which Christison developed.
 - 43 Prévost JL, Dumas JB. Examin du sang et de son action dans les divers phénomènes de la vie. *Annales de Chimie et Physique*, Paris 1823; **23**:90–104 (report of meeting of 15th November 1821 of the Société de Physiologie et d'Histoire Naturelle de Genève). See also: Mani N. La découverte de l'urémie expérimentale par Jean-Louis Prévost et Jean-Baptiste Dumas. Genève; 1821. *Méd Hyg* 1963; **21**:408–9.
 - 44 Cameron JS. Towards the millennium: a history of renal anaemia and the optimal use of epoetin. *Nephrol Dialysis Transplant* 1999 [suppl 2]; 10–21.
 - 45 Owen Rees G. Observations on the blood with reference to its condition in Morbus Bright. *Guy's Hosp Rep* 1843; **8**:317–30.
 - 46 Christison R. An inquiry on some disputed points in the chemical physiology of the blood and respiration. On the mutual action of blood and atmospheric air. *Edin Med Surg J* 1831; **94**–103 (published also in German in *Froriep Notizen* 1831 col 81–88).
 - 47 Osler notes that in chronic renal failure 'anaemia is more or less regularly present' (Canadian *Lancet* 1881; **13**:353–9) and Sir Nestor Tirard (a pupil of George Johnson's) in 1899 *passim* (Tirard N. *Albuminuria and Bright's disease*. London: Smith Elder; 1899; 148, 153, 205, 212, 219, 327). Otherwise, little or no mention is made of anaemia even by the careful observer Samuel Wilks in his later articles in the 1880s and 1890s. See also: ref. 44, and especially Brown GE, Roth GM. The anemia of chronic nephritis. *Arch Intern Med* 1922; **30**:817–40. Brown GE, Roth GM. Prognostic value of anemia in chronic glomerulonephritis. *JAMA* 1923; **81**:1948–50; Parsons L, Ekola-Stromberg M. Anemia in azotemia. *Am J Med Sci* 1933; **185**:181–90.
 - 48 Christison R. Properties of healthy urine; Functional disease of the kidneys; Gravel; Urinary calculus; Diabetes; Suppression of urine; Errors in the position and conformation of the kidneys; hypertrophy of the kidneys; Inflammation of the kidneys; Granular degeneration of the kidneys; Other chronic diseases of the kidneys; Diseases of the bladder and urethra. In: *A system of practical medicine comprised in a series of original dissertations*. Arranged and edited by Tweedie A. London: Whittaker; 1840; Vol 4; 215–99.
 - 49 Alexander Tweedie (1794–1884) was a contemporary of Christison's at Edinburgh as a student, and had been taught by Christison's father. In 1822 he moved from Edinburgh to London, to work in the London Fever Hospital. In 1831–1835, he brought out the multi-author *Cyclopaedia of Practical Medicine*, to which John Bostock contributed a section on Physiology, followed by his *Library of Practical Medicine* in 1840. These two works were the first multi-author textbooks of clinical medicine in English.
 - 50 Richet G. Daguerre, Donné et Foucault, trois franc-tireurs créent la microphotographie. *Hist Méd Sci* 1997; **13**:45–8.
 - 51 Abercrombie J. Observations on ischuria renalis. *Edin Med Surg J* 1821; **10**:210–22. This apparently is the earliest full description of intrinsic acute renal failure.
 - 52 Cumin W. Cases of severe burns, with dissection and remarks. *Edin Med Surg J* 1823; **19**:337–44. Cumin notes that such patients (his were mainly children) might develop anuria.
 - 53 John Charles Lever (1811–1859) of Guy's Hospital is usually credited alone with the first description of albuminuria during eclampsia in 1843 (*Guy's Hosp Rep* 1843; (2nd series) **1**: 495–517), but almost simultaneously James Simpson in Edinburgh noted it as well (*Edin Monthly J Med Sci* 1843; **11**:1015–22), as Christison says. One should also note that Rayer [see ref 20 above] described albuminuria during pregnancy, but did not associate it with an eclamptic syndrome.
 - 54 Osler W. *The principles and practice of Medicine*. New York: Appleton; 1909; 741–2. For more on the history of acute renal failure, see Eknayan G. Emergence of the concept of acute renal failure. *Am J Nephrol* 2001; **22**:225–30, although a full treatment is

- still awaited on this complex and interesting subject.
- 55 Christison R. Bright's disease of the kidneys (delivered 11 and 18 March 1851). *Edin Monthly J Med Sci* 1851; **12**:551–73.
 - 56 Johnson G. *On the diseases of the kidney, with their pathology diagnosis and treatment with an introductory chapter on the anatomy and physiology of the kidney*. London: John W Parker; 1852.
 - 57 Wilks S. Cases of Bright's disease with remarks. *Guy's Hosp Rep* 1853; new series, **9**:232–315.
 - 58 Wilks S. Cases of lardaceous disease, and some allied affections, with remarks. *Guy's Hosp Rep* 1856; 3rd series; **2**:103–32. In this paper, Wilks notes two cases of what he called 'simple amyloid' without any preceding infection – 30 years before the usually credited description of primary amyloidosis by Carl Wild in 1886.
 - 59 Frerichs T. *Die Bright'sche Nierenkrankheit und deren behandlung*. Braunschweig:Vieweg; 1859.
 - 60 Valentin G. *Repertorium für Anatomie und Pathologie*. Bern St Gall: Huber; 1837; **11**(2):290–1.
 - 61 Fogazzi GB, Cameron JS. Urinary microscopy from the seventeenth century to the present day. *Kidney Int* 1996; **50**:1058–68.
 - 62 The first microscopical studies of the diseased kidneys were published by Valentin (see ref 35 above) in 1837, followed by those of Gluge (1839), Hecht (1839), Becquerel (1841), Bowman (1842) – who studied diseased kidneys as well as normal ones – Henle (1842), Quain (1843), Canstatt (1844), Eichholz 1844–5, Johnson (1846: see ref 40 above), Simon 1846, as well as Toynbee (1846) – who however made no sections, but used microdissection. The limitations of thick sections, and absence of tissue staining until the mid 1850s, held up progress in the area of histology for two decades. A history of early attempts to study renal histology has yet to be written.
 - 63 Klebs TAE. *Handbuch der pathologische Anatomie*. Berlin: August Hirschwald; 1870:644–8.
 - 64 Johnson G. On the minute anatomy and pathology of the Bright's disease of the kidney, and on the relation of the renal disease to those diseases of the liver, heart and arteries with which it is commonly associated. *Med Chir Trans* 1846; **29**:1–24.
 - 65 von Rokitsansky K. *Handbuch der speciellen pathologischen Anatomie*. Vienna: Braumiller & Seidel; 1842–46, Vol II; 417–24.
 - 66 It is strange that Christison was unaware of amyloidosis, which was so much more common in the nineteenth century in Europe than today, given the heavy load of chronic infection at all levels of the population, especially the poor. However Wilks' excellent account (see ref 33 above) was five years in the future.
 - 67 Christison R. *A dispensatory or commentary on the pharmacopoeias of Great Britain, comprising the natural history, description, chemistry pharmacy, actions, uses, and doses of the materia medica*. Edinburgh: 1842 (second edition 1848).
 - 68 Johnson G. Lectures on the pathology, diagnosis and treatment of Bright's disease. *BMJ*. 1873; **i**:1–3, 27–28, 81–83, 109–111, 161–164, 191–194, 275–277, 303–305, 527–529, 579–580, 605, 606, 696–697, 725–726. This series of articles was published separately as a monograph: Johnson G. *Lectures on Bright's disease etc*. London: WT Elder; 1873.
 - 69 Berry DJ, Mackenzie C. *Richard Bright 1789–1858*. London: Royal Society of Medicine, Eponomists in Medicine; 1992:189 and 270.
 - 70 Christison R. Observations of the effect of *cuca* or *coca*, with supplement. *BMJ* 1876; **i**:527–31.
 - 71 Christison R. On the properties of the ordeal bean of Old Calabar, Western Africa. *Edin Monthly J Med Sci* 1855; **20**:287–94. The Calabar, 'ordeal bean' or *esere* created great interest in the 1850s. The beans of this secret plant, later named '*Physostigma venenosum*' were given to accused prisoners to prove guilt or innocence in parts of Nigeria. They contained an alkaloid, physostigmine named after the plant, which potentiates the activity of acetylcholine, inducing bradycardia and eventually cardiac arrest. Toxicity varied with the dose, and the outcome from recovery to death could in fact be determined in advance by how mature the beans were and how much was offered to the prisoner by the administering judge. More recently, similar compounds have been used as antagonists including the toxic 'nerve gases' such as Sarin (see also ref 2 above, and Anon. Histories: The killer bean of old Calabar. *New Scientist* 2003; **178**: 48–9).
 - 72 Christison R. On the capture of whales by means of poison. *Proc Roy Soc Edin* 1860; **iv**:270–1.
 - 73 R Christison, A Christison, D Christison. *Report on medical statistics of the Standard Life Insurance Company*. 1845–1880; Home department: Standard Life Insurance Company; 1884.
 - 74 Cameron JS, Hicks JA. Frederick Akbar Mahomed and his role in the discovery of essential hypertension at Guy's Hospital. *Kidney Int* 1996; **49**:1488–1506.
 - 75 Cameron JS, Hicks JA. High blood pressure and the kidney: the forgotten contribution of William Senhouse Kirkes. *Kidney Int* 2000; **57**:724–34.
 - 76 A further indication of how different the world Christison inhabited from ours, is his mention that, on coming up the Thames, the remains of publicly executed pirates were to be seen, hung in chains by the river as a deterrent.
 - 77 Nor, more surprisingly was there any notice in the *Glasgow Herald!* This may be the result of traditional inter-city jealousy.
 - 78 To contemporary eyes there appears to be interstitial expansion and glomerular alteration in this illustration; however, the material was probably examined unfixed and no illustrations of comparable normal kidneys are available, so this impression may be false. At best, the Valentin knife must have produced 'sections' of 100 microns thick or more.
 - 79 It is interesting to note that Christison, Johnson and Gull all received their knighthoods or baronetcies for personal services to the sovereign and her family, rather than purely for eminence in clinical medicine. The master himself, Richard Bright, died plain Dr Bright in 1858 – although he also served the Royal Family. As a dissenter, he lay somewhat outside the establishment of the day, and, of course, may have turned down an honour, which would have been in line with his character.