Research Paper

Wars, disasters and kidneys

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This paper summarizes the impact that wars had on the history of nephrology, both worldwide and in the Ghent Medical Faculty notably on the definition, research and clinical aspects of acute kidney injury. The paper briefly describes the role of 'trench nephritis' as observed both during World War I and II, supporting the hypothesis that many of the clinical cases could have been due to Hantavirus nephropathy. The lessons learned from the experience with crush syndrome first observed in World War II and subsequently investigated over many decades form the basis for the creation of the Renal Disaster Relief Task Force of the International Society of Nephrology. Over the last 15 years, this Task Force has successfully intervened both in the prevention and management of crush syndrome in numerous disaster situations like major earthquakes.

Keywords: acute kidney injury, trench nephritis, Hantaan virus, crush syndrome, Norbert Goormaghtigh

Although the term 'nephrology' was introduced only in 1960, at the occasion of the first World Congress of Nephrology in Evian (France), kidney diseases and, more in particular, acute renal failure (ARF), currently named acute kidney injury (AKI), must have afflicted humans from times immemorial, because of wars, trauma, and infections. As elegantly written by Eknoyan,[1] AKI, as with other diseases, predates medicine and its historical roots are buried in the misty beginnings of priestly medicine, which emerged as illnesses to be separated from other kinds of suffering.[1]

For all the destruction and chaos it wreaks, war also spurs advances in most medical domains and medical services have been associated with the military since the days of Ancient Greece. This relationship declined in the Middle Ages, but after a radical reorganization of medicine during the 1700s the links between the two grew stronger with each passing year.

There is much debate about how much influence war and medicine have had on each other, but in many cases war moves medical practices and innovation forward, or refocuses research into specific conditions. For obvious reasons, this happens most frequently in acute trauma medicine. Historically, trauma surgery, emergency care and infectious disease treatments leap the furthest ahead.

Some critics however, including British sociologist Roger Cooter, have made the argument that, 'for the most part, war has accelerated research into old medical problems of military importance, the bulk of which are highly specific to that context and of little value outside it.' During most modern wars, Cooter says, civilians' health needs have taken a back seat to the medical needs of the military.[2]

Already Hippokrates (460–370 BC) is quoted as saying that 'he who would become a surgeon should join an army and follow it' and second-century Greek physician Galen (AD 129 – c. 200/c. 216), court physician to Marcus Aurelius in Rome honed his skills not only in the sanctuary of Aesclepius, god of healing, but also as physician to the gladiators of Pergamon. He performed bold operations and gained an understanding of the human anatomy that was unsurpassed well into the second millennium.

Blood loss has always been the biggest killer in war. A big turning point came, in 1537, when a French barber called Ambroise Paré (1510–1590) was sent as a surgeon to the Siege of Turin. He was so horrified by what he saw, that he came up with an incredibly simple alternative, the blood vessel ligature. He would identify bleeding arteries, clamp them, and then tie the ends with silk threads. Prevention of blood loss through the use of tourniquets and ligatures, as well as amputation to prevent death by gangrene, was used as early as Roman and Arab times but the skills had been lost and it took time for Paré's work to change people's attitudes. A century later surgeons were still using boiling oil and cauterizing for bleeding wounds.

The idea of using specialized transport to evacuate the wounded from the battlefield came 200 years ago by Dominique Jean Larrey (1766–1842), surgeon-in-chief to Napoleon's armies who noticed that the French artillery were able to move cannons at high

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speed around the battlefield with horse-drawn carriages. He wondered if similar vehicles could be used to move casualties. At that time many soldiers were left to die where they fell and it could take 24 hours or more to get a wounded man to a field hospital. Larrey created what he called, 'flying ambulances'. These were horse-drawn carts which could carry the wounded in some comfort and at high speed to the waiting surgeons. The Duke of Wellington was so impressed he ordered his men not to fire at them.

Larrey also improved the mobility of the field hospitals and organized a system of triage, under which the wounded were treated according to their need for treatment and not because they were of noble birth.

When recorded medicine began in antiquity, it was the abnormal symptoms and external signs with which patients presented that formed the framework of the diagnostic taxonomy of what was then considered a disease.

Related to diseases of the kidney, dominant among those presenting symptoms were pain and changes in urine excretion and this often translated into the pain of urolithiasis and either increased or suppressed urine excretion.[3] Over time, increased urine output (polyuria) was termed diabetes in the 2nd century BC and emerged as a diagnostic entity by the 2nd century.[4] By contrast, that of suppressed urine output (oliguria) went unnamed and linked to the obstruction of urolithiasis that usually presented with pain. Nevertheless, by the time medicine matured and for the centuries that followed, suppressed urine output also came to be considered an ominous prognostic sign in several other diseases.[1,5]

In the 17th century the term 'ischuria', indicating either the suppression or retention of urine, was introduced. And, following the establishment of anatomical dissection, which allowed the early description of diseased organs, Morgagni (1682–1772), the acknowledged father of pathological anatomy, first proposed a classification of ischuria into four categories: *ischuria vesicalis, ischuria ureterica, ischuria urethralis* and *ischuria renalis*.[6] A fascinating case of acute renal ischuria was for example described by George Fife in 1840.[7]

As pointed out by Eknoyan,[8] the 'kidney infection' of Galen, the 'ischuria renalis' of Morgagni, and the subsequent use of 'nephritis' (a term introduced in the 16th century to mean 'inflammation of the kidneys') are the inclusive but wastebasket terms, often used interchangeably, that provided the framework within which diseases of the kidney in general, and those of ARF and AKI in particular, were grouped, described, and studied well into the 19th century.

William Heberden (1710–1801) in his *Commentaries on the History and Cure of Diseases* (1802) introduced a chapter on 'Ischuria', as 'a total suppression of urine has lasted seven days, and yet the patient has recovered. It has been fatal as early as the fourth day. However, in general those patients, who could not be cured, have sunk under the malady on the sixth or seventh day'.[9]

Richard Bright (1789–1858) described his eponymous disease of albuminuric end-stage kidneys in 1827, which was soon followed by its classification into acute and chronic forms of Bright's disease.[1] By the turn of the 20th century, acute Bright's disease became the taxonomic classification under which ARF was generally classified and discussed. In the late editions of his textbook *Principles and Practice of Medicine*, which appeared in the early years of this century, Osler stated that acute Bright's disease could be produced by various poisons, infections, burns, traumas, major surgery and pregnancy.[10] Francis Delafield (1841–1915) in an 1888 report titled 'Acute Bright's Disease' wherein he provides what can be considered an accurate description of the microscopic pathology of ARF, classified it as 'parenchymatous degeneration of the kidneys'.[11]

During World War I, German authors observed acute renal failure in soldiers who had been buried under heavy masses of earth when trench walls collapsed.[12,13] As only tubular lesions were seen on postmortem examination, the anuria was thought to be due to circulatory disturbances of the kidney ('vasomotorische Nephrose') or to tubular obstruction caused by myoglobin casts.

Terms as renal inadequacy, vasomotor nephrosis, lower nephron nephrosis, post traumatic shock kidney all emerged in the literature during the pre and post first world war period. An increasing number of traumatic shock cases occurred as a result of work-related accidents in the new industrial setting of the time, especially those of life-threatening car and train accidents. Because more operative procedures were being performed, post-surgical shock emerged as a clinical subject of investigation. In addition, changes of kidney function began to be noted and reported in cases of severe diarrhoea, transfusion reactions, and toxin exposure (for details see.[8] Whereas all described in variable detail some of the clinical, biochemical, and structural features of the posttraumatic shock kidney described during World War I, they did so in articles published in various specialty journals, each under different names that were not appreciated as a single disease until the years that followed the Second World War.[1]

Trench Nephritis

As we consider the 100-year anniversary of World War I, one should be mindful of the assaults that the soldiers faced from the diseases that prospered in the

trenches of this war. A neglected area of research is the group of diseases that bear the name of the trenches, namely trench fever, trench nephritis and trench foot.[14–16] Trench fever was a short-duration relapsing fever spread by lice; trench foot involved pain and swelling of the feet due to exposure to cold and damp, which could lead to gangrene. Trench nephritis occurred secondary to an unknown cause but there are arguments to believe that at least many cases of trench nephritis were caused by Hanta virus disease (see below). These trench diseases collectively led to about half a million casualties in the British and Allied forces.

This relatively 'new' kidney disease appeared early 1915 in British troops in Flanders and was quickly called 'trench nephritis' or 'war nephritis' in the British reports (which formed the majority).[17–19] Towards the end of June 1915, a total of 1062 cases was counted with a steady monthly increase afterwards. The 'nephritis' occurred in the soldiers after some months at the front, by which time the war had stagnated, and troops lived and died in a long line of cold, muddy, pestilent trenches which extended right from Switzerland to the English channel 500 miles to the North. For many veterans who are asked to recall their memories of life in the trenches the overriding feature that lingered in the mind was the problem – and horror – of trench rats. Rats – brown and black – thrived literally in their millions among trenches in most Fronts of the war, be it Eastern, Italian, Gallipoli – but primarily the Western Front. Trench conditions were ideal for rats. Aside from feeding from rotting food rats would invade dug-outs in search of food and shelter. Most soldiers who served on the Western Front would later recall how rats grew in boldness, stealing food that had been lain down for just a few moments. Rats would also crawl across the face of sleeping men.

The majority of the patients suffering from the 'trench nephritis' were in active duty in the trenches at the moment of their illness although some rare cases were also observed in the rear zone or in the base campements. Trench nephritis remained a serious sanitary problem for the British Expeditionary Force throughout the war, with thousands of soldiers to be sent back for convalescence, and leading to a bed occupancy of 25% in the internal medicine wards of the base hospitals at the end of the war. In the German Austrian troops, a similar outbreak was noted since the spring of 1915 and was called '*Feldnephritis*' or '*Kriegnephritis*'.[20]

The disease spread to French and even Canadian troops located South of Flanders as well, demonstrating many features of an infectious disease, being common in Summer and rare in Winter: on occasion, hospital orderlies and others who had never been at the front also could succumb.

A febrile prodrome of sudden onset was followed by pulmonary symptoms in a majority, and 'nephritis' sometimes with anuria occurred in about 20% of cases.[21] Blood pressure might be high but without eye fundal changes; the urine contained various casts and modest proteinuria. The condition was so common that specially designated 'nephritis wards' were set up in the British army field hospitals of northern France to investigate and treat the hundreds of cases, and the Army became seriously worried about its impact on the fighting ability of the troops – it is worth remembering that less than one quarter of fatalities in soldiers were from battle wounds.

When the US troops joined the war in 1917, they were not spared and on a total of 370 000 Americans, in Europe, 2002 (0.54%) cases of acute 'war nephritis' were noted (Dr Jan Clement, personal communication).

Looking back[22,23] it appeared that a similar condition had been seen during the American Civil war and probably the Franco-Prussian war, but not in the Crimean or Boer war – nor the Sino-Japanese war in Manchuria only a few years previously. During World War II, as many as 16 000 cases of a rodent-borne leptospirosis-like disease were noted during the 1942 German campaign in Finnish Lapland.[24,25] Because the snow melted, great numbers of lemmings and field mice invaded the German bunkers. Examinations in Munich and Berlin of these rodents, air-lifted from the war theatre, offered no clue. Confronted with some distinctive clinical symptoms (e.g. acute myopia and localized oedema) and with repeatedly negative findings for leptospirosis in the patients, a new field-like fever disease ('Kriegsnephritis') was suspected.[24]

Extensive investigations on both sides of the front during and after World War I yielded no clear aetiology, but a viral cause (a filter-passer) was already suspected early[15,21] (Dr Jan Clement, personal communication).

Although a combination of several conditions could have been responsible for these epidemies (acute tubular necrosis, acute interstitial nephritis, glomeronephritides) there is more and more, be it indirect and retrospect evidence, that Hantaan virus infection and Hanta virus nephropathy could have been a major cause (see below).

Korean Haemorrhagic Fever

In the Spring of 1951 the military doctors of the United Nations (UN) troops in Korea were confronted with a 'new' and frightening disease consisting of fever, haemorrhages, shock and renal failure. Many other diseases, including leptospirosis could easily be excluded and since an infection, hitherto unknown to Western medicine, was suspected, the

American Army Medical Services created a Haemorrhagic Fever Centre in South Korea to treat the affected troops under the best conditions and to start a very extensive research programme. In all the UN forces, more than 3000 cases occurred of what later was called Korean Haemorrhagic Fever (KHF). A mortality of approximately 10%, even reaching 15% in some localized clusters was observed. Despite the intensive research, KHF was the most important – but unresolved – nephrological problem of the Korean War. It was only 25 years later that the causative virus could be isolated from the lungs of the Korean striped field mouse, *Apodemus Agrarius Coreae*, a rodent very common in the region.[26] The virus was named after the Hantaan River, which transects the same endemic region where most of the cases had been noted and which runs in the Demilitarized Zone near the famous 38th parallel. Hantaan virus[26] is the cause of KHF. A milder form of the disease has been described in Scandinavia and in many other European countries and has been termed 'nephropathica epidemica' and is caused by an antigenically similar virus.[27–30]

Hantaviruses infect various animal species worldwide: rodents and insectivores, as well as mammals such as cats (Clement *et al.*, 1998). The natural reservoir of infection appears to be in rodents such as the fieldmice in Korea, the bank vole in Scandinavia and other European regions and rats. Rodents contaminate humans who inhale aerosols of virus-containing particles excreted through lung, saliva, and urine. In Europe, hantavirus disease is mainly due to the Puumala serotype, whose animal reservoir is the red bank vole, Clethrionomys glareolus. It is endemic and, occasionally, epidemic in Scandinavia (where it was known as Nephropathia epidemica), western Europe, the Balkans, and the western part of the Russia (where it was known as haemorrhagic nephroso nephritis).

Korean haemorrhagic fever is often severe, with haemorrhagic features and acute renal failure. The mortality is currently around 5 to 8%. The related illness, nephropathica epidemica, is milder, haemorrhagic features are unusual and the mortality is less than 1% (for recent and comprehensive review see J. Clement – Acute kidney disease and hantavirus disease-chapter OTCN in press, Oxford Textbook in Clinical Nephrology, Oxford University Press, 2014). The European cases appear also to be of this less severe variety.

In view of the discussion above, it is thus highly plausible that many cases of so-called 'trench nephritis' and the acute kidney disease in KHF were Hanta viral nephropathies.

The Role of Norbert Goormaghtigh

Professor Norbert Goormaghtigh was born on the 14th of February 1890 in Ostend, where he was raised and also went to school. He left his native town for Ghent where he studied medicine at the State University. He graduated as Doctor in Medicine, Surgery and Obstetrics magno cum laude in 1913. He became well-known for his studies on the structure of the adrenal gland. He started his studies on the kidney, more in particular the juxtaglomerular apparatus at the beginning of the 1930s carrying on from previous observations and in 1932 he provided evidence of its endocrine function.[31,32] His training and research were interrupted by the first World War. He was mobilized and assigned to a surgical mobile hospital. He took part in the retreat of the Belgian Army behind the river Yser, and functioned as surgeon in the Field Hospital in Hoogstade which was an English hospital, sent to Belgium by the British government in order to support the Belgian Army. In this hospital he met his future wife, Mable Lawrence, who was an English nurse belonging to the staff of the Belgian Field Hospital.[32]

The discovery of the unique structural relationships between the early distal tubule of the nephron and the vascular pole of its originating glomerulus and the subsequent demonstration of the functional and clinical import of this remarkable complex – the juxtaglomerular apparatus – is one of the principal achievements of nephrology.

Of the several investigators who made this possible, Norbert Goormaghtigh was not only one of its first observers but the only one to persevere in its investigation, to recognize and define the critical relationship of the complex he named the juxtaglomerular apparatus, and in what were clearly prescient insights to foresee correctly many of its functions that were to be documented in the ensuing decades.[31] Goormaghtigh belonged to the class of morhologists who believed that accurate structural studies provided a basis for the undertaking of functional studies. In fact, he often used in the text and title of his papers the term 'histophysiologie' (histo-physiology).

In his inaugural paper on the subject,[33] Goormaghtigh described in detail the afibrillar cells of the juxtaglomerular arterioles, principally in an 8-year-old girl who had died of scarlet fever. He characterized them as afibrillar granular cells and identified them with those lining the afferent arteriole described by Ruyter. In addition, he identified a second population of smaller, also afibrillar but agranular, spindle-shaped cells in the vascular pole, and highlighted the rich enervation of the entire area. The second type of cells he described were subsequently termed lacis cells because of their interlacing processes separated by basement membrane.

In the context of this paper, it is of interest that Goormaghtigh performed some of his numerous

studies on autopsy material submitted to him by pathologists of the Royal Canadian Army Medical Corps stationed in Belgium during the first World War. The victims were young enlisted men in the Canadian Army who had died 4 to 9 days after crushing injuries and after the development of marked oliguria and even anuria. In a seminal paper describing his results he added a case of 'traumatic uraemia' observed by him during the war of 1914–18 with a remarkable clinical description of a post crush syndrome complicated by oligo-anuric ARF.[34]

It is on this background in the state of the medical sciences that Goormaghtigh made his major contributions on the juxtaglomerular apparatus in the period between the two world wars, both of which to some extent influenced and shaped his personal life.

The Second World War (WWII) was equally defining in his life, when his favoured son was accused and imprisoned in Dachau in 1943. The following year, the Gestapo incarcerated him also, albeit for only a short period.

The toll of WWII on his work and productivity is reflected in the diminishing number of his publications. His subsequent administrative responsibilities as a rector (1947–1950) of the University of Gent, during a particularly difficult period in its history, further hampered and practically ended his investigative career. Following a series of progressively severe and incapacitating cardiac attacks beginning in November 1957, he died on 2 January 1960.

The Beginning of Chronic Dialysis

It is beyond the scope of this paper to repeat the well-known history of the development of both peritoneal and haemodialysis in the treatment of acute and chronic kidney disease. A number of websites can be consulted on this topic and some interesting books have treated in detail this fascinating story.[35,36]

The development of the artificial kidney by Willem 'Pim' Kollf in Kampen (the Netherlands) during the second World War and the rather slow but worldwide introduction of the first models in some selected university hospitals have been told many times. Whereas the first Kollf-Brigham artificial kidneys were successfully used in the treatment of acute renal failure patients in the Korean War (see below), chronic dialysis became only possible by the creation of a permanent vascular access by Scribner in 1960. The Scribner shunt was developed using the newly introduced material, Teflon®. With the shunt, it was no longer necessary to make new incisions each time a patient underwent dialysis.

Further improvement in chronic vascular access was realized by the surgical creation of the arteriovenous fistula by Drs Cimino and Brescia in 1966.

In 1962, Scribner started the world's first outpatient dialysis facility. Immediately the problem arose of who should be given dialysis, since demand far exceeded the capacity of the six dialysis machines at the centre. In another brilliant move, Scribner decided that the decision about who would receive dialysis and who would not – a matter of life and death for the patients involved – would not be made by him. Instead, the choices would be made by an anonymous committee composed of local residents from various walks of life plus two doctors who practiced outside of the kidney field. Although his decision caused controversy at the time, it was the creation of the first bioethics committee, which changed the approach to accessibility of health care in many countries.

The past 60 years has been a time of incredible advancements in the world of kidney medicine. Thanks to the efforts of Kolff and Scribner and other medical pioneers like them, people with chronic kidney disease are now able to live full and productive lives.

Professor Severin Ringoir – Pioneer of Nephrology in Ghent University Hospital

Dr Severin Ringoir was born in 1931 in the city of Aalst. He did his medical studies on the medical faculty in Ghent and graduated as Doctor in Medicine, Surgery and Physics as the diploma was named at that time in 1956. Besides his military service he started a training in internal medicine under the guidance of Professor Paul Regniers between 1957 till 1961. His choice for beginning a study of kidney diseases started already during his training in internal medicine and was prompted by the dramatic experience of observing some young patients slowly dying from chronic renal failure, despite so-called conservative therapy. Encouraged by Professor Regniers, Dr Ringoir was allowed to stay for several months in already then famous renal services abroad, Paris (Hôpital Hôtel Dieu under the leadership of Prof Dérot and the young Marcel Legrain), Géneva (Dir. Professor René Mach), and Houston (the renal division of Baylor College – Dir. Professor Morgen). From each training period he brought back experience in peritoneal dialysis, haemodialysis, and kidney transplantation. In the meantime he was working on his PhD thesis in the Laboratory of Normal and Pathological Physiology, between 1964 and 1966.

A particular interest for acute renal failure is already present from his beginning years in nephrology and is reflected in an interesting contribution in his Mémoire pour le titre d'assistant étranger de l'Université de Paris on 'Observations in 33 cases of anuria caused by acute tubular necrosis post-abortum'.

Under the stimulating leadership of Professor Ringoir and in collaboration with the department

of surgery, a young team of nephrologists started acute and chronic haemodialysis, peritoneal dialysis and kidney transplantation in the first 5 years of the 1960s.

It is without exaggeration one can say that under Ringoir's guidance the Ghent school of nephrology has acquired a certain national and international reputation and has contributed to the development of a great number of Flemish centres of nephrology.

In parallel with dialysis, an active kidney transplant programme was developed in close cooperation with the department of surgery under the direction of Prof Fritz Derom.

It has been a long way between the first haemodialysis patient in Ghent in 1963, the first kidney transplant in 1968 and the first continuous ambulatory peritoneal dialysis patient in 1977 and the actual number of 3926 haemodialysis, 122 peritoneal dialysis, and 2998 kidney transplant patients by the end of 2010 present in Dutch – speaking Belgium.

The University of Ghent Renal Division and the Renal Disaster Relief Task Force of the International Society of Nephrology

As mentioned above, there has always been a great interest in ARF in the Ghent nephrology division. It was then almost natural that the Ghent renal division was in the frontline when the International Society of Nephrology started the creation of a Renal Disaster Relief Task Force for renal interventions in case of disasters causing post-traumatic crush ARF.

Most cases of AKI that develop following natural disasters are a result of crush syndrome. Crush syndrome is a reperfusion injury that occurs after ischaemia of skeletal muscle caused by prolonged continuous pressure by rubble. The pressure causes destruction or disintegration of triated muscle, which is called rhabdomyolysis. This syndrome is characterized by muscle breakdown and necrosis resulting in the leakage of the intracellular muscle constituents into the circulation and extracellular fluid.[37,38]

After a victim is released from the rubble, water and sodium flow into the injured region, and severe dehydration and circulatory failure develop. Furthermore, large amounts of myoglobin and potassium are released into the circulation from the injured muscle, which can result in acute tubular injury and hyperkalaemia.

The first adequate description of muscle crush syndrome appeared in the English literature in the classic monumental report on casualties of the London Blitz which started in September 1940. Bywaters and Beal[39] described four patients with extensive mechanical crushing of muscles and myoglobinuric AKI resulting in renal failure. All patients were extricated alive from under the rubble, but died a few days later. Initially, some of these casualties developed shock and haemoconcentration with gross oedema of the crushed limbs, which was strongly suggestive of extensive sequestration of extracellular fluid by the damaged muscles. Furthermore, through an elegant series of experiments, Bywaters demonstrated that myoglobinuria led to nephrotoxic effects when the urine was acidic but not when it was alkaline.[40–42] On the basis of these observations, Bywaters was the first author to suggest that management of muscle crush syndrome should consist of copious rehydration combined with infusion and ingestion of bicarbonate ions to achieve alkalinization of urine.[42] Towards the end of World War II, London was bombed again. Bywaters later estimated that 95 of 186 patients with muscle crush syndrome in this second attack were prevented from developing myoglobinuric AKI as a result of treatment with copious rehydration and urine alkalinization during the predialysis period.[42] These results were achieved before development of the Kolff artificial kidney, which was introduced in London in 1946, and greatly improved the management of patients with myoglobinuric AKI. Furthermore, in 1946, mannitol (an osmotic diuretic drug) was the first agent introduced for protection against ischaemic renal injury and myoglobinuric AKI in humans and in experimental models.[43] The decades that followed completely vindicated the usefulness of Bywaters' regimen. Crush syndrome was first mentioned in US literature as late as 1958.[42] This delay probably reflects the near-absence of large-scale disasters or war within mainland USA since the civil war.

The 'Bywaters' regime of vigorous fluid resuscitation was also applied by Ron *et al.* in 1984.[44] Following the collapse of a building in South Lebanon, seven subjects (aged 18 to 41 years) were released from under the rubble within one to 28 hours. All seven suffered from extensive crush injuries with evidence of severe rhabdomyolysis and were treated by the induction of an alkaline solute diuresis immediately on their extrication from the debris. Historical controls with injuries of similar severity have showed a high incidence of acute renal failure and a high mortality rate, yet none of the fluid treated patients had azotaemia or renal failure. This success was attributed to the unprecedented early institution of intravenous appropriate therapy even before the complete body of the victim was extricated from under the rubble. Efforts to extricate trapped victims may be futile if the means to resuscitate and treat rescued victims are not available, as occurred following the 1988 earthquake in Armenia.[45] Many rescued victims in Armenia subsequently died of crush-related AKI and hyperkalaemia because of poorly organized relief and inability to provide

dialysis to all patients with AKI.[46,47] It was also evident that a poorly organized relief effort resulted in a chaotic influx of untrained, unsupported volunteers and materials that overloaded available distribution systems and interfered with transport of supplies, creating a 'second disaster'.[45–48] Consequently, it was clear that there was a need to organize an international response system to prevent and manage crush-induced AKI. The International Society of Nephrology founded the Renal Disaster Relief Task Force in 1989, as a response to the chaotic relief efforts of the Armenian earthquake.[49]

The organization of this task force was and still is in the hands of the Ghent Renal Division. The interventions in several disasters, the most important ones being the Marmara, Bam, Kashmir, and Haiti earthquakes have been described in detail elsewhere. The programme is embedded within the broader rescue support programme deployed by Médéçins sans Frontières, (Doctors without Borders).[50–54]

Based on the cumulative and extensive experience with several of these interventions where the principles of early fluid resuscitation were applied, the task force has published recommendations for the logistical and medical management of crush syndrome victims in mass disasters.[53–55]

During the London Blitz of 1940, crush syndrome was almost universally fatal, whereas by 1999 the mortality rate had been dramatically reduced to $<20\%$. In 2003, all 16 young adults (mean age 23 ± 13 years) who were treated with early vigorous fluid resuscitation for extensive crush syndrome following the Bingol earthquake in Turkey survived. Although myoglobinuric AKI occurred in four of these individuals, this complication was prevented altogether in the other 12.[56] An important point to note, however, is that such aggressive treatment would have been inappropriate in elderly earthquake survivors with multisystem failure, as such individuals are vulnerable to the adverse effects of fluid overload. Since fluid administration should be started on site before a patient is transported to medical facilities, there is a critical need to educate emergency staff, co-medical staff and general physicians about the risk of crush syndrome and the importance of fluid therapy. Such knowledge would facilitate early recognition of AKI and timely referral of patients who require renal replacement therapy.

In addition, nephrologists have also a key role in the management of chronic dialysis and transplant patients, following an earthquake.[57] Major disasters destroy dialysis facilities, leaving patients without lifesaving therapy in their local environment. This was a major challenge following Hurricane Katrina, Cyclone Yasi, the Kobe and Marmara earthquakes, and the recent Tohuku earthquake and tsunami, which was followed by the Fukushima nuclear power plant meltdown (for review see.[50,54] In these situations, if possible, dialysis-dependent endstage renal disease patients must be transferred to other dialysis facilities, often in other cities, to continue their dialysis treatment. For example, relocation of chronic dialysis patients places significant pressures on receiving dialysis units. Following Hurricane Katrina, 700 dialysis patients from New Orleans were added to the usual 1000 in Baton Rouge, LA. This may involve a number of days without dialysis while the patients are relocated or the facilities are repaired and brought back into service. During that period, chronic dialysis patients must be contactable and, if possible, conservative care preferably provided by experienced nephrologists should be prescribed.

The same concerns apply to transplant patients who may not have access to their antirejection therapy in the disaster area.

In conclusion, the Sarton lecture 2014 provided an opportunity to summarize some aspects of the reciprocal impact of wars and disasters on medicine in general and nephrology in particular.

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