

Professor Hugh MacLean: one of the first British military research nephrologists and the pioneer of the first United Kingdom veterans' renal clinic

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Few people have been as successful in bringing together basic research, clinical science, and a contribution to military medicine as Professor Hugh MacLean. However, today he is almost forgotten. During World War 1, practicing within the realms of the new field of renal medicine, with minimal resources and in a military hospital, he conducted one of the first large-scale Medical Research Committee investigations into war nephritis involving 60,000 subjects. After

the war he set up and practiced, amongst other specialties, in the field of veteran medicine and established the concept of the one-stop renal clinic. After achieving significant academic recognition, he was unfortunately affected by mental health problems, possibly related to his wartime experiences, which brought an illustrious career to an untimely end.

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Introduction

Many would assume the first substantial Medical Research Council (MRC) (or its forerunner the Medical Research Committee (*vide infra*)) studies involving thousands of subjects began in the late twentieth century, or that one-stop clinics were a modern feature initiated at the end of that same century. However, one of the first large MRC studies was performed during World War 1 involved 60,000 subjects, and the innovation of the day clinics was the result of pioneering scientist, clinician, and teacher Professor Hugh MacLean (Figure 1).

Early life

Hugh MacLean was born into a rural family in Kincardine, Scotland on 23 April 1879; his father was a gamekeeper. His family moved shortly thereafter when Hugh was three years old, settling as tenant farmers on the Aberarder Estate in Inverness-shire. For senior schooling he walked 15 miles to attend the Inverness Royal Academy, lodging locally during the week, but walking home again at the weekend.¹

Identified as having the potential for a brilliant academic career, he studied medicine at the University of Aberdeen where he was encouraged to concentrate on the physiological aspects of clinical medicine.² He graduated M.B., Ch.B. from Aberdeen in 1903, then M.D. with honours the following year.

Figure 1 Professor Hugh MacLean (Provided with permission by Drs J and A Shneerson, family of Hugh MacLean)



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He pursued an academic career, with his first research post as the senior assistant in physiology at the University of Aberdeen. MacLean's first papers in 1906: *Observations on Fehling's Test for Dextrose in Urine*³ and in 1907: *On the Influence of Kreatinin in Modifying Certain Reactions of Sugar in Urine*⁴ established his interest in the biochemistry and quantification of the constituents of urine, which would set the scene for the next two decades of his life.

In 1908, Dr MacLean travelled to Berlin as a Carnegie Fellow, publishing two papers in German on phospholipids^{1,5,6} before returning to Liverpool University, England where he performed similar work, qualifying for his M.Sc. in 1910.

His next move was to the Lister Institute in London as a senior assistant in the Biochemical Department working towards his D.Sc.. This is where he met Ida Smedley, an extraordinary, clever, charismatic woman. She had studied science at the University of Cambridge (women were not allowed to graduate in the 1890s) and would go on to found the British Federation of University Women and the International Federation of University Women, perform vital scientific work in World War 1, publish over 25 papers (mainly on fatty acids) and become the first woman to chair the Biochemistry Society. She became Mrs Ida Smedley-MacLean in 1913,⁷ celebrating their marriage by sharing a publication that same year.⁸ The couple were now financially secure, Hugh having been appointed as a chemical pathologist at St. Thomas's Hospital, London the previous year.^{1,2}

During this same decade, the British Government passed the National Insurance Act (1911) creating a national system of insurance to protect working people against loss of income relating to sickness or unemployment.⁹ This also created a national fund for medical research, with the aim of financing and retaining exceptional researchers under the auspices of the Medical Research Committee and Advisory Council (later to become the MRC) set up in 1913.¹⁰ This Committee would soon come to have a significant impact on Dr MacLean and his work.

World War 1 – war nephritis

The First World War began for Britain on 4 August 1914, when Britain declared war on the German Empire. The British Expeditionary Force which embarked for the Continent comprised the standing regular army and existing volunteers of the reserve (Territorials). As such, the health of those deployed was generally good. However, within a year over 1,000 cases of acute nephritis had been identified in British troops as trench warfare consumed the Western Front in Belgium and France. The first cases began to appear towards the end of the first winter of the war (February 1915). Arrangements were made for a number of these patients (58 cases) to be brought from France to St. Bartholomew's Hospital, London, at the request of the Director General of the Medical Research Committee. They were placed under the care of Captain W Langdon Brown of the Royal Army Medical Corps (RAMC) Territorial Force for investigation.¹¹

Acute nephritis, or Bright's disease as it was often then called, was not a common illness in the civilian population at that time. Langdon Brown commented that only 26 cases in men aged between 20 and 40 years had been admitted to St. Bartholomew's Hospital in a period of five years before the war; a hospital that was admitting over 7,000 patients annually at that time.¹¹ In one of the first papers on the subject, *Report on Fifty-Eight Cases of Acute Nephritis Occurring in Soldiers of the Expeditionary Force, Investigated at St. Bartholomew's Hospital for the Medical Research Committee*¹¹ (1915), Langdon Brown describes the symptoms and signs clearly: striking dyspnoea, oedema (renal dropsy) and albuminous urine which also contained blood and casts on microscopy. Despite extensive investigations, no cause for the nephritis was identified, no therapeutic strategy proved successful and although only one death occurred in this group, the potential for the disease to have a slow recovery time or to become chronic in nature predicted the significant impact this disease could have on the British fighting force and for the future of the war.

In 1916, particularly in the winter months, considerable numbers of what became known as 'trench nephritis' or 'war nephritis' continued to occur.¹² Not surprisingly, therefore, in February 1917 the Director General of the British Army Medical Services (at the suggestion of the MRC) invited Dr H MacLean as a biological chemist to work on the subject of 'war nephritis'¹³ and commissioned him with the rank of Temporary Honorary Captain RAMC.

Captain MacLean departed for France in early 1917 and established himself at Étapes, then the principal depot and transit camp for the British Expeditionary Force, with a significant series of hospital complexes to which the wounded or sick were transported. This included the 46 Stationary Hospital which provided the required laboratory space for examining urine samples.

There MacLean set about investigating 50,000 troops, recording age, length of service, occupation pre-service (grouped into sedentary or active occupations), examining their urine for albumin and casts, assessing the effect of training on their urine, and documenting any past medical history of scarlet fever, syphilis, or gonorrhoea. The enormous task was completed between May and October, 1917.¹³

Urine samples were collected at an early morning parade, thus avoiding the problem of daily exercise increasing albuminuria, which was understood by MacLean but reconfirmed in a subset of 200 soldiers in his Étapes study. The soldiers passed their urine sample into a cleaned 'Ideal' milk tin, one of the brands of condensed milk provided in World War 1 rations.

Specially trained medical orderlies initially screened the urine samples for albumin using salicyl-sulphonic acid: six drops of a supersaturated solution added to a small quantity of urine in a test tube, and any that proved positive were retained for quantification using a six-point scale (Very Marked, Marked, Fairly Marked, Distinct, Faint, Trace) and centrifuged for

microscopy to look for casts.¹³ Using this method, up to 600 specimens could be processed each day.

To investigate the impact of early training on recruits' kidneys, immediately after his investigations in France Captain MacLean returned to England to a basic recruit centre in Aldershot and undertook a repeat of his investigations. Here he identified 2,132 men who had less than one month's service and a larger number (5,837) of young, 18-19 year old soldiers from a further 10,000 recruits who all had their urine examined.¹³

Captain MacLean was able to compare his vast data with those published by another RAMC Medical Officer, a Captain McLeod (although spelt MacLeod in his report) in 1916; McLeod had investigated albumin in the urine of British and French troops freshly returned (<24 hours) from the trenches with a longer service history (>12 months).¹⁴ McLeod possibly used different analytical methods to those of MacLean and certainly used a different three-point scale for albuminous urine in his paper, which unfortunately rendered absolute comparison difficult. The numbers of participants in McLeod's study were also relatively small, although still comprised 4,081 soldiers. Based on the evidence presented by McLeod, Captain MacLean's report suggested that the incidence of albuminuria in those returning well and directly from the trenches did not differ from that found in soldiers during their training.

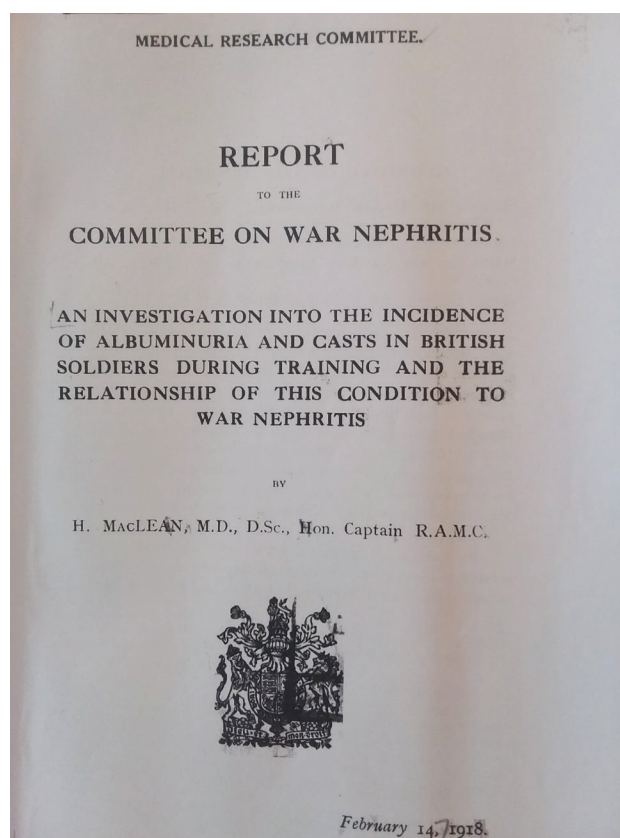
Although no formal statistical analysis was offered, the summary from the report included:

- The general incidence of albuminuria in trained troops was 5%.
- Albumin in the urine which is produced by sudden and severe exercise passes off on resting.
- The presence of casts in the urine of trained troops was 1.8%.
- Of those soldiers therefore deemed fit for 'active service' there was within their ranks 1% who had some degree of kidney disease (both casts and albumin being present).
- No relationship was found between the presence of albumin or casts and: pre-service occupation; duration of service; or age (although albuminuria was more common in those aged 18-22 years old).

The conclusion was that the investigation performed by Captain MacLean supported the view that no injurious effects on the kidney was associated with training for active service, and that 'trench nephritis' was due to some factor operative in the fighting area (Figure 2).¹³

During the study performed at Étapes, Captain MacLean created a card index system of the soldiers whose urine was investigated, with arrangements made such that any soldier returning with nephritis to any of the military hospitals in France would have notification passed back to the record and any relationship between pre-existing albuminuria and

Figure 2 Report to the Medical Committee on War Nephritis by Captain H MacLean 1918



subsequent nephritis could be established. At the time of the report (February 1918) insufficient notifications had been received to ascertain if any such relationship existed.

'War nephritis' rather than 'trench nephritis' became the more accepted term for this condition, as it was seen in troops serving outside the trenches. By late 1918, report cards of patients previously studied by Captain MacLean at Étapes were returned. In early 1919 MacLean published¹⁵ a report stating that of the 161 patients admitted with war nephritis, 28 had shown albuminuria at the time of training, and 133 had not, concluding therefore that albuminuria was neither a marker for war nephritis exacerbating an existing chronic disease nor for developing acute war nephritis. *The History of the Great War, Medical Services, Diseases of the War* states that no cause for this disease was ever identified despite the enormous investigative attempts made at the time,¹² a fact that remains true to this day. The report went on to highlight the need for patients with war nephritis to be followed up, recognising that the later development of chronic nephritis was insidious, although care was to be taken to ensure primary nephritis was distinguished from secondary disease arising from either infection or infected wounds.

In a more complete and specially commissioned report to the MRC by Captain MacLean on *Albuminuria and War Nephritis Among British Troops in France*, published in 1919,¹⁶ he provides a chapter on the prognosis and clinical tests which could potentially define the long-term outcome for patients with war nephritis. He suggests that whilst many cases

apparently 'clear up entirely, it is probable that some patients are more susceptible to develop later renal disease'. Even during the war, the possibility for troops who had nephritis to return to active service was limited. Follow-up research by the MRC¹⁶ and a Captain Dyke¹⁷ suggested that 40% of a total of 121 patients were either invalided out of the services or the re-establishment of normal renal function was incomplete.

In the same MRC report,¹⁶ MacLean discusses tests which could be performed to indicate 'kidney efficiency'. In addition to a physical and routine examination of the urine for albumin, blood, and casts, four further tests were recommended: estimation of urea in the blood, a 'new' urea concentration test (calculating the kidney's ability to excrete ingested urea), the diastatic test (the power of the urine to hydrolyse starch) and measuring urinary chlorides. This system, it was proposed, could define the function of the kidneys and ascribe an accurate prognosis. This latter statement and those tests were to play a significant part in Dr MacLean's future career.

Post War – The Veterans' Renal Clinic

After the war, Hugh MacLean returned to work as a chemical pathologist at St. Thomas's Hospital, London. He was, however, soon approached by the Ministry of Pensions, who, recognising his work on war nephritis appointed him as a consulting physician tasked to look at that disease and its implications for veterans in receiving a war pension.^{1,2} The final number of veterans recorded as receiving a war pension for nephritis was 15,837 or 1.8% of total war pension recipients.¹⁸ To assess veterans for a pension required MacLean to develop a clinic they could attend, allowing a great number to be tested daily, required the least possible time for the veteran, and 'the least interference for the patient' (avoiding blood tests, including those for blood urea, and injections). This is possibly one of the first examples of a focused, one day, one-stop outpatient clinic run for the benefit of both the patient and society (the Ministry of Pensions), almost 70 years before such clinics became routine.

The following assessment was developed, and was ultimately used throughout the country in the clinics of the Ministry of Pensions.¹⁹

- The veteran was examined clinically for their general condition, cardiovascular condition (blood pressure, apex beat both position and nature, cardiac sounds), condition of the arteries (described as normal or stiff) and for the presence or absence of oedema.
- A urine sample was taken for examination for protein (using the method adopted in Étaples in 1917) and centrifuged for microscopy looking for casts and blood.
- A diastatic test was performed on the urine sample. This test relies on the production of diastase (now termed amylase) by the pancreas and its subsequent excretion in urine. The ability of the urine, or more precisely the concentration of diastase in the urine, to convert an amount of starch into

sugar in a set time was understood to reflect the efficiency of the kidney. A high diastatic value is an indication of efficient renal action. MacLean himself attached slight importance to this test, particularly when applied to a single sample as opposed to 24-hour collection.¹⁹

MacLean placed much greater importance on the 'urea concentration test' which he had developed with his colleague Dr De Wesselow from Étaples and St. Thomas's Hospital.²⁰ In this test, the veteran emptied his bladder then 15g of urea was ingested by mouth (in 100ml water) following which the bladder was emptied at one and again two hours later. The two separate urine collections were then analysed for the urea concentration, expressed as a percent. The method used involved a fixed quantity of both urine samples being mixed separately with sodium hypobromite, which reacts with the excreted urea in the urine to produce nitrogen gas. The volume of nitrogen produced reflects the concentration of urea in the sample. The higher the concentration of urea excreted again reflects the efficiency of the kidney.

Dr MacLean stressed that as many as 50 patients could undergo examination in one day and that he personally had supervised over 10,000 examinations by 1921.¹⁹ He further recommended that this process, with or without the refinement of measuring blood urea, should be adopted by every practitioner in managing suspected cases of renal disease. The methods used, and the description of the clinic, along with a background to diagnosis and treatment of renal disease were published in his book in 1921 (Figures 3 and 4).¹⁹

Dr MacLean's career was on the rise; he had demonstrated himself to be a sound researcher and teacher and although lacking clinical experience, he was appointed as the inaugural head of the St. Thomas's Hospital Medical Unit and Professor of Medicine, University of London in 1921.^{1,2}

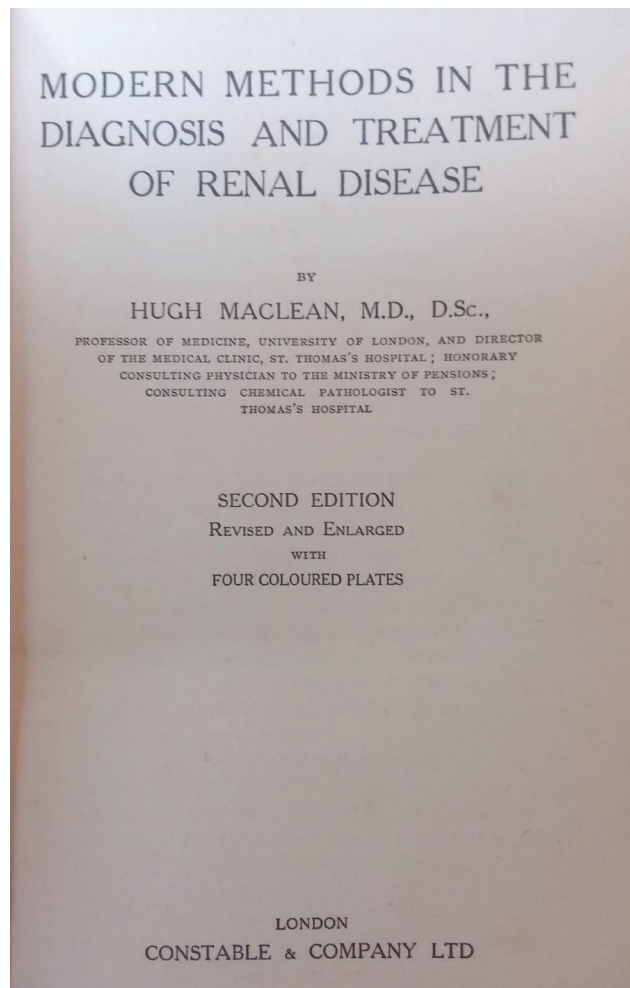
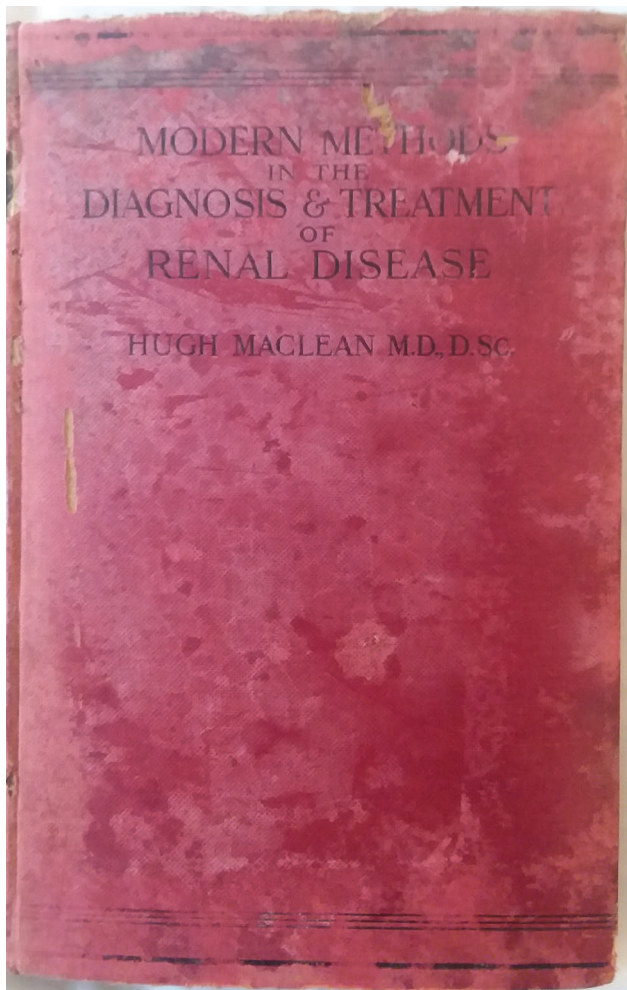
Mental health and later years

Throughout the 1920s Hugh and Ida appear to have enjoyed an idyllic academic and family life; two children had arrived, Kenneth and Barbara, and Hugh developed a successful private practice. Ida toured the United States lecturing, and she and Hugh published a book together.²¹ Hugh continued to develop his expertise in renal disease, contributed significantly to the understanding of diabetes and gastric diseases, and redesigned outpatient clinics.^{1,2} Hugh also toured the United States, raising a considerable amount of money for St. Thomas's Hospital. In 1929 he toured Australia whilst the family took their summer holiday in Europe.⁷

For relaxation, Hugh enjoyed golf and fishing and excelled at shooting, almost certainly reflecting his early Scottish and rural upbringing.^{2,7}

Suddenly, in 1930, timed to the first day of his summer holiday in Scotland in one account,¹ although possibly with a prodrome of a self-diagnosed stomach ulcer in another,⁷ Hugh

Figures 3 and 4 McLean H. *Modern Methods in the Diagnosis and Treatment of Renal Disease*. 1924



was affected by what was described as severe depression. After initially obtaining medical advice in Scotland and then returning to London for a further opinion, within two weeks he was admitted to a nursing home. For the next five years, Professor MacLean found himself in and out of several nursing and psychiatric institutions, interspersed with time at home being supported by Ida. It is possible his mental health related to his wartime experiences as guilt was described as a feature of his illness.⁷ Étaples and the hospitals had been bombed badly during the war but probably after he had left; one of his brothers had died serving in the War;⁷ and of course he had been exposed to the hospital environment during the war and to veterans subsequently. In support of this theory, he was admitted at one point to The Cassel Hospital for Functional Nervous Disorders, Penshurst, Kent. The hospital was founded in 1919 to support those traumatised by the War. Hugh was admitted under the care of Dr T A Ross, an expert on war neuroses, although the hospital did care for those with other mental health problems.^{7,22} His symptoms did not resolve and just over a year after becoming ill he resigned from his post at St. Thomas's Hospital, almost certainly under some pressure from his employer.^{1,2,7}

It was not until 1935 that Professor MacLean was able to return to full time clinical work, both in private practice, several public hospitals in London and to work in his wife's laboratory.^{2,7} However, he never reached the heights of academic brilliance achieved in the previous decade. During the Second World War and in a blackout in 1943 Hugh fell down steps at his home in London, suffering a fractured skull.^{1,7} Although making a full physical recovery, the injury either precipitated or coincided with a return of his mental health problems, again described as depression.^{1,7} The death of his wife a year later from cancer required his admission to another psychiatric hospital, St. Andrews, Northampton where he remained until his death in 1957 at the age of 78. Remarkably, given his early career and commitment to renal medicine his death was ascribed to uraemia.¹

His legacy is to have created the circumstances in combining both clinical examination and the ability to rapidly and accurately measure renal function in an appropriate outpatient setting to set the scene for the development of the new specialty of renal medicine. ①

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