In this book, Ulrich Tröhler documents the origins of systematic efforts *"to improve the evidence of medicine"* (in the words of the 18th century physician, George Fordyce), demonstrating that a quantitative and critical approach to the evaluation of medical practice became established far earlier than previously thought.

Long before Pierre-Charles-Alexandre Louis and his colleagues in 19th century Paris began using comparative statistical analysis to evaluate the effectiveness of therapy, James Lind, the Scottish naval surgeon (whose controlled trial of oranges and lemons for scurvy is so well known) and many other clinical investigators in 18th century Britain had pioneered the introduction of observation, quantification, and experimentation in medicine and surgery.

Professor Tröhler's book provides a fascinating account of the way that doctors who often had begun their clinical careers outside the medical establishment, used quantified observations to challenge therapeutic dogma based on theory and to introduce new treatments. He explores a number of contemporary health care problems and their solutions as seen by the pioneers of a critical approach, and by their opponents. As well as painting a vivid picture of 18th century medical practice, readers will find that many of the issues discussed are equally pertinent to health care, clinical practice and therapeutic evaluation in the 21st century.

"TO IMPROVE THE EVIDENCE OF MEDICINE"

The 18th century British origins of a critical approach

ULRICH TRÖHLER

"TO IMPROVE THE EVIDENCE OF MEDICINE"

The 18^{th} century British origins of a critical approach

ULRICH TRÖHLER

Published by the Royal College of Physicians of Edinburgh
9 Queen Street
Edinburgh EH2 1JQ
www.rcpe.ac.uk

Printed in Scotland by Metro Press Euro Limited.

for Marie Claude

CONTENTS

ILLUSTRATIONS

PREFACE

The scholarly basis of this book was established 20 years ago in my 1978 London PhD thesis, *Quantification in British Medicine and Surgery 1750-1830 with Special Reference to its Introduction into Therapeutics*. Why then prune an old thesis to write a new book? There are three main reasons.

First, in the mid-1970s the history of quantification of medical experience was hardly explored, with the main exception of the field cultivated around 1830 in Paris by Pierre-Charles-Alexandre Louis. His *méthode numérique* was then seen as the inventive first step towards statistical-comparative analysis of aggregated data for the elaboration of a new type of evidence for therapeutic (in)effectiveness. My study on earlier British medicine and surgery challenged this traditional view. Numerous scholarly works have since been published and a fuller picture of the origins and further ups and downs of the statistical approach to therapeutic evaluation can be drawn. My interpretation of the meaning of the 18th century British movement of "clinical arithmetic observation and experimentation" has evolved in this light.

Second, evidence-based medicine, the legitimate, albeit late-born, child of this 18th century movement, has risen to "the top of the hierarchy of evidence" as the *Journal of the American Medical Association* wrote in 1992.* However, this place is contested from both inside and outside the health care world. To form one's own judgement, it is valuable to know its parents and their milieu; this will also help us to understand the further development of critical appraisal in therapeutics. (A book setting out to inform historians and such a large spectrum of the public must necessarily be short. I have therefore selected only representative examples from my thesis and included only the references of the original quotations. However, I have added an annotated list for further reading, which includes the recent secondary literature, and the full text of the original thesis is now available on the website of the Royal College of Physicians of Edinburgh: *www.rcpe.ac.uk.*)

The third and most important reason for this book to see the light of day is Iain Chalmers. He has been its real initiator and indefatigable source of momentum. It was impossible to escape his argumentative force, his power of judgement, his contagious efficiency – with the consequence that during a few (holi)days of

* EBM Working Group (1992), Evidence-based medicine. *JAMA* **268:**2420-5, p. 2420.

intense collaboration in Germany and France we dove with increasing enthusiasm back into 18th century Britain. My most heartfelt thanks, those of a friend, go to him – not least also for having established the contact with the Royal College of Physicians of Edinburgh and its Publications Department, headed by Juliet Miller. With great professionalism equalled by her friendliness she has, together with Anne Borthwick, made it miraculously possible to publish this book in this shortest time ever, despite the need to transform my understandable yet sometimes rocky Swiss English into elegantly flowing British English. Iain Milne, the College Librarian, has been of unwearying help in tracing down references and finding illustrations; and the President, Jim Petrie, has supported the project from the outset. Margaret Andergassen has kept pace with the ever-increasing amount and speed of exchanges between Edinburgh and Freiburg.

I also wish to thank many colleagues with whom I discussed issues in the history of epistemology. I am particularly grateful to Irvine Loudon, Holger-Andreas Maehle, Lutz Sauerteig and Thomas Schlich for critical discussion and very valuable comments on an earlier draft of the manuscript.

When and wherever work was done on my numerous 18th century "number-heroes" my wife, Marie Claude, has created the ideal atmosphere: We have indeed met them time and again during 25 years of our married life ...

ULRICH TRÖHLER

FOREWORD

IT is widely believed that a quantitative and critical approach to the evaluation of medical practice originated in Paris, among Pierre-Charles-Alexandre Louis and his colleagues, during the first half of the 19th century. Many professional medical historians, however, know otherwise, because they have come across an unpublished London University PhD thesis completed by Ulrich Tröhler in 1978. At that time, Dr Tröhler had already made his name as a researcher in renal physiology in Bern; but he had been bitten by the history bug, and the award of a stipend by the Swiss Science Foundation enabled him to study for three years at the Wellcome Institute for the History of Medicine in London.

Dr Tröhler's research there tested his hunch that quantification of the results of surgical and medical treatment must have become established earlier, and that there might be British origins, particularly in the Army and Navy. His research showed conclusively that James Lind, the Scottish naval surgeon whose account of his controlled trial of oranges and lemons for scurvy is so well known, was only one of many imaginative clinical investigators in 18th century Britain. Indeed, by the beginning of the 19th century, a quantitative and critical approach to testing therapeutic claims had become taken for granted in many quarters, although there was opposition in others.

These facts deserve to be more widely known and we are delighted that Dr Tröhler, who is presently Professor of Medical History at the University of Freiburg in Germany, was successfully prevailed upon to write a very readable book based on his insufficiently known research. Although his book will certainly be of interest to historians, it is addressed above all to general medical readers. They will be intrigued by the many parallels between aspects of medicine in 18th century Britain and the evaluation of medical practice today.

Dr Tröhler's book provides a fascinating account of the way that doctors who often had begun their clinical careers outside the medical establishment, used statistics derived from quantified observations to challenge therapeutic dogma based on theory. Many of these men were Scots or Scottish graduates. Perhaps it is no accident that, 200 years later, the work of the Scottish Intercollegiate Guidelines Network is a manifestation of a renewed commitment to challenge therapeutic dogma when it is unsupported by empirical evidence.

PROFESSOR JAMES PETRIE CBE
President, Royal College of Physicians of Edinburgh

SIR IAIN CHALMERS
Director, UK Cochrane Centre

XVI. *An Attempt to improve the Evidence of Medicine.* By GEORGE FORDYCE, M.D. F. R. S. *Fellow of the Royal College of Physicians, and Reader on the Practice of Physic in London.*

THE evidence on which medical knowledge is founded has hitherto been principally deductions from the practice of medical practitioners, made by themſelves, and communicated to the public. The caſes themſelves from which theſe deductions were made have ſeldom been publiſhed; and when they have, they have principally been of extraordinary diſeaſes; and theſe have commonly been ſtated, with a view to ſome particular point, in ſuch a manner that they cannot be brought as evidence ſufficiently accurate to be depended upon.

The following ſcheme is intended to make the evidence in caſes more compleat, by diſſecting them, placing the progreſs of each particular ſymptom by itſelf, and ſhewing its connection with, and the relation it bears to, the other ſymptoms of the diſeaſe.

INTRODUCTION

"Where's the evidence?"

THE question posed by the title of William Silverman's end-of-millennium challenge to clinicians[1] will be familiar to everyone who recognises that things done in the name of health care, although often helpful, are sometimes useless and occasionally harmful. People will answer the question in different ways: students may recite 'textbook knowledge'; inexperienced clinicians may refer to the opinions of their more experienced colleagues; more experienced clinicians, and patients with experience, may refer both to their intuition and to evidence from research. Increasingly, however, all of these actors – and others, such as policy makers – are taking account of the cumulative results of relevant research about the effects of health care.

Those who actually think about the nature of the evidence they have at hand, and the way it was generated, will know that it is transient, the best available at the time, in constant need of improvement, and that it represents probable, rather than certain knowledge. During the past half-century in particular, methods have been gradually developed to achieve exactly this – a constant improvement of evidence. There are many motives for working in this direction, and numerous motives for not doing so. These are currently being pitted against each other in sometimes fierce debates about 'evidence-based medicine', on grounds ranging from philosophy, through clinical practice and morals, to politics, economics and the law.

Many of the issues at stake are linked to the fundamental difference between two types of experience described nearly half a millennium ago by Francis Bacon. Bacon distinguished "ordinary experience", based on chance observations and therefore subjective, and "ordered experience", founded on the results of methodological investigation and aspiring to be objective. Whether subjective or objective, all experience is empirically gained knowledge. By contrast, 'knowledge' based on mere authority, tradition or pathophysiological theory, or deduced from higher 'insight', may be called dogma, which one is expected uncritically to take for granted. The history of the church and the law come to mind immediately when dogma is mentioned; but medical history too has abounded with dogma since antiquity – and still does.

What about the history of empirically gained knowledge? As in many walks of life, the change from dogmatic and certain knowledge, reflecting the wisdom of the ancients (preferably in agreement with the holy scriptures), towards empirical yet probable results based on new observations and interventions, started in the 16th century. It began with studies of human anatomy. These were followed by studies (often animal experiments) to elucidate the function of the newly discovered bodily structures. These two steps are exemplified by the writings of Andreas Vesalius on human anatomy, and by William Harvey's description of the circulation of blood. Their findings were gradually accepted, not only by the medical professions, but also by the churches and the general public. A further century passed before new disease entities were described, for instance by Thomas Sydenham, who has been appropriately referred to as "the British Hippocrates".

Physicians – who constituted the academic profession of medicine up to the 19th century – tended to regard empiricism as the sphere of quacks and surgeons, and indeed an empirical approach was first introduced into therapeutics by surgeons. Out of necessity, surgeons had been more open to direct observation of their essentially localised treatments than theory-driven physicians had been of the systemic approaches that they used to treat disease. In 1536, for example, the military surgeon Ambroise Paré, who grew up near the Château du Houssay in the west of France, described how he had assessed the effects of a remedy for burns using a within-patient controlled comparison:

> *One of the Marshall of Montejan's Kitchen-boys fell by chance into a Cauldron of Oyl, being even almost boiling hot; I being called to dress him, went to the next Apothecary's to fetch refrigerating medicines commonly used in this case: There was present by chance a certain old Countrey woman, who hearing that I desired medicines for a Burn, persuaded me at the first dressing that I should lay two raw Onions beaten with a little salt; for so I should hinder the breaking out of blisters or pustules, as she had found by certain and frequent experience. Wherefore I thought good to try the force of her medicine on this greasie Scullion. I the next day found those parts of his body where the onions lay, to be free from blisters, but the other parts which they had not touched, to be all blistered.*[2]

Efforts to evaluate the effects of other surgical treatments began earlier and were more international than efforts to evaluate medical treatments, and in the third chapter, I outline the development and evaluation of the predominantly surgical treatments for bladder stones and injured and gangrenous limbs.

There are many reasons for the 'delay' in introducing an empirical approach in medicine (as opposed to surgery). One is the fact that, since antiquity, the mark of distinction of a learned man had been the certainty of his knowledge. A doctor *knew* – he did not need to test his kind of knowledge empirically because this would imply acknowledgement of uncertainty. Another reason for the delay was that no new therapeutic strategies had been proposed until the end of the 17th century, when one result of the voyages of discovery was that pharmacopoeias – such as that developed in Edinburgh in 1699[3] – were revised to incorporate the additional herbal drugs that had been collected during circumnavigations of the world. The most prominent of these drugs was Peruvian bark, the bark of the cinchona tree, which we now know contains quinine. It became recommended for 'fever', the most prevalent 'disease' at that time.

In contrast to the much earlier origins of empirical surgical evaluation, it was not until the 18th century that Bacon's distinction between "ordinary experience" and "ordered experience" started to be applied in medicine, and that an empirically-based challenge to previously unchallenged therapeutic dogma began to gather momentum. Unlike the multinational origins of empirical evaluation of surgical therapy, this book makes clear that the introduction of an empirical approach to the evaluation of medical treatments was a largely British initiative, in which the principal actors were medical graduates of Edinburgh University.

The most celebrated of these graduates is probably James Lind. He was born in Scotland in 1716, and like many of the pioneers in the early history of empirical evaluation in medicine, he had only been an apprentice to a local surgeon before becoming a naval surgeon. At the end of the Austrian War he studied medicine in Edinburgh, graduating in 1748 and settling there until 1758, when he was appointed physician to the Haslar Naval Hospital near Portsmouth, a position he held for 25 years.

Lind's prospective clinical experiment, performed in 1747 aboard a ship of the British Navy, is widely known. In order to test the validity of his strong impression about the best treatment for scurvy, which was killing more sailors than military action, Lind took 12 patients, *"as similar as I could have them"*, and assigned two each to one of six treatments, all of which were justified either by dogma or ordinary empirical experience.[4] The two sailors who received two oranges and a lemon daily improved dramatically more quickly than the other ten (see below, page 70).

This book will show that this milestone in therapeutic evaluation did not come 'out of the blue'. It considers the medical and social contexts in which it took place, and what its consequences were. After all, Lind lived until 1794: what did he do after 1747? As a hint, it may be noted here that fruit juice was not introduced into the British Navy for preventing and treating scurvy until 1795, that is, nearly 40 years after the publication of Lind's experiment. Why? Every present day reader could imagine several reasons for the results of clinical trials not being implemented in practice. But what were the reasons in the 18th century? Lind used his position at the Naval Hospital at Haslar to make observations –

mass observations even – particularly in relation to the prevention and treatment of scurvy. However, the use of observations as a scientific tool pre-supposed the will – or the obligation – to record them and Lind realised early that a given therapy was only effective in a certain proportion of cases of any disease. This induced him to design comparative clinical experiments that he analysed numerically. Lind had a number of distinguished pupils, such as the two Scotsmen, Robert Robertson and Gilbert Blane, who by the beginning of the 19th century had completely reorganised the naval medical service, not least with a view to improving scientific knowledge. The introduction of simple arithmetical analyses was clearly of great relevance to the health of the seaman: the scourge of scurvy had been controlled successfully by 1814.

Lind is just one of many pioneers in the British Navy, Army and civilian life who initiated systematic approaches to the assessment of therapy during the second half of the 18th century. The new features of the British scene at that time which facilitated the emergence of these initiatives are outlined in the following chapter, together with the traditional hindrances. For example, dispensaries (outpatient facilities for ambulant patients) and hospitals, both military and civilian, were a unique feature of British health care at that time. Some of these cared for all kinds of ‘curable’ ailments; others were specialised, for example in fevers, childbirth, children’s ailments and rheumatic diseases. Many doctors working in these institutions strove to improve practice and, by introducing measurement into clinical assessment, show how medicine could become elevated to the ranks of the natural sciences. Promoting these changes, they reasoned, would also help to distinguish medicine from old fashioned, theory-driven dogmatism, as well as from superstition and quackery.

Quantitative methods were discussed and implemented – on ships, in the dispensaries and hospitals, and also in private practice – for testing the efficacy of smallpox inoculation and vaccination, old and new drugs (such as foxglove, arsenic and a secret remedy for bladder stone), operations, bathing, and some of the nastier, yet ‘well founded’, systemic treatments such as bleeding and purging. The research methods used ranged from mathematical analysis of case series to prospective experiments with untreated or placebo controls. Proportions, ratios and averages were calculated and probabilities estimated; and the limitations of these investigations, including selection biases, insufficient numbers of observations, and frank cheating, were actively discussed.

Adequate record keeping was propagated as indispensable for medical advance and methods for doing so were developed, even though they could not be enforced in civilian medicine. Indeed, the whole enterprise of methodical numerical assessment of therapy depended on individual and group motivation, which was usually driven – in the words of the practitioners themselves – by values such as candour, honesty, openness of mind, attention to social as well as individual well-being, and a concern to care for the underprivileged, including women and children. The pioneers in these developments in the methodology of therapeutic evaluation indeed saw themselves as reformers of medicine for the public good.

This is not to suggest that they were uninterested in their own status within the profession, particularly as they were typically not from the medical establishment, and were often provincial, usually Scottish.

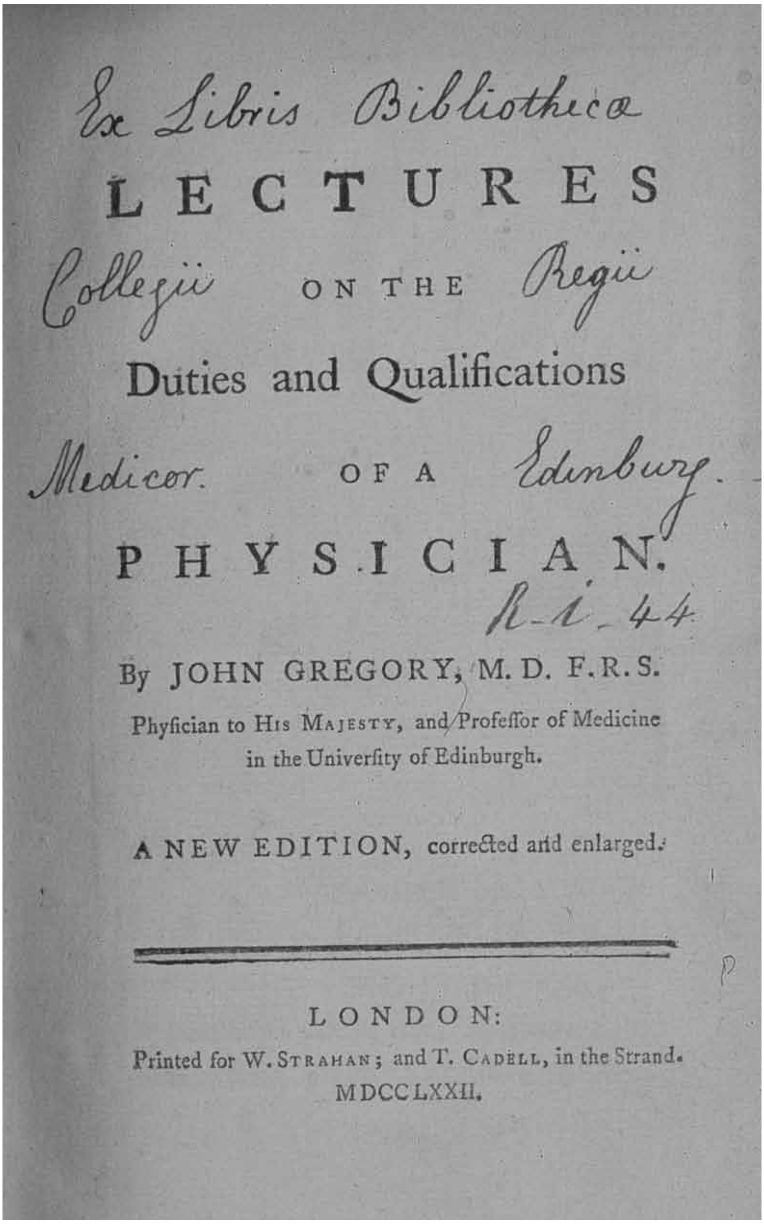
In the hope that it will meet the needs of a general readership more effectively, I have organised most of the text of this book to show how these developments played out in the evaluation of therapies for particular health problems. For example, the treatment of 'fevers', one of the most frequently occurring 'diseases' and the focus of the main therapeutic debate during the 18^{th} century, became more effective as a result of empirical research in both military and civilian medicine. Numerical analysis of hospital reports played a fundamental role in challenging hitherto unquestioned copious bleeding, replacing it with the use of Peruvian bark (cinchona), and re-stressing its value a few decades later. Syphilis was another field in which the value of traditional treatment, in this case with mercury, was challenged using prospective comparative experiments. However, in spite of the demonstration that less toxic treatments were effective for managing early stages of the disease, one member of the London medical establishment criticised the use of British soldiers for experimental purposes. In response, James McGrigor, an Edinburgh-trained Scotsman, head of the Army Medical Service and one of the pioneers celebrated in this book, emphasised the value of military statistics and responded that his investigation was meant:

> *... strictly in that spirit of patience, liberality, candour and fidelity that ought to characterize the inquiries after truth – a spirit altogether remote from the precipitancy of innovation, the acrimony of disputants, or the sticklers for any particular doctrine.*[5]

Discussion of the various issues that I have touched on in this introductory chapter continues today, three centuries after the challenge to therapeutic theories and dogma began in earnest. But have the motives and arguments, as well as their social connotations, changed?

In this book I document the origins of systematic efforts *"to improve the evidence of medicine"* – in the words of another Edinburgh-trained author, George Fordyce.[6] The following chapter gives a brief overview of medicine in 18^{th} century Britain, with an eye on the intellectual and structural context within which these developments took place. In the third chapter, I explore a number of contemporary health care problems and their solutions, as seen by the 18^{th} century pioneers of a critical approach, as well as their opponents. While this part of the book is organised according to disease categories, each example also focuses on particular practical, conceptual, or ethical issues of general importance.

In a concluding chapter I draw together some of the themes that have emerged throughout the book, most of which seem to me to be pertinent to health care, clinical practice and therapeutic evaluation in the 21^{st} century.



Ex Libris Bibliothecæ

LECTURES

Collegii ON THE Regii

Duties and Qualifications

Medicor. OF A Edinburg.

PHYSICIAN.

R-1-44

By JOHN GREGORY, M. D. F. R. S.

Phyſician to HIS MAJESTY, and Profeſſor of Medicine in the Univerſity of Edinburgh.

A NEW EDITION, corrected and enlarged.

LONDON:

Printed for W. STRAHAN; and T. CADELL, in the Strand.

MDCCLXXII.

MEDICINE IN 18TH CENTURY BRITAIN

Challenging dogma, seeking evidence

IN the second half of the 18th century there was a desire to bridge the age-old schism between the dogmatist's and the empiricist's way to truth. This new approach was sometimes called 'rational empiricism', 'intelligent empiricism' or 'systematic empiricism', because it would try to meld apparently rational notions derived from theory (rationalism) with observations made in the real world (empiricism). Previously, by pursuing independent agendas, dogmatists and empiricists had failed to develop a shared framework for obtaining and interpreting reliable evidence.

How did a critical approach evolve under circumstances that blurred some of the differences between the two camps? By 1800, both saw themselves as the true heirs of a Baconian tradition, emphasising planned observation and the piling up of facts. How did the rationalists' need to synthesise their thoughts into a dogmatic system influence the empiricists' demand for observation and experiment in ways that would lead to statistical analysis of well observed facts?

The climate described above was not peculiar to any one country, but it was particularly prevalent in Britain. This reflected the influential challenges to (dogmatic) rationalism by Francis Bacon and John Locke in the 17th century, and the reaction of Scottish Enlightenment 'common sense' philosophy to the scepticism and empiricism for which David Hume argued in the 18th century.

In medicine, early examples of the emerging concept of rational empiricism include Francis Clifton's *Tabular Observations Recommended as the Plainest and Surest Way of Practising and Improving Physick* (1731), and William Hillary's *Inquiry into the Means of Improving Medical Knowledge, by Examining all those Methods, which have Hindered or Increased its Improvement in all Ages* (1761).

A number of British works published between 1760 and 1800 were specifically devoted to this subject. John Gregory formulated the modern principles of rational empiricism most clearly in his *Observations on the Duties and Offices of a Physician* (1770). John Aikin included them in a section of his *Thoughts on Hospitals* (1771), addressed to John Haygarth and read by Thomas Percival, who had himself written two brilliant essays on the dogmatist and the empiricist physician in 1767. James Sims followed with a *Discourse on the Best Method of Prosecuting Medical Enquiries* (1774), and John Coakely Lettsom with *The Improvement of Medicine in London* (1775). John Millar described the method in *The Duty of Physicians* (1776), Thomas Kirkland in his *Inseparability of the Different Branches of Medicine* (1783), George Fordyce in his *Attempt to Improve the Evidence of Medicine* (1793), and an anonymous author in the *Edinburgh Medical and Surgical Journal* under the title *"Is there any certainty in medical science?"* (1805).

Medical societies and their publications

A characteristic feature of the time was the participation of medical men in medical societies. Societies began to become common in Britain around the middle of the 18th century. They were founded both to provide better education than the traditional privileged licensing bodies and also to encourage the communication and comparison of 'facts', whether clinical cases or contributions to biological sciences.

With its group of practitioners led by Alexander Monro *primus* and its (students') Medical Society, Edinburgh had set the example for both types of societies as early as the 1730s. This example was adopted in different parts of Britain, helped not least by migrating Edinburgh students. In London alone at least 12 voluntary associations of medical practitioners were formed from 1746 onwards – some ephemeral, some long lasting. Their names characterise them somewhat: *The Society of Physicians* (1752), *The Society of Licenciate Physicians* (1764), *Guy's Hospital Physical Society* (1771), *The Medical Society of London* (1773), *The Society for the Improvement of Medical Knowledge* (1782), and *The Society for the Improvement of Medical and Chirurgical Knowledge* (1783). By 1830, there were over 40 societies in Scotland, at least 16 provincial societies active in England – for example, at Colchester (1774), Plymouth (1794), Leicester (1800), and Leeds – and two in Ireland.

The Medical Society of London deserves special mention in the context of this book. John Millar (a Scot), its first president, and John Coakley Lettsom, its founder and subsequently president several times, not only presented enthusiastic papers on arithmetic as a basis of judgement in therapy, but put their plans into practice in a way well adapted to the standard of clinical medicine of their time. James Sims, another of the Society's presidents, took up several of his predecessor's ideas. He stressed the importance of mass observation and of simultaneously monitoring untreated cases as a standard of comparison for medical treatment. During Sims' long lasting presidency, William Black was invited to give the annual oration in

1788, and this led eventually to the publication of his important book *Arithmetical and Medical Analysis of the Diseases and Mortality of the Human Species* (1789).

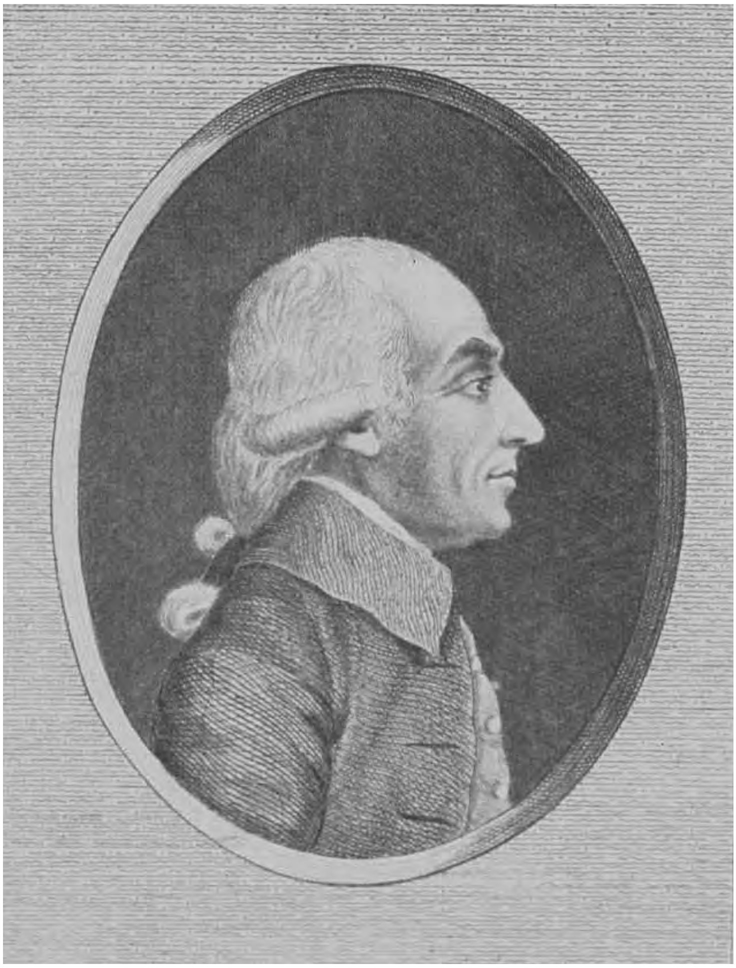
The papers published in the Medical Society of London's *Memoirs* (1787-1805) were comparable to those of the preceding *Medical Observations* of the Society of Physicians (1757-1784), at least as far as the quantitative basis of the arguments presented was concerned. This would suggest on the one hand that the scientific activities within the two societies were not different. On the other hand, in Millar's words, the Medical Society's *"professed design ... [was] to encourage the dissident, to aid the diligent"*, indicating that some of the members saw themselves as outsiders. Indeed one form of 'dissent', the doubt over the value of traditional therapy, was finding open expression within this society. The members present at Black's oration of 1788 also heard of a possible new solution:

> *Physicians have been too long running astray in speculative or frivolous employments of philosophick drudgery ... Medical arithmetick establishes on a solid foundation a multitude of the fundamental principles ... of medical architecture; and erects platforms for compleating the entire superstructure ... In its most extensive application ... [it] may be termed what trigonometry, geometry and the telescope are to the arithmetician and astronomer, or the compass and quadrant to the navigator.*[7]

Black concluded: *"By this criterion we should prove our superiority over the physicians of the Continent"*,[8] thus distancing himself from learned dogmatists in other parts of Europe who, like the famous Herman Boerhaave in Leyden, had published aphorisms rather than actual facts.

These London societies also welcomed communications from corresponding members and from provincial societies without their own outlet for publication, and their periodicals contained papers selected from those read at the meetings. The preface to the first volume usually stated the programme of the society, stressing its methodological direction away from mere abstract reasoning, and insisting instead on observation and the publication only of precisely recorded facts.

A less stable but very influential group – which we can refer to as 'The Warrington Group' – met regularly in this Cheshire town in the 1780s *"in order to explain our professional difficulties and success, and to consult together what might be the best remedies for such dangerous disorders as had occurred in our practice"*. Warrington had a well-known non-conformist academy in the 18th century. Some of the members of the Group had been pupils there, and all were Unitarians.[9] There were thus similarities with the non-conformist membership of the Medical Society of London. But the parallel can be drawn even further. The Warrington Group, too, included physicians and surgeons alike, reflecting the Edinburgh medical scene, where both groups had been able to study at university.



William Black
1749-1829

Again led by Edinburgh, where Alexander Monro's group started publishing society proceedings, many of these societies made an effort to publish regular *Memoirs* or *Transactions*. This new type of medical publication soon superseded the customary methods of issuing printed pamphlets or making casual communications to the unspecialised Royal Society. Before 1790, 23 periodical publications – some ephemeral – appeared in Britain. Between 1791 and 1820, at least another 24 medical journals were started (the *Lancet* appeared in 1823).

The Edinburgh *Medical Essays and Observations*, published in five volumes between 1733 and 1744, reached a fifth edition in 1771, and was praised and translated throughout Europe. The *Medical Observations and Inquiries* published by the London Society of Physicians (in six volumes from 1757 to 1784) saw itself as *"a continuation of that valuable work."* The preface stated that it did not want to be liable to the objection of 'lack of specificity' that had been made against both the *Memoirs* of the Academy of Sciences in Paris and the *Philosophical Transactions* of the Royal Society. One of these 18th century journals – *Medical and Philosophical Commentaries* – was a quarterly review of relevant medical literature, launched in 1773.[10] It was edited by Andrew Duncan, nominally on behalf of "A Society of Physicians in Edinburgh", and was translated into several other languages. The journal was published continuously under a succession of changed titles until (as the *Edinburgh Medical Journal*) it ceased publication after the Second World War.

The Medical Society of London published six volumes of *Memoirs* from 1787 to 1805, and *Transactions* of *Proceedings* from 1810 onwards. After an important group of members had split from them in 1805 to form the Medical and Chirurgical Society, this new body printed *Transactions* from 1809. The Society for Improvement of Medical Knowledge and the Lyceum Medicum Londinense were associated with the *London Medical Journal* (1781-1790), which continued until 1800 as *Medical Facts and Observations*. The Fordyce-Hunter Society issued three volumes of *Transactions* from 1793 to 1812. Even the privileged Royal College of Physicians of London, concerned through the 18th century more with political questions than with promoting scientific advance, issued six volumes of *Medical Transactions* from 1768 to 1820.

Medical periodicals revolutionised the exchange of ideas in medicine. Doctors who would not have been able nor willing to pay for expensive treatises were often regular readers of such periodicals. Furthermore, doctors who would never have dreamed of undertaking the task of writing a treatise could – and often did – write short papers recording their experiences and opinions. Finally, periodicals provided a means whereby individual doctors, hospitals, and dispensaries could publish numerical data and comparisons.

Hospitals and dispensaries

The evaluative and educational mission of the societies and their publications was pursued at a time when political, social and institutional factors seem to have been propitious for the use of statistics in medicine. Although some of these conditions may have been present in other countries, they appear to have been particularly convergent in Georgian Britain.

The crucial missing element in promoting a more statistical approach to the evaluation of medical practice (at least in civilian life) had been the necessary framework for compiling meaningful amounts of clinical and pathological data in less than the lifetime of an individual practitioner. This changed with the development of hospitals and dispensaries, which emerged with the growth of great towns.

The charity hospitals and dispensaries for outpatients are an outstanding feature in the medical history of the reign of George III (1760-1820). In 1760, London had seven general hospitals, six special hospitals and two asylums, with three new hospitals founded over the succeeding 60 years. In the provinces, by contrast, whereas there had been 16 hospitals and one asylum before 1760 (mostly founded after 1736), by 1820, 45 new hospitals and eight new asylums had been established. Naval hospitals also flourished, in Greenwich, and especially with the opening of the Haslar Naval Hospital near Portsmouth and the Royal Naval Hospital in Plymouth, in 1754 and 1758 respectively. Haslar had room for 800 inpatients by 1755, rising to 2,000 by 1780, and there were 1,250 inpatients in Plymouth by 1795. Besides the Chelsea Hospital for retired soldiers, there was an increasing number of facilities for treating active members of the Army. By the end of the Napoleonic wars (1815), every overseas military base had a hospital of some sort, and the Army collaborated with the Navy in using these outstations.

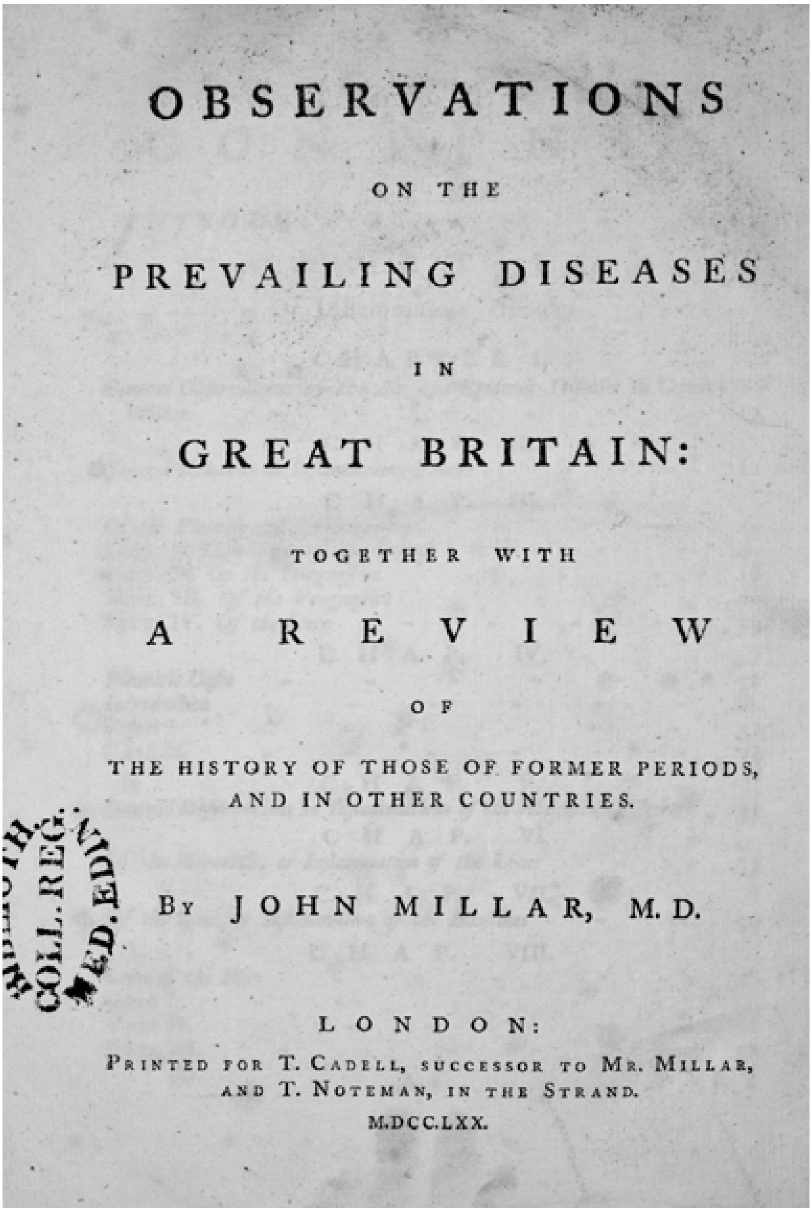
This period also witnessed the foundation of a number of hospitals specialising in the treatment of particular diseases. By 1800, ten maternity hospitals had been founded (four of them in London, not including a department at Middlesex Hospital), two hospitals for venereal disease, one for smallpox and inoculation, one for sea bathing and air therapy for tuberculosis, and at least four fever hospitals (in Chester, Dublin, Manchester and Liverpool). An institution for research into the cure and prevention of contagious fever (the London Fever Hospital) was opened in 1802 and one can speak of a "fever hospital movement". Similarly, a special cancer ward was established at the Middlesex Hospital in 1792, and an "Institution for Investigating the Nature and Cure of Cancer" was opened in 1801.

Administratively, there were differences between these specialised institutions and the all-purpose hospitals, such as the great London hospitals and the provincial infirmaries. General hospitals tended to be dominated by lay governors, whereas the smaller, specialised institutions were usually run by the doctors who established and staffed them.

This distinction also holds true for a number of the dispensaries established for outpatients over the period, most of which emerged as a result of initiatives taken by individual, socially conscious physicians such as John Coakley Lettsom, John Millar, and James Sims in London, John Clark in Newcastle, and Andrew Duncan in Edinburgh. London had no dispensary in 1760, but had 16 by 1800 and 34 by 1820, with 22 and 36 respectively established in the provinces by these dates.

These institutional structures were *a priori* favourable to the application of quantifying methods. However, the qualitative input – that is, the will to take advantage of these institutions by making and recording observations, undertaking experiments, and introducing new therapies – was still needed. But this spirit of research and innovation was not lacking either, as the next chapter will illustrate for the major ailments from which people were suffering at that time.

These developments in hospitals and dispensaries reflect a change in emphasis from simple caring to attempted curing in institutions, as well as the availability of new surgical and medical approaches to treatment requiring appropriate evaluation, in the rational empiricist spirit of the period.



OBSERVATIONS

ON THE

PREVAILING DISEASES

IN

GREAT BRITAIN:

TOGETHER WITH

A REVIEW

OF

THE HISTORY OF THOSE OF FORMER PERIODS, AND IN OTHER COUNTRIES.

BY JOHN MILLAR, M. D.

LONDON:

PRINTED FOR T. CADELL, SUCCESSOR TO MR. MILLAR, AND T. NOTEMAN, IN THE STRAND.

M.DCC.LXX.

EVIDENCE, QUANTIFICATION AND THERAPY

Introducing quantification: The context

THE first two chapters of this book have outlined the intellectual and structural context within which a quantified approach to evidence relevant to clinical practice in 18th century Britain could grow, and some of the forces operating against such a trend. In this introductory section, I consider in general terms how quantification was exploited.

In his *History of Life and Death* (1623), Francis Bacon proposed quantitative descriptions of life span, causes of death and of longevity, size of families, and so on. In his utopian description of the ideal scientific society, *New Atlantis* (1627), there was a collaborative research institute, Solomon's House, where he intended that compilers and abstractors (should we call them statisticians?) would condense such information into *"Titles and Tables to give the better light for the drawing of Observations and Axioms out of them."*[11]

Forty-one years later, Bacon's proposals were taken up by John Graunt, a tradesman who was close to everyday life and death events and to the practical and systematic use of numbers in commercial bookkeeping (or 'shop arithmetic'). Graunt's *Natural and Political Observations Made Upon the Bills of Mortality* (1662) bridged the gap between a 'modern' learned world and the work of the fieldworkers and administrative clerks who had been responsible for the bills of mortality for over a century. Graunt's work appeared with no close English precedents and little warning. This earliest scientific health report was welcomed heartily in the circle of the young Royal Society, as it fitted closely with the prevailing outlook of the members, who self-consciously followed the Baconian injunction of counting, weighing and measuring. Sir William Petty, for instance, was an enthusiastic sponsor of Graunt, and 'political arithmetic' – indeed, the collection and interpretation by very elementary processes of mass observations in the interest of the state or of a policy, got its name from him.

This *"art of reasoning by figures upon things relating to government"*, as political arithmetic was still defined a hundred years later,[12] was not restricted to official circles. Counting and accounting were seen as an important way of thinking in many worlds, and medicine was one of them. Petty himself had calculated in 1676 the economic loss of premature death and drawn attention to the gain, to the state, of a large and healthy population. Doctors and lay sponsors became concerned with the well-being of the whole population or with specific groups within it – such as the labouring poor, soldiers, women, or children – rather than with individual patients only.

The British hospital and dispensary movement of the 18th century was one consequence of this concern and there was a natural bridge to numerical accounting of recovery and death rates within these institutions or the success rates of specific cures – e.g. taking the Bath waters (see below, page 87). So this quantifying culture did not die out in the 18th century, neither in state affairs nor in medicine; quite the contrary. While bills of mortality recording diseases had been issued regularly since 1657, they began to record age and sex in 1728. However, by the mid-18th century, they were justly deemed inadequate, for only the burials of conformists were recorded, and nurses or even ignorant domestics, supplied the diagnoses. From the 1770s, several doctors, such as Thomas Percival in Manchester and William Black in London, suggested practical improvements for collecting and presenting the data for the bills of mortality in order to constitute a 'data bank' usable for clinical research (see below, page 55). Black created, in 1788, the notion of "medical arithmetic" by clear analogy to Petty.

The example of smallpox inoculation illustrates the continuing connection between the prosperity of the state, care for a group of the population, a medical intervention, numerical reasoning, and accounting, over three quarters of the 18th century. In addition, the evaluation of the merits of inoculation – that is, the transfer of lymph from pox pustules from one child to the other – also reflected Bacon's views on the advancement of learning. Just as Bacon had recommended the collection and analysis of descriptive data, so had he postulated the need for enquiries into the effects of diet, exercise and medicine; in other words, approaches to therapy. The practice of inoculation was introduced into Europe by the wife of the British ambassador in Constantinople. The numerical analyses provided the subject matter for a heated controversy, which began in the early 1720s and continued during the greater part of the 18th century. Building on Graunt's example, James Jurin, then secretary to the Royal Society, initiated these quantitative investigations based on the returns from a substantial network of reporting correspondents across Europe. These activities were the first attempts to assess the value of a medical practice by sophisticated mathematical means. Indeed, the first instances of the application of the calculus of probability to a medical problem by two mathematicians, Daniel Bernoulli in Basle and Jean Le Rond d'Alembert in Paris, occurred around 1760.

A later example of the use of numerical data in elucidating means to prevent disease in a group of the population was Charles White's quantitative evaluation of his practice of cleanliness and ventilation in Manchester as prophylaxis against puerperal sepsis, a common cause of death following childbirth. One year after the publication of White's book on obstetrics in 1773 (now considered a milestone in the history of obstetrics), John Coakley Lettsom wrote:

> *In the nurture and management of infants as well as in the [preventive] treatment of lying-in women, the reformation hath equalled that in the smallpox; by these two circumstances alone incredible numbers have been rescued from their grave.*[13]

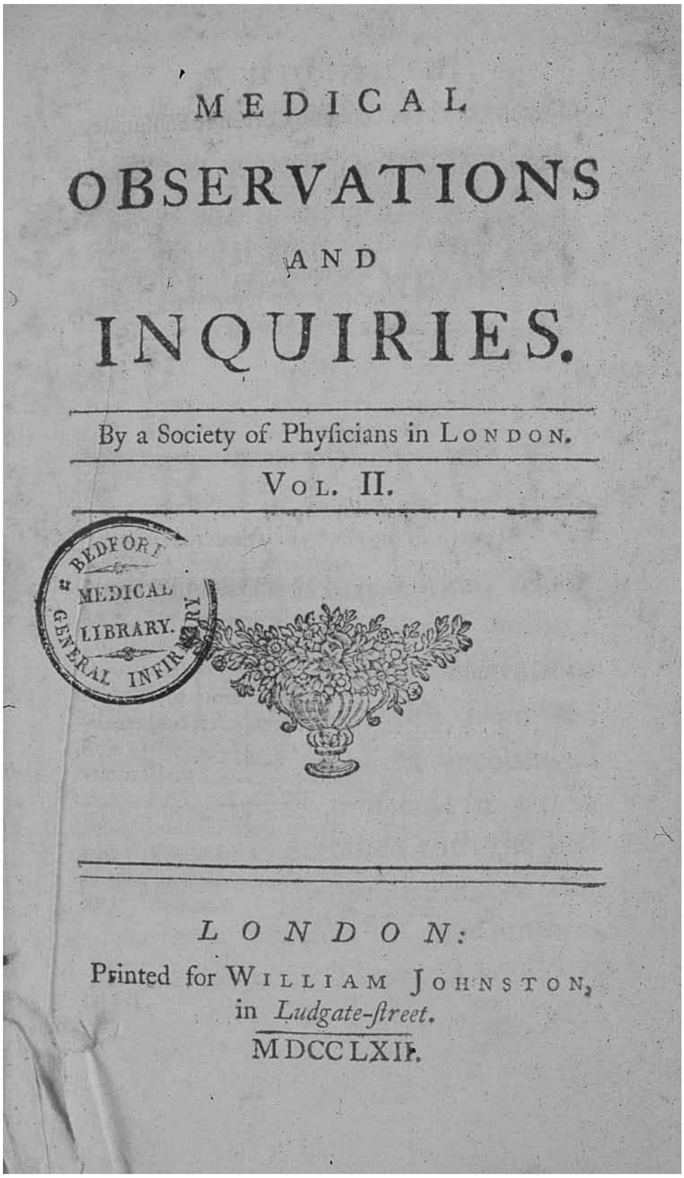
And a further 20 years later, Alexander Gordon of Aberdeen likewise used a numerical approach in his *Treatise on the Epidemic Puerperal Fever of Aberdeen.*

In the previous century, only a few physicians had attempted to adapt statistical – that is, probablistic – methods used to inform disease prevention measures to the analysis of clinical problems. Most physicians followed Sydenham in looking for absolute truth. They understood neither that probabilities could help them, nor that these were inevitable. Truth was certified by the testimony of authoritarian witnesses, a technique still found in many 18th century writings. It was not easy for numerically-minded physicians to break through the encrusted ways and ideas of the traditional medicine of the classicists. By 1750, however, such received medical doctrines were doubted and rational empiricism was being promoted.

The direct link between preventive measures, statistics, and clinical medicine was also made in the second half of the 18th century. In 1780, John Clark, a Scottish dispensary physician at Newcastle-upon-Tyne, (see below, page 43) suggested that statistics on inoculation also provided a good example of how to evaluate therapeutic theories.

This changing atmosphere can be illustrated by the example of the research programme initiated by John Ferriar. He was attached to the Manchester Infirmary, opened in 1752, and a member of The Warrington Group. As he wrote in 1792, it was the work in public hospitals that afforded:

> *... the most favourable opportunities for ascertaining with precision many facts in the history of diseases and for appreciating the value of established methods of cure ... Something may be added to the stock of science, by unwearied attention to a considerable number of patients, indiscriminately taken in a great town.*[14]



MEDICAL

OBSERVATIONS

AND

INQUIRIES.

By a Society of Physicians in LONDON.

VOL. II.

LONDON:

Printed for WILLIAM JOHNSTON,
in *Ludgate-ſtreet.*

MDCCLXII.

Ferriar emphasised that the method *"so fashionable at present of publishing single cases, appears not well calculated to enlarge our knowledge, either of the nature or cure of diseases"*. Indeed, however faithfully recorded and analysed a single instance of success might be, and although the best writers since Bacon had recommended minuteness in descriptions, these were an insecure basis for practice. Ferriar maintained that serial observations (resulting from experiments, clinical cases and autopsies) would become reliable only if they were written down in a journal, regularly updated and including both favourable and unfavourable outcomes of a treatment. This was *"absolutely necessary"* if the physician wanted to avoid those false conclusions he would arrive at *"if he trust[ed] to memory alone"*. Furthermore, data obtained in this way could and must be compared with those of other physicians.[15]

Ferriar believed that medical writers had tended to establish theoretical systems embracing dogmas, and suggested that *"these gentlemen ... would do well to read Mr Locke's chapters on abuse of language. A system ought to be nothing more than the arrangement of [empirical] facts, in convenient order for the memory"*.[16] Ferriar acknowledges in his writings his obligations to Francis Home, a former military surgeon who was then professor of *materia medica* at the University of Edinburgh and one of the physicians at Edinburgh Infirmary.

The armed forces also presented opportunities for mass observation relevant to the prevention and treatment of disease. In the British Army and Navy, as in other countries, there were systems of regular administrative returns and sick lists and duties to keep records. Reports were made to the Army Medical Board of Controul *(sic)* and the Navy Sick and Hurt Board. Both of these were nominally directed by 'amateur' figurehead commissioners (that is, London physicians in private practice) until they were reorganised around 1800, when they became firmly established, with full time personnel.

As John Millar, who had founded the Westminster Dispensary in London, wrote in 1783:

> *When the success of the various methods of treating diseases was first compared, by arithmetical calculation, there were few records on which the comparison could be founded ... [I] was, therefore necessarily led to consult the army returns, as being particularly adapted to that purpose.*[17]

As noted earlier, he and his friends were soon to create their own returns from their civilian institutions.

There was no obligation or direction as to the use of Army returns for scientific purposes. Until the end of the 18th century this was left to the personal initiative of individual surgeons or physicians, mostly men who had not received a higher medical education, but who were commissioned surgeons with craft training.

Prestigious physicians, in contrast, considered filling in forms as belonging to the domain of clerks and administrators rather than as a possible means of advancing their professional knowledge.

In the words of John Thomson, who in 1806 became the first professor of military surgery in Edinburgh, military medicine greatly contributed to the gradual rise of a new approach to medicine:

> *… which, by dissevering all connection with the science of abstract quantity, and allowing medicine to rest on observation and experience alone … threw into the shade all other means of acquiring medical knowledge and regulating medical practice.*[18]

Of the nine personalities Thomson credited by name, only one was not linked with military medicine, and the six Scots among them had all studied in Edinburgh.

As in civilian life, all the pioneers of a quantitative approach in the Army and Navy came from modest backgrounds. They were individualists, motivated, as they said, by humanity and by their love for observations of fact, as distinct from the mass of surgeons who held warrant rank only, and were often known for their tendency to drunkenness and debauchery. Indeed, after 1749, any surgeon who had served in the Army or Navy for at least three years was allowed to enter independent practice outside London without further exams, and this led to a decrease of standards in the country – for at the outset of a war the entry examinations tended to be rather perfunctory! Scotsmen especially, for whom it was otherwise very difficult to set up practice in England, chose this way. Of the approximately 300 naval surgeons listed in 1779, only four had ever published anything. Yet among these were the great pioneers in their respective fields.

Another reason that military medicine, as well as the new hospitals and dispensaries in civilian life, were potentially favourable milieux for the application of quantification was that soldiers, sailors and the poor were regarded rather impersonally in the 18th century as 'lives'. They could therefore be presented by impersonal numbers, and treated according to standard protocols. In contrast, 18th century officers and private patients were attended by their own private physicians, and, in the Hippocratic tradition, were considered as very individual cases indeed.

All these reasons evoked for the development of statistical methods in military medicine held also for the Honourable East India Company, which, as a private, profit-oriented enterprise, insisted on bookkeeping, including records of disease and death of passengers and crew. As from 1770, surgeons had to keep day-books, which were sent eventually to India House in London.

ℵ

In summary, 'observation' made in the real world rather than acceptance of theory-based dogma became a key word in 18th century British medicine and surgery. Although the *quality* of observation was decisive for the description of phenomena, there was a certain trend to lay weight on the *quantity* of observations. This represented a shift away from the search for absolute truth and certainty to the discussion of probabilities. John Gregory taught his Edinburgh students:

> *The advancement of the sciences … requires only an attention to probabilities, to leading principles, … a quick discernment where the greatest probability of success lies, and habits of acting in consequence of this with facility and vigour*.[19]

An analysis of a series of British medical periodicals from 1733 to 1829 has shown the gradual reduction in dependence on single case reports and a growth in the publication of ever larger case series, some of which were analysed by proto-statistical methods. In the following sections of this chapter, there will be many examples showing how this was reflected in arithmetical calculations and trials relating to the treatment of a variety of medical and surgical conditions frequently encountered in the 18th century. The question of certain versus probable knowledge is, of course, of basic relevance. I now consider the debates about how 'reliable' evidence in therapeutics should be generated, and the arguments used to foster various types of evidence, and to dismiss others.

Herman Boerhaave
1668-1738

Certainty versus probability: Sorting out fevers

THE 18th century struggle against fever can be compared with our present day efforts against cancer. Both are major killers of the times. A great deal is known about them, yet there continue to be fundamental disputes regarding their nature and treatment: How many kinds of tumours are there? Just how, in essence, does one kind differ from another? How should they be classified? What are their causes? What is it that makes a tumour malignant?...

If we replace "tumours" with "fevers", these were the questions 18th century doctors asked. And despite a huge mass of relevant partial truths, their ignorance, as ours about cancer, was enormous. The problem was consequently seen by many contemporaries as complex and confused.

For the 18th century physician, fever was a disease rather than a mere symptom. Herman Boerhaave, the outstanding Leyden physician of the early 18th century, defined fever as a triad of rapid pulse, shivering, and heat, with only the rapid pulse being present from the beginning to the end. Fever was a fundamental phenomenon affecting the whole body. This definition, simple as it was, was sufficiently broad to allow for a great variety of complaints to be classified under its heading. Moreover, the pathophysiological mechanisms supposed to underlie the increased pulse were speculative and vague, as also was the long list of causes. These causes had to be envisaged in terms of fluids and systems that would be capable of influencing the state of the whole constitution, that is, the circulatory and/or nervous systems.

The most important British fever expert of his time was probably Richard Mead, a fellow student of Boerhaave at Leyden and, while physician to St. Thomas's Hospital in London, his friend and correspondent. Mead directed his attention to contagion as a possible remote cause of fevers, rejecting the traditional explanation of fevers as being acts of God. Contagion was for him the passage of some unidentifiable chemical substance from one person to the other. Fevers were initially classified using time, the degree of continuity being more important than overall duration. Thus there were *intermittent* fevers, characterised by a succession of paroxysms or fits with complete remissions in between (the duration of the intervals distinguished tertian, quartan, and double tertian fevers). In *remittent* fevers there was a slight but incomplete remission, and in *continuous* fevers there was no remission at all. This three-category classification of fevers was used throughout the 18th and early 19th centuries.

The classification was founded on patients' subjective complaints, that is, their description of their sickness, and on external appearances observed by the doctor. But from about 1790, doctors began to reclassify fevers as distinct disease categories according to post-mortem evidence related to clinical conditions. This anatomo-clinical method allowed, for instance, the distinction between typhus and typhoid – the two main constituents of the former category of 'continuous fever'. This new approach relating *in vivo* observation at the bedside to post-mortem findings in the morgue continued to play a large part in the classification of fevers until the advent of bacteriology in the 1870s, and brought about the classification by causative agents still in use today. This development illustrates the increasing reliance on observations made by doctors, first at the beside, later in the laboratory, which *they* considered objective and therefore more valid.

This snapshot of the history of classification of fevers hints at the difficulty, impossibility even, of retrospective diagnosis – a fact that is clear to every doctor today when thinking of diabetes 50 years ago. It should be borne in mind also when reading about 'scurvy', 'dropsies' and even injuries in the later sections of this book.

As today, 18th century doctors did not feel able to stand idly by; they had to treat their fever patients. Their therapy in the earlier part of the 18th century reflected their pathophysiological theories about fever and speculations about its remote causes. For Boerhaave, therapy consisted chiefly in the elimination of the morbid matter through saliva, vomit, urine or faeces, and cutting short the initial irritation by moderate bloodletting. In his theory and his therapy, Boerhaave followed Thomas Sydenham and the classical authors of antiquity. This can be seen, for instance, in his stressing the need for an individual approach to each patient, an approach that was reinforced by the absence of precise categories of fevers.

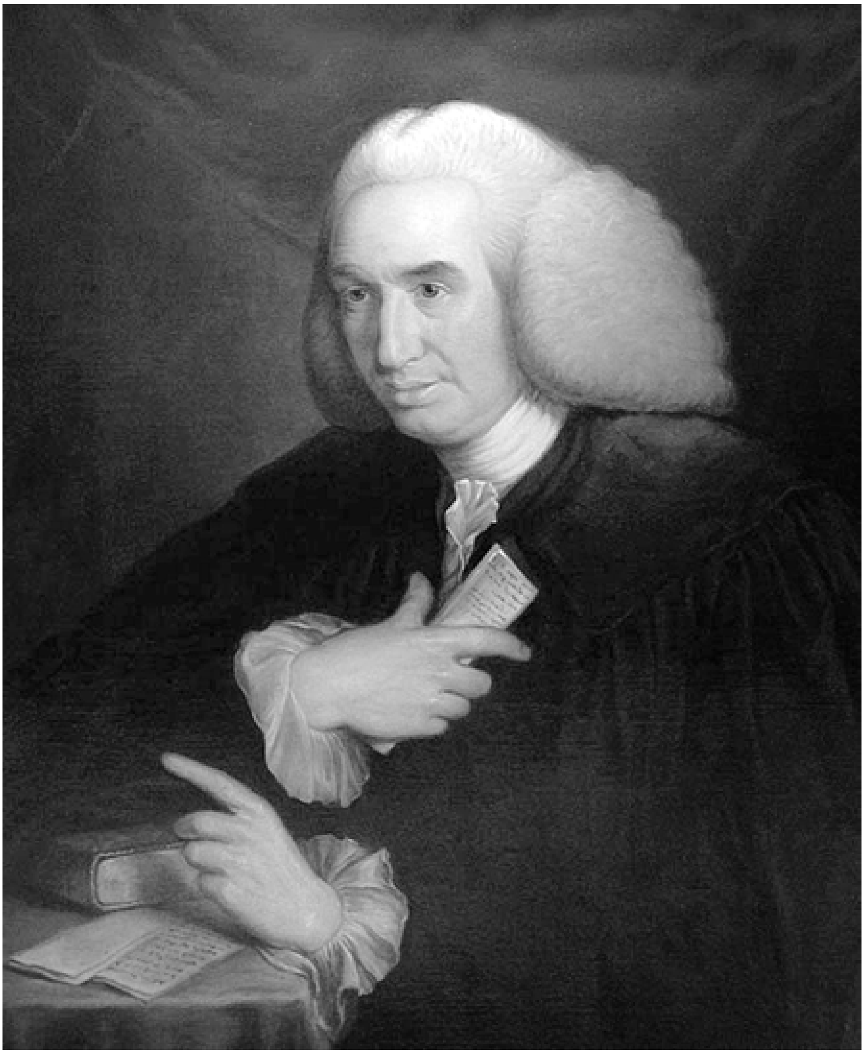
Certain less vague clinical groupings were suggested by the generation of Boerhaave's and Mead's pupils, not least as a consequence of mass observations in the Navy and Army. One influential authority on fever was John Huxham. Though never a regular naval surgeon, he practised at Plymouth among a largely seafaring population, and accompanied the fleet on many occasions. Huxham distinguished between intermittent fever (ague, or malaria), and the 'low nervous' fevers, which when aggravated were called putrid, malignant or pestilential (the latter being accompanied by petechiae). He contrasted this type of general fever with local inflammatory fevers.

Although his classification was still rather confused, Huxham's skill as an observer was apparent throughout his *Essay on Fevers* (1750). His view also had therapeutic consequences, for he recommended cinchona bark for intermittent fevers in accordance with Sydenham, whilst defending more copious bloodletting in inflammatory and other 'general fevers'. Since for him the cause of all fevers was the heat of the blood, venesection was a fundamental and logical therapy.

A more definite step forwards was made by John Pringle (another of Boerhaave's successful pupils and a Fellow of the Royal Society). He did not worship at the Hippocratic shrine but tried to advance knowledge, within the existing framework, by his own observations; and he was not afraid to suspend judgement and to acknowledge his ignorance instead of filling in a gap with ingenious speculations, as Boerhaave would have done. He held theoretical views based on *in vitro* experiments and gave an excellent description of the malignant continuous fevers in camps, jails, ships, and hospitals, which may well have been typhus. Pringle's contribution was more one of attitude, general approach and method, than of detailed contents or discoveries (see below, pages 36 and 107).

Later, it was the great 18th century Edinburgh clinician and teacher William Cullen who aimed to make things orderly and neat in this field. As a systematist, he classified fevers into distinct categories, thereby envisaging them as separate entities. His *pyrexiae*, or febrile diseases, included most of the conditions now thought of as distinct infectious diseases exemplifying the various kinds of relationship between inflammation and fever. Thus, in a first attempt, Cullen distinguished symptomatic fevers, accompanying topical inflammation, from essential, or primary, fevers. The latter were already divided into two groups, the familiar intermittent and the continuous fevers. And finally, there were the exanthemata (the rashes of smallpox, measles and scarlet fever) with their specific cutaneous eruptions.

Cullen also attempted to correct the theory of fevers inherited from his forerunners. Influenced by the rudimentary neurophysiology of his time, he attempted to explain the pathogenesis of fevers by substituting Boerhaave's "lentor of the fluids" with an equally hypothetical "spasm of the arteries". As to the many causative factors of the earlier 18th century, he dismissed a number of these by his emphasis on contagions. Indeed, impressed by the epidemic character of many fevers, he thought that *"some matter floating in the atmosphere and applied to the bodies of men, ought to be considered as the remote cause of fevers*".[20] These effluents were of two sorts, the *contagions* originating from the bodies of humans suffering from a particular disease and capable of exciting the same disease in another person; and the *miasmata* arising from marshes and moist ground – that is, environmental sources. Cullen did not believe that there was a variety of specific contagions, attributing the differences between the various febrile states of continuous fevers to environmental circumstances (seasons, climate) rather than to distinct contagions. This view was challenged in the 1770s and 1780s because of similar descriptions by naval and military surgeons



William Cullen
1710-1790

from very different climates. Cullen himself was not dogmatic, recognising that jail or hospital fever seemed somewhat different from other forms.

Neither was Cullen dogmatic in terms of therapy. He did not add any significant practical contribution. He knew that therapy would not attack the contagious material directly. Symptomatically, the spasm of the arteries had to be removed, which would be accomplished by the familiar remedies: rational hygienic measures, bloodletting practised with discrimination, purges and blisters. This was followed by correction of the prostration (or 'debility') as well as by combating putrefaction with stimulants including cinchona bark, wine and 'antiseptics'.

These were, interestingly enough, the same principles that remained in vogue until well into the 20th century. Bloodletting had, as we shall see, its ups-and-downs and finally lost its popularity in the 1850s, but until the discovery of antibiotics, the inability directly to combat contagion remained.

By 1800, observationist doctors tended to favour the view that there were specific fever categories. Yet it must be pointed out that the specificity was not derived from the supposed specificity of a causative agent (which was still hypothetical until the advent of bacteriology) but rather from that of the clinical picture, particularly the cutaneous findings.

The specificity of fevers also became reflected in therapeutic recommendations. For typhus, for instance, the picture of a contagious fever, associated with clinical debility and cutaneous eruptions, had been built up during the second half of the 18th century. Because of the weakness accompanying this and other contagious diseases, patients would not bear bloodletting, although this was used by some practitioners in endemic diseases of 'miasmatic' origin, such as the yellow fever of the tropics.

Yet once more the views on fever changed. Specific identities were lost around 1810 during what has been called the "British bloodletting revolution". Under the influence of Londoners such as Henry Clutterbuck, John Armstrong and others, not only did specific fevers lose their identity, but even the varying 'types' of fevers in different years or seasons tended to become less identifiable. Based upon autopsy findings of 'inflammation' in cases of typhus (later in other forms of fevers, too) this was now seen as a congestive, inflammatory disease, thus overloading the patient's strength. This meant that the clinically observed debility was 'indirect' and could be relieved by bleeding and purging away the excessive congestion. This view seems to have prevailed for continuous fevers right into the 1830s in Britain (see below, page 47). Meanwhile, the nature (basically, the contagiousness) and the cure of tropical fevers still remained controversial, as reflected in the heated debates over the utility of quarantine in the 1810s and 1820s.

It is against this changing background of identification, classification, patho-physiological mechanisms and causative explanations of fever, that the therapeutic issues, which I discuss next, must be seen. As fevers were so important as the great killers of the day, there is an overwhelming volume of literature on the subject. Fevers are a difficult and muddling part of medical history – and were indeed already considered so by critical 18th century men. I will now concentrate on documenting those aspects that illustrate the whole range of approaches to quantification that were introduced to disentangle the subject of fevers in order to familiarise the reader with the general theme of this book.

SPECIFIC REMEDIES FOR DISTINCT TYPES OF FEVER

At the beginning of this section it is worth saying something about the rationale for venesection, since, from a present day point of view, one easily thinks that bleeding could only do harm. Its persistence until the 1850s was certainly in part due to ancient authority, but this was not the only reason.

Today we recognise that blood is wholly precious and that – rare diseases apart – it is benign and one cannot have too much of it. In the 18th century, however, blood was perceived both as essential to life and also, at certain times and in certain ways, as a potentially evil substance in that it was the direct cause of inflammation, and of all inflammatory diseases.[21]

Thomas Watson in his *Lectures on the Principles and Practice of Physic* (1843) wrote that *"… an inflamed part contains a preternatural quantity of red blood …"*. To Watson and his contemporaries it seemed obvious that the redness, heat and swelling that typified an inflamed area must be directly due to an excess of blood and the pressure with which it was forced into the inflamed area. Logic suggested that removing blood was the only way to diminish the pressure and quantity of 'bad' blood, and hence cure the inflammation.

If the inflammation was purely local, blood could be removed by leeches. If the inflammation was general, as in an inflammatory fever, one could see the blood in the red face of the patient, feel its heat in the form of fever, and note a strong rapid pulse. It seemed self-evident that an inflammatory fever must be due to an excess of hot inflammatory blood driven with excessive force. Therefore, venesection was called for. But this was only the case in this type of fever, never in the 'aesthenic' or 'nervous low' fevers. In the latter, the patient looked pale, lay still in the bed (in inflammatory fevers the patient was usually restless) and was too weak to sit up, with a cold sweat and a weak pulse. For such low nervous fevers, venesection could be fatal and would never do any good. Unfortunately, there were sometimes individual patients whose fever seemed to be inflammatory on Monday, low nervous on Tuesday, and inflammatory again on Wednesday. Judgement was then very tricky, but who said medicine was supposed to be easy? Incidentally, the concepts of a disease or group of diseases in which there was too *little* blood – the anaemias – hardly existed before the 1850s.

Only after taking account of this kind of thinking does it become possible to understand how intelligent doctors could believe so strongly in venesection. And this underlines the importance of the methods required and used to demonstrate that, contrary to accepted standards with an apparently strong logical basis, bleeding was not (or was less) effective in curing fevers. Indeed, even James Currie, who propagated cold water treatment as an alternative or complementary therapy (see below, page 51), was himself bled (too copiously) when he suffered from fever in 1805 – and succumbed.

James Lind was not only an authority on scurvy, but used his position at Haslar Hospital for an extensive study of fevers. The first outcome was *Two Papers on Fever* (1763), which dealt mainly with jail, hospital and ship fever. The introduction echoes that to his *Treatise on the Scurvy*:

> *A very extensive practice in fevers during three years in one of the first hospitals in Europe, qualifies me, in some measure, for making researches into the dark and abstruse subject of infection, [to elucidate] a chaos of contradicting precepts.*[22]

Lind was a practical man, with a duty to perform, and he had little patience with the then innumerable attempts to classify or to account for fevers theoretically. He classified fevers according to where they occurred rather than by their accompanying symptoms. He realised that jail fever, hospital fever and ship fever were the same, that they had the same aetiology, namely crowds, dirt, close contact, and semi-starvation. A number of statistical returns from ships and from his hospital illustrated his opinion that fever was *"of all diseases … the most destructive of mankind"*.[23]

These statistical returns also supported his view that the common ship fever was infectious, as all his epidemiological conclusions and hygienic recommendations were based on such numerically stated facts. To reduce contagion he adopted strict measures of isolation and burned infected clothing. He fumigated the wards with brimstone, tobacco or gunpowder; and introduced separate fever wards at Haslar 20 years before John Haygarth did so in Chester, thereby initiating the 'fever hospital movement' (see above, page 12). Lind was keen to record the result of this innovation, especially the containment of contagion. He wrote:

> *As the best proof of the efficacy of any method, is the success with which it is attended, I here give you an account of the mortality amongst the nurses, servants and all other persons in the hospital (exclusive of the patients), from June 1758 to January 1760.*[24]

As to therapy, Lind made some judicious statements, too*: "I have often thought"*, he wrote, *"that publishing only one or two singular or particular cases, does more harm than good".* If the mode of treatment was said to be useful on the basis of such evidence, Lind contended that this was not convincing enough to exclude the possibility that the patient's constitution alone had led to recovery. Conversely, if it was said to be ineffective, this did not preclude its efficacy in many other cases – for, as he stressed, *"… all the maxims of physic are limited, and there is in it no universal infallible method or remedy"*.[25]

In other words, although Lind was clear that a general plan could be derived from a large series of observations, this did not mean that such a plan would apply to every case.

In practical terms Lind recommended bleeding only occasionally, in cases of light fever, and thought it dangerous in malignant pestilential fever (typhus). For this he recommended certain antimonial medicines as febrifuges (see below, page 53), local blistering, and enemas, still hoping that a specific therapy might be found (as cinchona bark had been for the intermittent fevers). In accordance with his general outlook, Lind claimed that his observations merited attention as they were not founded on private opinion *"or on any one particular case, which might prove an exception to a general established principle in practice. They are the result of some thousand patients, whose cases are still preserved in the hospital"*.[26] In fact, during the visit of the Russian fleet in 1769, 1,521 cases of typhus (among 4,200 men) were landed at Haslar, and only 86 of them died.

In 1768, Lind published the first edition of an *Essay on Diseases … in Hot Climates*, a standard work of which there were still editions produced in Britain 40 years later and in America even in the 1810s. A long 'Appendix' dealt with agues (intermittent fevers, malaria). In practice, Lind's plan consisted in bringing about a remission of the first febrile convulsion by tartar, blistering and opium, but not bleeding; then continuing with cinchona bark. As with scurvy, he listed over 50 other possible treatments that might occasionally be helpful, but suggested that his simple plan would usually suffice for all types of agues. He gave his numerical results, but not in great detail: *"Of between four and five hundred patients with remitting or intermittent fevers, under my care in the year 1765, I lost but two; neither of whom had taken the bark."*[27]

The choice of bark for intermittent fevers probably needed no special justification in Lind's opinion, since Sydenham had already recommended it. His use of opium to abort the first febrile convulsion, however, was based on the following trial: In one fever ward, Lind had given it to all 25 patients, 19 of whom had felt immediate relief; with three there had been no change, and the three remaining had not taken it (no results stated). Upon this success, Lind administered opium to another dozen patients the next day, in 11 of whom it removed the headache and abated the fever, so that bark could be started earlier than usual. Since that time he had (at the moment of publication of his *Essay*) given opiates *"to upwards of three hundred patients labouring under this disease"*[28] and noticed its effect on the febrile convulsion. After Alexander Monro (see below, page 95), Lind was perhaps the first physician to publish success rates obtained in one group of diseases, with one known method, in one hospital, during a given time.

PERUVIAN BARK AND BLOODLETTING: FROM SPECIFICS TO PANACEAS

Evaluations in London dispensaries

While the value of Peruvian (cinchona) bark in intermittent fevers was obvious – rather like penicillin in lobar pneumonia in the 1950s – questions about its use in other categories of fever were hotly debated throughout the second half of the 18th century. John Coakley Lettsom, for instance, founder of the Aldersgate Dispensary in London, described the issue and how he had found a way to solve it in his *Medical Memoirs* (1774). He wrote that, prior to his election as physician:

> *... a painful sensation was ... excited in my breast at the loss of patients by the usual ro[u]tine, when I reflected that another method of treatment might probably have proved successful. By my election to the General Dispensary, a more extensive field of practice afforded me daily opportunities of ascertaining the doubts, and clearing up the difficulties, under which I had laboured ...*[29]

Having criticised the current antiphlogistic therapy with emetics and bleeding for some time, Lettsom was now able to claim that this old practice, frequently fatal, had given way to an almost uniform success by using of cinchona bark and ventilation. And this was no haphazard conclusion arrived at in a casual way:

> *From the useful hints suggested by my ingenious friend Dr Percival ... I was induced to keep an exact register of the diseases and deaths which fell under my observation in the ... Dispensary, agreeable to the following tables which include a period of twelve months.*[30]

From those tables, one could see that he had indeed lost only a few of his fever patients between April 1773 and March 1774: 3 out of 22 from *febris intermittens*, 3 out of 65 from *febris nervosa*, 8 out of 192 from *febris putrida*, none out of 82 from *febris remittens*, and none out of 29 from *febris simplex*. This dispensary report provided monthly figures of patients admitted and discharged as 'cured', 'irregular', 'improper', or 'dead', from which an average annual proportional mortality was calculated (1:37.5 in the present case). Applying Thomas Percival's suggestions for the improvement of the bills of mortality (see above, page 16) to his own dispensary practice, Lettsom drew up two additional tables. In the second, he divided all cases he had seen into diagnostic categories and computed their total incidences in one year. In a third table he listed, again in monthly distribution, the numbers of fatal cases of each disease; even recording with symbols the marital status and age of each of the deceased.

Another advocate of the replacement of bleeding and vomiting (by the administration of antimonials) by cinchona bark was John Millar, a Scot associated with the Westminster Dispensary in London. A historical review of the various methods of cure for putrid inflammatory fevers proposed since Hippocrates first suggested to him that cinchona bark might be the only dependable remedy. For recent evidence he referred among others to Lind's trials at Haslar Hospital (see above, page 29). A comparison of the description of the agues and remittent fevers by military and naval surgeons from different places on the globe further suggested to Millar that remittent fevers might also be managed successfully without the traditional evacuating cures. Were they not related to the ague, in which the bark showed good effects, according to the accounts of Lind and George Cleghorn? Millar had also started prescribing cinchona bark for remittent fevers, against Boerhaave's authority, and claimed several years' success. He reported 19 cases in which those treated with the new method survived, whereas the others died. But the final vindication of his theoretical and practical views came only in 1777 from the analysis of his dispensary practice, which had provided the opportunity to put his research programme into effect.

Millar's *Observations on the Practice in the Medical Department of the Westminster General Dispensary...* (1777) suggest how he actually did it. Since, as he claimed, opposition was feared, a clerk was appointed (so that nothing might depend on the testimony of physicians) to keep the records and make out the returns. Such an account of an institution which was, in addition, open for public inspection, was for Millar part of the demystification, or the reformation, of medicine, just as the Reformation in religion had put an end to the withholding of the Scriptures from the laity. For, in his opinion:

> *... the priests of the Temple of Aesculapius [still] continue their oracular ambiguity, involve their art in tenfold obscurity, and in hiding it from others, conceal it from themselves.*[31]

Millar acknowledged the complexity, greater than in any other science, of asserting the *"comparative merit of different medicines and methods of cures"*.[32] This explained the success of mountebanks and even permitted an established Licentiate of the Royal College of Physicians of London (Dr Robert James: see below, page 55) to withhold the recipe of the medicine he sold and extolled. As with Lettsom, both practices were thorns in Millar's side. To resolve such questions he believed that one needed demonstrations by "incontestable evidence", declaring that *"Error ought not to be sanctified by custom ... nor concealed by mystery and reserve; nor the test of arithmetical calculation evaded"*. For this latter:

> *... detached cases, however numerous and well attested are insufficient to support general conclusions; but by recording every case in a public and extensive practice, and comparing the success of various methods of cure with the unassisted efforts of nature some useful information may be obtained; and the dignity of the profession may be vindicated from vague declaration and groundless aspersions.*[33]

There could hardly be a stronger plea for numerical analysis!

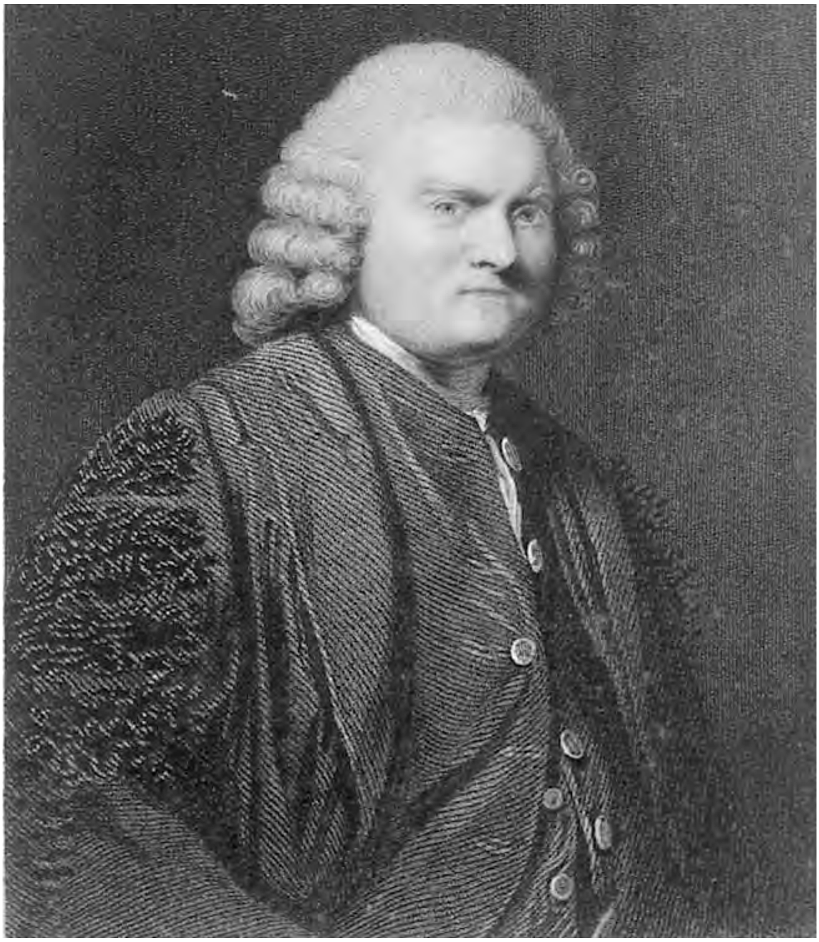
Millar published two tables of all cases treated in the first two years of practice at the Dispensary, compiled from monthly returns, featuring for each disease the numbers of patients admitted, cured, relieved, and discharged into other hospitals. Separate columns indicated the numbers of 'improper subjects' (that is, those not likely to receive any benefit), of cases too advanced for treatment, irregular attenders, and deaths. These latter groups were further analysed according to diagnosis and 'event'.

Such returns, Millar thought, ought not only to be introduced in all charity establishments but also in the Army and Navy. In a wholesale attack on military surgeons, in which he used comparative figures (sometimes uncritically, a blunder which he must have known himself when one considers his criticism of others), he evidently intended to promote a change in the military's handling of fever in the forthcoming American War. At the same time he hammered into people's minds that arithmetical analysis of recorded data was the sole basis for evaluating a therapy. This he pursued with unceasing insistence, and engaging considerable private financial means, until 1802. Although he was verbose and repetitious, some of his passages were remarkably shrewd; and he had positive numerical evidence for his fight against the advocates of bleeding (early and copious), blistering, and purging in fevers.

Millar first compared general mortality rates of big cities (for example, London 1 in 20 inhabitants, Vienna 1 in 19.5, Berlin 1 in 45), with those of the Army in the Seven Years' War in Germany (1 in 16, 1 in 8, and 1 in 6, for 1759, 1760, and 1761, respectively). This difference, he thought, might partly be accounted for by a difference in air and manner of life. Yet he declared that doctors ought to reconsider their practice, too; for from some hospital returns which an anonymous friend had procured for him, and from the death lists of the British regiments, it transpired that 1,300 out of 20,000 soldiers had died from wounds obtained in action, but 6,500 from diseases – a mortality among the sick of over 50%. This was about double the mortality in the British military hospitals in Flanders during the earlier War of the Austrian Succession, for which Millar compiled a table from the returns delivered to the commander in chief of the Army. For Pringle's hospitals, for instance, he calculated the following figures:

Physician	***Hospital***	***Year***	***Period***	***Admitted***	***Dead***	***Proportion***
J. Pringle	*Brussels*	*1744*	*28/4-24/12*	*1,259*	*89*	*1:15*
J. Pringle	*Maastricht*	*1746/7*	*26/7-28/2*	*1,165*	*119*	*nearly 1:9*

The average mortality he calculated to have been at least 1 in 9. But the mortalities in the hospitals in the Seven Years' War (that is, 50%) looked even worse when compared with those in civil hospitals in Britain (where they varied between 1 in 13 and 1 in 20), in Amsterdam (1 in 7) and in Paris (1 in 7 in the Hôtel-Dieu). The situation seemed yet more dreadful if compared with that in



Sir John Pringle
1707-1782

the dispensaries. Lettsom's Aldersgate Dispensary had a mortality of 1 in 33, Millar's own Westminster Dispensary 1 in 110. Even if the deaths omitted due to Millar's peculiar listing were considered, one arrived at 1 in 30 at the worst. Information on British hospitals was available from analysts of vital statistics, such as the Reverend Price and Thomas Percival, while he had obtained that about Paris and Amsterdam from a medical friend who had travelled on the continent.

Millar used these figures to prove that the mortality of fevers treated without antimony and bleeding could be kept very low. He had to assume that camp fever (typhus?) had been the most prevalent disease in both military and civil institutions, for although he and Lettsom had published specific mortalities of fever, such figures were not available for the Austrian and Seven Years' Wars. In 1779 and 1783, however, Millar would be able to make a specific comparison.

Perhaps it was Millar's aggressive tone, perhaps his deliberate struggle against authority, which incurred the wrath of some established authors, such as Donald Monro and Sir John Pringle. This was expressed in pamphlets and papers written against Millar's publications of 1770 and 1777 in which they justified their own practice polemically, yet without his kind of data. (Pringle was involved in this, it seems, even though his brother had been cured of fever by Millar in 1762.) Millar's presentation of unspecific results provided easy opportunities for criticism, but such criticism was philosophical rather than based on factual evidence. In 1778, opposition also arose against the whole system of record keeping at the dispensary and Millar lost his clerk, Thomas Dickson Reide. In 1779, he wrote that the registers now kept were useless for scientific purposes.

Nevertheless, after his 1777 report, Millar continued his assiduous campaign for the abolition of "vampyrism" in the Army, for which statistical returns were crucial. In the following year, he made this clear in his *Observations on the Management of the Prevailing Diseases in Great Britain, Particularly in the Army and Navy*, privately printed and freely distributed in early 1779 to the official departments concerned. Having further confirmed his conviction about the importance of reliable registers at the Westminster Dispensary, he wrote that an *"abstract of the returns of the military hospitals in Flanders and Germany renders it easy to reduce to numbers, and compare the effect of a contrary practice"*.[34] In these *Observations* he thus reprinted all the tables already included in the 1777 report with appropriate references and two important additions regarding the method to generate the right kind of evidence.

Firstly, Millar thought that:

> *... as a standard for comparing the various success of different methods of cure, it will be proper to ascertain the ordinary termination of disease when left to the unassisted efforts of the constitution ... Hippocrates has given an account of the progress of fevers under careful domestic management and this may be taken as a standard ...*[35]

Millar then subjoined the numerical details of 42 cases from a Hippocratic text – also used later for the same purpose by Gilbert Blane (yet another Edinburgh-trained Scotsman) and Francis Bisset Hawkins (see below, pages 79 and 126). He asserted that the antiphlogistic treatment, confirmed by authorities such as Boerhaave, could actually be traced back to Galen in the second century AD, the greatest doctor of later antiquity. According to Millar, Galen had narrated:

> *... in his manner, a miraculous story of the effects of bleeding, which were so palpably evident, that the spectators exclaimed, O! wonderful Doctor! Since then, the practice has always been general but never successful.*[36]

Secondly, Millar looked at fevers from a new point of view. There was no disease more fatal than putrid fever: its mortality in the last war had been even greater than that of the plagues of London in the 17th century, as calculated by Graunt. This indicated, he felt, a *"degeneration of medicine"*, which brought the practice of physic into discredit, and increased that of quacks. Did the established physicians such as Donald Monro, Pringle and their friends consider such high mortalities normal? They even wondered how in Professor Haen's practice in Vienna only 12 out of 500 ill with malignant fever could have died, bluntly pretending that the diagnosis must have been mistaken, that the fevers in Vienna were probably less acute than in London, and that Haen's petechiae were only flea bites! Millar replied with a statistical argument against these assertions:

> *It may be fairly presumed that in an equal number of fevers at Vienna and London, or elsewhere, an equal proportion of slight and dangerous cases would originally occur.*

He claimed that mortality was lower in Vienna because Haen had treated his patients properly, that is, only with unspecific cordials in light cases and the bark in difficult ones. He apologised to Pringle for having been obliged to quote him so often in a bad light and concluded with a classical quotation familiar to a learned gentleman: *"Amicus Socrates, Amicus Plato, sed magis Amica vertitas" (sic).*[37] [You're a friend Socrates, you're a friend Plato, but our greater friend is Truth.]

In fact, Pringle himself had already yielded to evidence, for in a published appreciation of the explorer James Cook (see below, page 75) in 1776 he had admitted that bleeding was not indispensable. This was noted with satisfaction by Millar in 1779. By then he was also able to give additional evidence for his case in the form of specific mortalities of fevers from different sources. He relied chiefly on statistical reports, such as those from Lettsom's Dispensary (which showed a decrease of fever mortality after the introduction of bark in 1773), from John Clark's *Observations*, and from the naval doctor Robert Robertson (see below, pages 39 and 43). Finally, Millar advocated his use of recorded mass observation for the evaluation of therapy (similar to that of Lettsom: see above, page 31) be adopted by the Army.

This work, stormy in style and farsighted in presentation of the data and in its outlook provoked a mixed reception. Soon after its publication, William Hunter, the prestigious London physician, obstetrician and part-time Commissioner of the Navy Sick and Hurt Board (see above, page 19), wrote to Millar:

> *I have already read the whole; and, admitting the facts (and no doubt you will take care to be accurate) anybody but myself would be surprised. The publication would be of great use at this time, especially in America. The Lord in his mercy keep us out of the hands of ... [Pringle?] in this world, and the Devil in the next.*[38]

In December 1778, Hunter arranged that Millar's *Observations* be given to Lord Amherst, the commander in chief. But this plan was allegedly obstructed by ministers and by officers until the 1790s, whilst the traditional anti-inflammatory evacuation therapies (bleeding, vomiting and purging) for fevers and dysentery continued.

The North American Campaign (1775-1781) turned out to be a disaster under General Cornwallis, both militarily and medically. Millar suggested that there was a relationship between the two, accusing the military administration of mismanagement and failure to recognise what had already been clearly proven. In 1783, in a *Reply* to Donald Monro's vehement self-defence, Millar again illustrated the advantage of 'mild' treatment of fever with a striking series of numerically stated results; these were drawn together in a table showing the comparative success of different methods of treating fevers, taken chiefly from the recent writings by Robertson, whom he had met in 1779 and others, even from Monro himself. In terms of mortality this table again showed the clear advantage of bark treatment over bleeding and evacuation therapy (BE), other medicaments, and the practice of allowing the disease to take its natural course. Millar did not refrain from including non-numerical statements, such as *"almost all (or none) died"* in the table (reproduced overleaf).[39]

After the American War, Millar continued his crusade for improving medicine by rendering the results of medical practice more transparent, *"with the same zeal and ardour ... [as] the indispensable duty of a citizen of the world"*. His account of his trip to France in 1788, of how the publication of his plan in Paris was withheld by the intervention of the English Government with the aid of Mirabeau, is almost unbelievable and deserves separate study.[40] However, at the onset of the Revolutionary War in January 1792, Millar was finally received at the Secretary of State's office in Whitehall, where he presented a *Memorial* to the President of the Board of Control. He underlined the advantages of the precise control of medical practice by including in his *Memorial* the reports of his former pupils Thomas Dickson Reide and John Marshall, and Clark's analysis of the returns instituted by the Honourable East India Company in 1770. On considering the Memorial, the President of the Board of Control ordered a plan to be immediately made out along the lines of the East India Company. It was delivered

Place	***Therapy***	***Patients ill***	***Death rate***	***Reference***
San Juan	*BE*	*400*	*"almost all"*	*T. Dancer*
Senegal	*BE*	*?*	*"almost all"*	*Schotte*
New York	*camphor*	*36*	*"nearly 1 in 7"*	*R. Robertson*
Rhode Island	*antimonials*	*26*	*"more than 1 in 7"*	-
Gibraltar	*antimonials & camphor*	*570* *437*	*1 in 10* *1 in 13*	- -
Coxheath	*BE, antimonials bark later*	*?*	*1 in 17*	*D. Monro*
St.Lucia	*antimonials, cooling medicines, bark*	*105*	*1 in 15*	*J. Rollo*
Senegal E	*bark*	*?*	*"almost nil"*	*Schotte*
HMS "Edgar"				
1779/80	*bark, early*	*475*	*1 in 80*	*Robertson*
1781/82	*bark, early*	*177*	*nil*	-
HMS "Juno"	*bark, early*	*216*	*1 in 215*	-
HMS "Juno"	*unspecific cordials (i.e. natural course of the disease)*	*296*	*"nearly 1 in 49"*	-

** The underlined figures are in Millar's original table or in the descriptive text of his 1783 monograph. The other figures have been added from the original references quoted by Millar.*

by Millar three days later and transmitted to the Secretary of War and the Chairman of the Company. His own estimation of the plan can be seen in Millar's statement that *"It would be improper to publish that plan at the present, lest the advantages to be derived from it ... should be improved against us by our enemies"*.[41]

Nevertheless, in 1798, Millar published "*An Appeal to the People of Great Britain on the State of Medicine in England ...*". This was intended to show the reader that medicine was no longer the concern of individual physicians but was extremely relevant to political economy and military affairs, and was necessary for the successful direction of the business of the state. As such, medicine was in turn influenced by them and ought to adopt their modern techniques, such as arithmetic:

> *Where Mathematical Reasoning can be had, it is a great folly to make use of any other, as to grope for a thing in the dark, when you have a candle standing by you.*[42]

Millar was perhaps the most aggressive of the civilian physicians fighting for the overthrow of the anti-inflammatory therapy of fevers as based on the mere authority of Boerhaave and Pringle. He argued for its replacement by Peruvian bark, whose superior value, he maintained, had been proved by numerical comparison. But he was not alone. Besides Lettsom, there were also, for instance, Robert Robertson in the Navy, John Clark in the East India Company, and Thomas Dickson Reide, John Marshall and William Rowley in the Army, who all continued numerical reporting when later in hospital or private practice.

Work in the Navy

Robert Robertson, like John Millar, has been unduly neglected or misrepresented by historians. He was a Scot who entered the Naval medical service with the low rank of surgeon's mate in 1760. He was thus on active duty during the Seven Years' War and remained so until the end of the American War in 1783. Early in his career he started keeping accurate registers, not to be *"cursory remarks made for amusement in the idle ... hours"* but clearly meant as a:

> *... specimen of a plan for obtaining a further knowledge concerning diseases, by recommending to gentlemen of greater abilities and experience, especially surgeons of the Royal Navy, the keeping of accurate registers of diseases, their symptoms and cure, in the course of other voyages.*

He referred to Lind, who had stressed that *"knowledge in physic can only be obtained by a series of observation"*, and who had thus shown how to separate *"experienced truth from hypotheses"*. Robertson, too, declared that one could judge the true pathognomonic symptoms and the effect of a cure not from one but from a great many cases; that all cases, the successful and especially the unsuccessful ones had to be related minutely to permit a positive judgement; and that mere general assertions could contribute little towards promoting the real knowledge of medicine. This programme, concerned with obtaining "greater certainty" about diseases and the effect of cures, accompanied the publication in 1777 of Robertson's *Journal* for 1772-1774.[43] Lind had already included a part of it in his *Diseases Incident to Seamen in Hot Climates*.

Robertson's arrangement of his *Journal* detailed not only the sick but also the weather and climate: readings of the thermometer and barometer, and the exact position of the ship in degrees longitude and latitude, were listed daily. But in his monthly review of the prevailing diseases (a development by Huxham of Sydenham's annual review) he went a step further than Huxham: his incidences were numerically stated, and he compiled a summary of the number of sick and dead according to a list of diagnoses.

Robertson drew practical conclusions from his statistics. He reduced the number of fevers to five, distinctly defined. In his opinion, further subdivision of the remittent fevers was irrelevant. From his own experiences in England, Africa and the West Indies, he also maintained that these fevers were the same the globe over. As for curing them, he opposed indiscriminate bleeding and advocated instead liberal use of the Peruvian bark, the effect of which he presented numerically. With this practice he had not lost any of 62 patients with remittent fever. It is noteworthy that the year after the publication of his *Journal*, Robertson *"was introduced to an acquaintance with Dr Millar"*.[44] Afterwards he became engaged even more strongly in proving the superiority of bark treatment in "typhus" with the aid of comparative tables of results. He also acknowledged John Clark's work along this line in the East India Company (see below, page 43).

Robertson's next book, *Observations on the Jail, Hospital or Ship Fever* (1783), was dedicated to William Hunter, whose lectures had excited the *"attentive spirit of enquiry, which now prevails among the navy surgeons"*. As in all his subsequent writings Robertson repeated his programme, defending it against those who thought it *"dry and insipid reading or altogether useless in the practice of physic"*.[45]

In this work, although he tabulated the monthly incidence of all diseases, he concentrated on continuous fever. The data (number of patients, deaths, and evacuations to hospital) were presented for the period from April 1776 to May 1782. Having shown numerically in his journal, in an uncontrolled *post hoc – propter hoc* manner, that typhus could successfully be treated with bark, he promptly made his case even stronger with comparative results when external circumstances forced him temporarily to abandon this method. (Bark was expensive, and not liberally provided by the Sick and Hurt Board.) When Robertson was a surgeon of the "Juno" his stock of bark lasted from April to December 1776, after which he had to rely on various other methods until July 1778. In a table he compared the results of the two treatments (obtained on the same ship), such tables representing for him conclusive evidence on the subject.

Continuous fevers

Under the bark method *(April 4 - December 31 1776)*		***Under all other methods*** *(Jan 1 1777 - July 30 1778)*	
Were treated on board	*Died on board*	*Were treated on board*	*Died on board*
216	*1*	*296*	*6*
		[Were treated on shore]	*[Died on shore]*
		[62]	*[9]*

Sixty-two patients were subsequently sent ashore, where treatment without bark continued at the New York and Rhode Island military hospitals. Nine of those under either antimonial or camphor treatment died. The overall proportional mortality of the bark group was therefore 1 in 216, whilst that of all other methods amounted to "more than 1 in 16". This group included even those patients who had taken bark on board but recovered only on shore, *"which added considerably to … [the statistical] success"* of the other methods.[46]

Following his transfer to the "Edgar" in 1779, Robertson wanted further to ascertain the efficacy of bark in typhus *"regardless of the expense which I knew must attend the experiments, tho' I could ill afford it"*.[47] This time he compared his results aboard ship with those of the Gibraltar Garrison Hospital with which he had been in touch in early 1780 (on an occasion on which he had briefly met Gilbert Blane). Robertson again used bark, whereas the practice at the Hospital consisted of antimonials, camphor and bloodletting. I have simplified his tables, but all the figures, including the proportions, are original.

On board the "Edgar" *(1 Jul 1779 - 1 Aug 1780)*		***In Gibraltar Hospital*** *(19 Jan 1780 - 20 Apr 1780)*			
		From the British Fleet		*Spanish prisoners of war*	
Fever patients	*Died*	*Fever patients*	*Died*	*Fever patients*	*Died*
475	*6* *or* *1 in 79*	*570*	*57* *or* *1 in 10*	*437*	*33* *or* *1 in 13*

Although 28 patients had been sent from the ship to hospital for 'convalescence', this was a numerical attempt at comparative evaluation of a therapeutic 'experiment' and Robertson was right in stating that *"few practitioners in physic will have so many cases come under their care, as the preceding observations are founded on; and consequently as few readers will ever have experimental authority to deny the validity of them"*.[48]

With his comparisons Robertson did not aim to criticise the hospitals in the manner of certain of his contemporaries. His aim was the comparison of treatments. Thus he had given "irrefragable proof" of the superiority of bark in continuous fever and would only submit to objections based on similar comparative trials on a large scale. Even if the advocates of Dr James' powder, a contemporary patent medicine (see below, page 55) claimed that many of their patients had died because of too low a dosage, it could be argued that deaths under bark might be equally due to the same defect. Besides, he stressed, it was an unalterable fact that for one fatality under bark management, 15 died under other methods of treatment. Robertson conceded, however, that the nature of the disease or the properties of the bark might change with time and that a new evaluation would then be necessary in order to investigate this.

In the second edition of his *Observations* (1789) Robertson was able to acknowledge Millar's approval of his kind of evidence. By then, he was able to recommend not only the liberal use of bark, but also its early prescription, as of importance for the cure of all varieties of fevers. From 1783 to 1789 he had been engaged in private practice in Hampshire, but he had also undertaken three voyages to America on "HMS Salisbury". In his country practice he admitted to having been unsuccessful with the treatment of fever. His annual mortality there varied between 1 in 33 and 1 in 6, yielding an average of almost 1 in 14 out of a total of 228 patients, whereas he had lost none out of 159 on his trips on board the "Salisbury". As Robertson himself emphasised, *"The contrast between the success stated... [in these two tables] is so striking as to attract every reader's attention"*. He attributed it to the fact that in the Navy the doctor was consulted early in cases

Peruvian bark

of fever, and that he saw the patients often and had authority over them. In private practice, on the other hand, he was often called too late and encountered *"the obstinate disposition of the lower class of my patients. A very melancholy and important lesson to the community"*.[49]

In a further *Essay on Fevers* (printed at his own expense in 1790) Robertson advocated the extension of his plan *"beyond the limits of navies and camps to civil service at large"*, in peace and war. He had in mind especially the great metropolitan hospitals for which only overall mortality figures were available, which were not broken down by diagnosis and did not indicate the methods of treatment. He concluded his plea: *"For God's sake, let mere theory or hypothesis no longer regulate the profession of a science upon the success of which the interest and lives of mankind depend"*.[50]

Having graduated MD at Aberdeen as late as 1779, Robertson became physician at Greenwich Hospital and thus senior physician of the Navy, a position he held until 1807. His *Diseases Incident to Seamen* (printed in four volumes from 1804 to 1807) contained his previous works and the results of his practice at Greenwich Hospital, again with detailed statistical information. An abridged version in two volumes was published in 1810-11. Robertson resumed active service from 1814 to 1819. He became a Licentiate of the Royal College of Physicians in 1783 and Fellow of the Royal Society in 1804. A more detailed study of this humane naval physician would be well worthwhile. From the point of view of this book he deserves credit for introducing the numerical method as a basis for evaluating therapy in the Navy. For Robertson, clinical medicine was a "science", regulated (as all sciences) by "experiments".

From the Army to the dispensary

John Clark had a similar career to Robertson, although starting as a surgeon in the Honourable East India Company (1768-1772) before gaining an MD from St. Andrews University and settling at Newcastle-upon-Tyne, where he founded a dispensary in 1777 in the face of opposition from the older, established Infirmary. He wrote several books based on records from both positions.

In his *Observations on Diseases in Long Voyages* (1773), Clark related how he had abandoned Pringle's recommendations and changed to Peruvian bark for the treatment of ship fever, having seen three patients become deeply unconscious when copiously bled. When comparing the mortality on his own ship, the "Talbot Indiaman" (11 deaths out of 108 patients), with that of another ship sailing at the same time and by the same route (40 deaths out of 117), the difference was especially striking – just as his reporting of a concomitant comparison appears to us.

When preparing a second edition of this work (1797), Clark commissioned a young colleague to go through all the Company surgeons' day-books for 1770-1775, kept at India House in London. His motivation for this typical retrospective study (in our modern terminology) was to verify the foundation of his recommendations regarding treatment of fevers, given 20 years earlier! In total, he could report 189 cases in which treatment and 'event' could be precisely traced: of which, 84 patients had died, and 105 recovered. In all of the latter, Peruvian bark had been prescribed. In quick recoveries, bark had been prescribed alone; in slow recoveries, combined with antimonials and bleeding. In many of the fatal cases, the bark had also been given, but in only two cases at the onset of the disease. In all the other fatal cases, bark had been given only 1-2 days before death. Thus, *early* administration of the bark seemed to be the successful therapy.

At the same time, Clark suggested an improvement in the Company's day-books, which had consisted only of a chronological recording of cases. Now he also favoured monthly analyses, grouped according to diagnosis, with a similar but longer summary at the end of each voyage. This would give the ship surgeon and his superiors insight into the morbidity and success of treatment; but more importantly, it would allow a central report containing material from all sources to be drawn up. The periodic publication of such a report would encourage the medical officers, and treatment would attain the highest possible perfection, enabling an immense number of lives to be saved for the community. This was exactly the method used since the 1770s by Robertson in the Navy, and by Lettsom and Millar in the dispensaries. It is hardly surprising, therefore, that Millar, who gathered evidence for the validity of his arithmetic method wherever he could find it, repeatedly expressed his appreciation of Clark, whose work had so singularly paralleled his own, and *vice versa*.

This applies also to Clark's reports from Newcastle. In his *Observations on Fevers* (1780, republished in 1809) there were not only 48 detailed cases illustrating his therapy but Clark also felt that:

> *... in order to determine its success from the result of general practice, it will be proper to give an account of the proportional number of patients who recovered, to those who died.*

During the two years from October 1777 to 1779, Clark treated 203 patients with continuous fever, 196 of whom were cured, one discharged *"for irregularity"* and six died (fatalities which were analysed in detail).[51] Similarly, Clark gave the results of all the scarlet fever patients he attended who had ulcerated sore throats, both in the dispensary and in his private practice.

In an appendix to his book, Clark added *"remarks on the method of improving medical returns"*, in Miller's style. It included five tables summarising his practice at the dispensary during the first two years. Three of the tables drew on Lettsom (listing all cases according to diagnosis and event on a month-to-month basis), and one on Millar (the results given with the additional category of *"relieved"*, that is, of incomplete cure). The table of the fatal cases included sex, marital status, and age of the patients (after Lettsom), and furthermore the day in the course of the disease on which death occurred. Additionally, there were two tables of deaths according to the seasons in Clark's practice and, in order to increase the number of observations, in the practices of all other physicians working at the Dispensary. Nevertheless, Clark admitted that two years was too short a time for any conclusions as to the disease-season relationship.

Thomas Dickson Reide's *View of the Diseases of the Army ...* (1793) appeared just before the reopening of a campaign in the West Indies in the same year. Reide had been a *protégé* of John Millar at the Westminster Dispensary. He had made out the early statistics of Millar's practice there in the mid-1770s and, on becoming an Army surgeon in 1776, adopted his system of noting every case and of analysing them at given periods. His work was full of tabular compilations, such as monthly and annual returns of the sick and dead according to diagnosis, and the proportionality of deaths to the whole numbers of the sick. The number of enlisted men was also regularly tabulated, so that other proportions could be calculated.

Reide had served from 1776 to 1791 in Britain, North America and the West Indies, and his book attempted to give an objective view of the mortality in these different climatic zones. He arrived independently at Robertson's and Clark's view that it was unnecessary to subdivide fevers into more than three types, all of which seemed to him to yield to one single plan of treatment: the early and liberal use of bark. This was the chief design of his book, for Reide had adopted Millar's method of treatment, having apparently been rather unsuccessful with others. He listed not only his own results, but compared them (favourably) with those of Blane, Rollo and Robertson, which showed that he had been very successful indeed.

There is no better summary of the situation concerning the therapy of fevers by 1793 than that by Reide (which, in addition, is a masterly example of British common sense). He said that many treatments of tropical diseases had been recommended in the past few years. All authors spoke of successful cures, although none agreed with any of the others. How was the young practitioner to decide between them, since many were mere assertions, *"unsupported by [the] least shadow of proof"*? The answer lay in the application of 'shop arithmetic'. A physician without the assistance of regular registers could form no idea of the result of his own practice, and much less of its comparative success; and yet, partial registers were worse than none, as they were not only defective but also fallacious:

> *How ridiculous would it appear [for a merchant] to judge of the advantages or disadvantages of particular branches of commerce from reasoning and conjecture, whilst the result can be reduced to certainty by keeping regular accounts, and balancing them at stated periods.*[52]

John Millar later narrated the intrigue around the attempted prevention of the publication of Reide's work by government authorities, partly ascribable to the tendency to save money on the medical preparation for campaigns, by deeming prevalent diseases to be 'incurable'. A promotion, which was to be granted to Reide by the Duke of York as recognition of his clear success in the West Indies, was apparently withheld. Reide, thus expelled from the Medical Service, became a captain and regimental adjutant in Ireland, *"a station to which thousand were competent"*, as Millar commented angrily. According to Millar, John Marshall, another of his pupils who became an Army surgeon and adopted his plan of publishing returns, seems also to have been prevented from re-entering the service at the outbreak of the Revolutionary Wars, being considered *"a Jacobin, leveller, republican and democrat ..."*.[53] Reide, however, was to be rehabilitated as the first true Army statistician by Henry Marshall in 1833.

William Rowley, trained at St. Thomas's Hospital in London, had started as an Army surgeon in the West Indies during the Seven Years' War. In 1766 he set up practice in London and became associated, as a man-midwife, with one of the lying-in charities, and later with the St. Marleybone Dispensary, which opened in 1785. Like Lettsom and Millar, he dedicated his first report (1788), dealing with fevers, to the supporters of the Dispensary. Rowley's experience in Jamaica taught him that Boerhaave was wrong in considering that all fevers were inflammatory and should therefore be treated with bleeding, vomiting, purging and antimonials. While there *were* some localised inflammatory diseases, Rowley looked upon the majority of fevers as general diseases. These were contagious and arose from "marsh miasmata", dirty clothes and close contact between people. Consequently, Rowley would allow traditional anti-inflammatory therapy only for localised fevers, recommending bark, fresh air and cleanliness for general fevers, ideas similar to those of Lettsom and the originators of the fever hospital movement (see above, pages 12 and 31). If this method were adopted, *"supported by reason and successful practical facts, the whole practice of medicine may undergo an entire revision, very condusive to the future welfare of society, and to the honour of the art"*.[54]

The proof was simple. In 1793 Rowley compared the case fatality of the standard therapy with that of his method at the St. Marylebone Infirmary (as the Dispensary was now called). The former was between 70% and 80%, according to a *"true statement of indisputable observation"*. For his own institution, Rowley calculated the mortality to be less than 8%. Therefore, he asked:

> *Will any person presume to say, that there is not an extraordinary difference in the dead list? Will it not be acknowledged, that saving above ninety lives out of every hundred, by a new mode of treatment, is better than losing seventy or eighty ... by the old methods, however sanctioned?*[55]

Rowley's writing challenged authorities, past and present. According to him, Boerhaave had been totally wrong. Cullen and Gregory had a laudably mixed practice, but still relied too much on the great Leyden master. He took issue with

John Brown, the Scotsman (possibly a pupil of Cullen) whose theoretical system had become popular in Europe since the 1780s, because it attempted to justify on the grounds of theory the use of alcohol and opium as therapeutic agents in most diseases. In Rowley's view, Brown scarcely merited any attention from men of science and experience – except that his errors had proved destructive to an incalculable number of human lives.

Rowley had a personal motive for challenging contemporary authority: He had been refused an MD at Oxford (despite receiving an MB from there in 1788) and the Royal College of Physicians had consequently not accepted him as a Fellow. As did other 'marginal men', like Lettsom and Millar, Rowley therefore fought for recognition of his merits: *"By their works shall ye know men, not by professions: and, by a comparative view of the malpractices, erroneously adopted, with the present improvements in curing [these] diseases"*. Thus, as for Lettsom and Millar, the data presented above were for him the only proof of the value of success, be it for his personal practice or for science generally: *"If it be proved that thousands are destroyed by the malpractices; and as many preserved by judicious treatment, which ought the practitioner to follow?"*[56]

As had Millar, Rowley persistently pursued a passionate campaign against bleeding and in a new *Treatise* in 1804, he had two more reasons to raise his voice: bloodletting had just started to become fashionable again, and Britain was at war. His tone reminds one often of John Millar, for instance when he wrote that:

> *... the field of slaughter ... was left to the furious venaesectionists ... and calomelists, with little or no opposition, and havoc, of course was dreadful ... but when the patients died, a prompt subterfuge was ready, namely that they were not bled or purged enough.*[57]

If we can trust his data, Rowley had excellent grounds for his opposition to bloodletting and allied therapy. By then, he had practised for nearly 20 years at St. Marylebone and from a register kept for many years by a colleague he was able to claim that they had never lost more than 6 in 100 patients from putrid infection in the old establishment: In the new dispensary, with more fresh air and "sweet wards", they had lost only two out of between 400 and 500 patients in a recent epidemic, compared to the hundreds who had died in other institutions.

The bloodletting revolution

I have just mentioned the reintroduction of bloodletting for fever in Britain in the early 1800s, especially for continuous fevers (see also page 28). In this reverse of practice, statistics played a great role in the supposed proof of its efficacy. In 1793, George Fordyce had written: *"Practitioners also have not compared cases of fevers in which it [bloodletting] has been practised, and of fever treated otherwise in* *the same manner in which it has not been practised".*[58] Such comparisons were now undertaken. The *Edinburgh Medical and Surgical Journal*, for instance, reprinted and commented at length on the results presented from Irish fever hospitals for and against bloodletting. Thomas Mills, an Edinburgh MD, analysed the records of the Dublin Fever Hospital. He wanted to compare mortality rates from different physicians and at different times with his own practice there in 1813, when he had used venesection. His analysis convinced him of the superiority of bleeding, but his opponents also used the Hospital's records, with more objectivity, to argue against it. However, the chorus of bloodletters from both specialised and general hospitals in many countries became ever louder and more influential.

In 1806, the military setting gave Thomas Sutton (trained in London, Edinburgh and Leyden) the opportunity to submit bloodletting to a thorough clinical trial. He examined what he believed to be a single disease in one military hospital (Deal), comparing the mortalities of four groups of fever patients. The results, which were highly in favour of the bloodletting as the principal remedy, are tabulated below. They suggested that the more one used the lancet, the lesser the mortality.

Therapeutic regimen	***Patients***	***Deaths***	***Mortality***
The usual treatment for "typhus" (Peruvian bark, wine, etc.) at the onset of the disease	*37*	*11*	*1:3*
The same treatment administered later in the course of the disease	*92*	*18*	*1:5*
As above, but with moderate bleeding at the onset of the disease	*20*	*3*	*1:7*
Bloodletting as the principal remedy	*[?]*	*[?]*	*1:20 (never exceeded)*

Several naval surgeons soon published similar numerical 'proofs', for instance, in 1812 from the Royal Naval Hospital at Plymouth (remarkably for the time, this report also listed pulse rates, i.e. beats per minute) and in 1816 from the hospital ships of the Russian fleet, directed for some time by Sir David James Hamilton Dickson, the future chief medical inspector of naval hospitals and fleets. Dickson had earlier recommended the antiphlogistic method, that is, bleeding and vomiting, to his subordinate naval officers, although without his own trials.

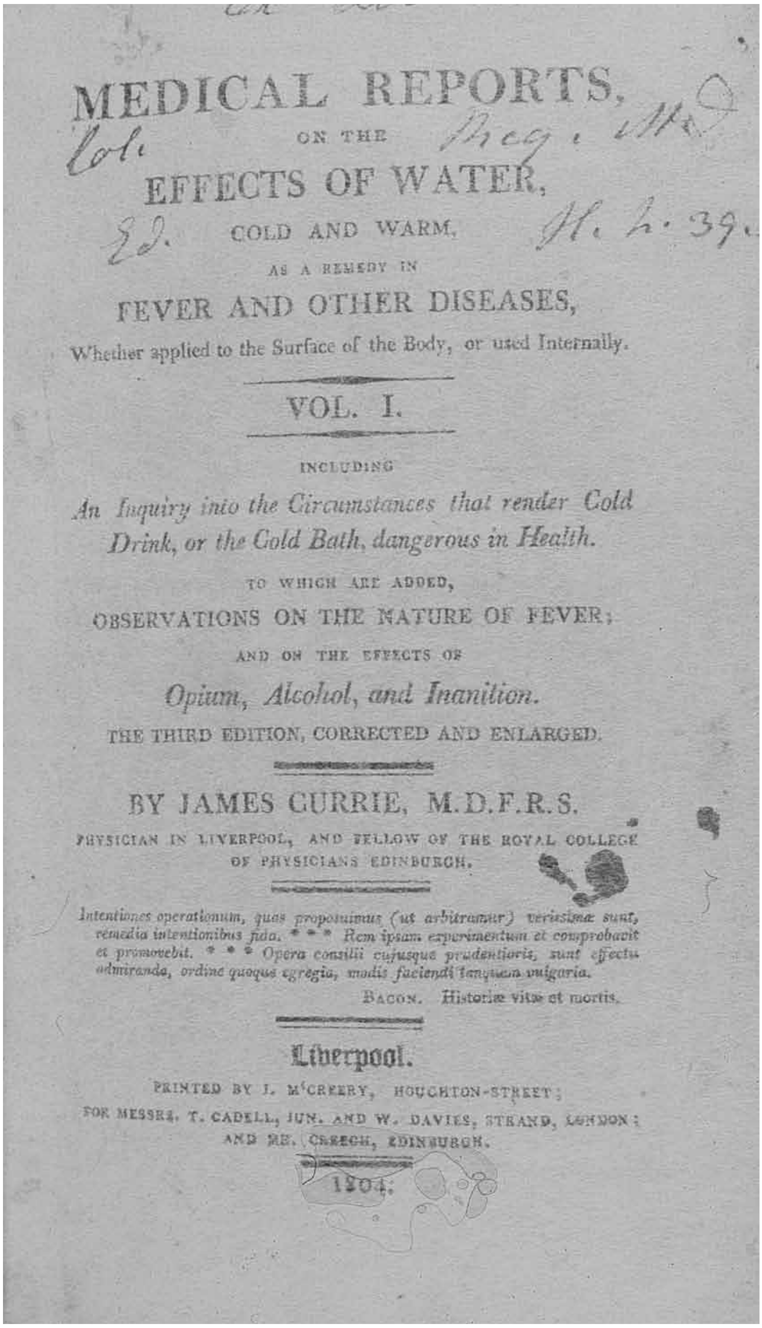
Edinburgh had no fever hospital when it was seized by an epidemic in 1817. Massive hospitalisations in the Royal Infirmary became necessary. It was then realised that no data were available on admissions and cures of fevers during previous years, as there were in the specialised institutions of Dublin, Cork, Manchester and London. This was quickly addressed, and dispensary-like data from the Infirmary and from an *ad hoc* fever hospital were published. At least seven Scottish authors wrote treatises in 1818/19, which were reviewed in the *Edinburgh Medical and Surgical Journal*. In 1818, the *Journal* reviewer considered bloodletting as the unanimously accepted therapy.

Indeed, there seems to have been little resistance to bleeding: as we have seen, the tradition of bloodletting for continuous fevers had never died out in the Navy and Army. But now, the practice was an attack by supporters of the retrograde inflammatory theory on the more modern – and more complicated – approach based on the theory of contagion. The latter consisted of hygienic measures, and attempts to lower the body temperature (measured by thermometer) by internal and external cooling, and treatment with Peruvian bark (thought to be a 'cooling medicine').
In 1821, taking into account more detailed and numerically tabulated facts from the *ad hoc* fever hospital in Edinburgh, the *Edinburgh Journal* reviewer was beginning to doubt the usefulness of bloodletting. It might suspend the symptoms of the fever for about a week; but what was this good for, he asked, if they returned, albeit less severe, in the third week? The bloodletters considered such instances as fevers "cut short, followed by relapse". Yet, he said, one could also look at them as fevers "suspended and protracted", especially when the relapses were as frequent as approximately one in four. Clearly, for the reviewer, numerical statements had supported his belief that the bloodletters had been misled by their speculative opinions, or by their partiality for a particular practice, and that general, unspecific treatment had been neglected. He felt too that *"there was still very much to learn concerning the combination of anodynes, stimuli, and tonics with the depleting practice*", a field in which numerical analysis could be a powerful tool.[59]

A comparative trial even more sophisticated than that suggested by Fordyce in 1798 was described in the Edinburgh doctoral thesis of Alexander Hamilton (1816). At the suggestion of their Chief, James McGrigor, Hamilton and two military surgeons wanted – in the midst of the bloodletting revolution – to assess the effect of this old remedy during the Peninsular War against Napoleon. The trial involved 366 sick soldiers:

> *It had been so arranged, that this number was admitted, alternately, in such a manner that each of us had one third of the whole. The sick were indiscriminately received, and were attended as nearly as possible with the same care and accommodated with the same comforts. One third of the whole were soldiers of the 61st Regiment, the remainder of my own [the 42nd Regiment]. Neither Mr Anderson nor I ever once employed the lancet. He lost two, I four cases; whilst out of the other third [treated with bloodletting by the third surgeon] thirty five patients died.*[60]

This is one of the earliest accounts of "alternate allocation" to generate comparison groups found to date, and constitutes the most advanced methodological step achieved during this era. However, as it was printed only in an MD thesis, it was probably hardly known outside Edinburgh and Army medical circles.



MEDICAL REPORTS,
ON THE
EFFECTS OF WATER,
COLD AND WARM,
AS A REMEDY IN
FEVER AND OTHER DISEASES,
Whether applied to the Surface of the Body, or used Internally.

VOL. I.

INCLUDING
An Inquiry into the Circumstances that render Cold Drink, or the Cold Bath, dangerous in Health.
TO WHICH ARE ADDED,
OBSERVATIONS ON THE NATURE OF FEVER;
AND ON THE EFFECTS OF
Opium, Alcohol, and Inanition.
THE THIRD EDITION, CORRECTED AND ENLARGED.

BY JAMES CURRIE, M.D.F.R.S.
PHYSICIAN IN LIVERPOOL, AND FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS EDINBURGH.

Intentiones operationum, quas proposuimus (ut arbitramur) verissimæ sunt, remedia intentionibus fida. * * * *Rem ipsam experimentum et comprobavit et promovebit.* * * * *Opera consilii cujusque prudentioris, sunt effectu admiranda, ordine quoque egregia, modis faciendi tanquam vulgaria.*
BACON. Historiæ vitæ et mortis.

Liverpool.
PRINTED BY J. M'CREERY, HOUGHTON-STREET;
FOR MESSRS. T. CADELL, JUN. AND W. DAVIES, STRAND, LONDON; AND MR. CREECH, EDINBURGH.
1804.

Vol. Reg. Ed. H. 2. 39.

The issues of cinchona bark and/or bloodletting were at the forefront of the debates concerning first-line therapies, at least for inflammatory fevers. Second-line therapies were also used for the same reasons as today: incompatibility, cost, non-availability. There were also alternatives, old and new, being discussed for the other fever categories, and a range of treatments were available. These were not mutually exclusive, ranging from a physical measure (cold water bathing), through herbal purgatives, to inorganic drugs and a secret patent powder.

INTRODUCING COMPLEMENTARY THERAPIES

Cold water bathing

The concept of physically cooling the body rather than using 'cooling medicines' such as Peruvian bark was introduced by James Currie in Liverpool. He was another Edinburgh-trained Scot, younger than Percival and Haygarth, but nevertheless their friend from the Warrington meetings. He also met and corresponded with John Clark, and was a member of the Medical Society of London. Currie developed two new aspects of the clinical management of fever, which were later adopted in the London Fever Hospital and elsewhere: namely, diagnosis by use of the thermometer, and treatment of elevated body temperature by cold water baths, the effectiveness of which he monitored using the thermometer. Facilities for fever treatment were opened in Liverpool in 1787 in the form of two fever wards, first at the infirmary and later at the workhouse, and he used these for therapeutic experiments. The principal purpose of his *Medical Reports on the Effects of Water, Cold and Warm as a Remedy in Fever, and Febrile Diseases* (1797) was *"to establish the use of [this] new and powerful remedy in fever"*.[61] How did he proceed?

Currie's *Medical Reports* were influenced by the clinical writings of his older friends, Percival, Haygarth, and Clark. He presented the monthly admissions at the Public Dispensary since its opening in 1780 in tabular form, and he made a similar table for the occurrence of "typhus". Numerical 'proofs' of the utility of the Manchester Fever Hospital (which opened in 1796) and of the fever wards that he had directed in his own Infirmary in Liverpool (since 1787), and of the Liverpool workhouse (since 1783) rounded off this report. Currie wrote that he had got the idea of cold bathing for fevers from the Army surgeon William Wright, who had described three successful cases (among them himself!). In fact, it was deep-rooted in popular culture for very diverse disorders.

In 1787, the year the Liverpool fever wards opened, Currie successfully tried cold bathing seven times, losing one patient (who had also been treated with bark). From then onwards, he always used bathing therapy whenever the patient's strength was not too reduced. By 1797 he had recorded 153 cases in which he attributed cure chiefly to this remedy. But later, showing a commendable empirical spirit of enquiry, he concentrated on recording the failures of his method, contrary not only to the usual approach of the dogmatists, but also to those like Robert James (see below, page 55), who had a vested commercial interest in their patented drugs:

> *Having satisfied myself of its extraordinary efficacy, and of the precautions necessary in using it, I have found it the shorter method as well as the more instructive, to record the instances [only] in which, it has proved unsuccessful.*[62]

Indeed, the results in his fever wards in the four years from 1793 to 1797 were good: 51 of 530 patients died – an average mortality of 1 in 10.

In a second volume bearing the same title, published in 1804, Currie kept to his former pattern of presentations, that is, a general numerical survey and ample illustration by detailed cases, including all his unsuccessful ones. By then he had also used bathing for dysentery (110 cases in 1801 with 10 deaths) and tetanus. Currie admitted that in all these cases other remedies had also been used, *"for it would be unjustifiable for the sake of experiment to neglect any means of safety"*, but they had been of the most simple kind.[63]

Typical of the work of some of his predecessors was his recognition of the insufficiency of his efforts and of the need for further investigation. Currie deemed his *Observations* not extensive enough to provide *"a complete view of the subject of which they treat"* and although *"in this rapid sketch assertions are sometimes given instead of experiments and proofs ... it will be found that the issue is clearly formulated so that it can be easily brought to the test of experiment"*.[64]

Such honesty showed itself again when he quoted the only negative account of the effects of bathing he had ever read and which, he emphasised, should not be concealed. Other literary evidence however, some of it numerical, permitted him to conclude on an optimistic note. For instance he cited evidence from two epidemics of yellow fever in Philadelphia. The first epidemic (1793) was the famous instance when William Cobbett, an English pamphleteer and politician, used statistics to prove the fatal effects of Benjamin Rush's method of bleeding and purging. During the second epidemic (1798), morbidity was four times less, but the mortality was the same. For Currie this was not due to insufficient bloodletting, as Rush claimed, but to the fact that no cold bathing had been practised.

It is perhaps not inappropriate to conclude this synopsis of Currie's work with such a speculative statement to round off the picture drawn of him. As indicated above, he was himself aware of the limited value of his evidence, yet with that presented his contribution stood epidemiologically higher than that of many of his contemporaries.

Purgatives

James Hamilton, a physician to the Royal Infirmary at Edinburgh, was as thoroughly traditional in his treatment of fever as in the type of evidence he cited of its efficacy. He presented only successful cases to prove the *Utility … of Purgative Medicine in Several Diseases* (1805). For him, the value of the cold bath was ascribable only to its purgative effect. But, as indicated in my introductory remarks on fevers, the 'bloodletting revolution' supported Hamilton's views of the value of purging with its own statistics, so that by 1829 his book was in its eighth edition.

By contrast, Currie's cold water bath was abandoned even by his friends from the London Fever Hospital, despite its initially enthusiastic reception and its documented efficacy.

Tartar emetic

Tartar emetic was the term used in the 18th century for antimony potassium tartrate, a traditional drug. Richard McCausland, an Army surgeon stationed at Niagara during the American War, evaluated this drug between 1775 and 1781, when he was obliged to use it because of a shortage of Peruvian bark. He compared the outcome in patients treated with tartar emetic, as a solution or as a pill, with patients treated previously with Peruvian bark. The ratio of cures to relapses was about 4:1 in the former, compared to about 2:1 in the latter group. He interpreted and weighed this overall evidence very carefully, taking the composition of the test groups and the seasons into account, and concluded: *"the arguments on both sides seem so nearly balanced, that we may venture the table as it stands."*[65]

James Lind also used his hospital facilities for a number of trials of febrifuges – for instance, comparing *vinum antimoniale,* tartar emetic, and hot water alone as an untreated control group. However, as in the comparisons of various antiscorbutics (see below, page 69), he did not present the results with precise numbers, the only exception being the trial of opium.

Arsenic

Arsenic in the form of *Solutio Fowleri* is still prescribed, for example in dermatology. The man behind the drug's name is Thomas Fowler. Having taken up medical studies in Edinburgh as an apothecary at the age of 38, Fowler became physician at the Stafford Hospital until 1791. Between 1785 and 1795 he published a series of three *Medical Reports*. These concerned the effects of tobacco, arsenic, bloodletting, sudorifics and blisterings in defined diseases according to a clear programme, for which he referred to Bacon's plan for the improvement of universal science. Some of these books were re-issued in English and translated.

Fowler's programme advocated the following:

(1) Recording the effects of the drug upon every patient;

(2) Studying the medical effects of natural products, for these were considered less variable and uncertain than those of the druggists;

(3) In order to avoid prolixity of repetition, reporting only a few detailed cases, but also including in an abstract (tabular) form an account of the whole practice;

(4) Finally, if the plan were successful, extending to other medicines.

Fowler also emphasised the necessity of distinguishing between the "operational effects" (such as vomiting or diarrhoea) and the curative effects of a medicine. This would also allow the physician to differentiate between a poison and a good medicine with "side effects". He thus declared:

> *It becomes highly requisite that the Public should speedily be made acquainted with such effects as far as they are known; together with such Precepts, Cautions and Restrictions, as may tend to unite the greatest Degree of Safety with its Efficacy. Nothing of this sort, has yet been done.*[66]

Such a task would be difficult. Therefore, he advised that:

> *... the memory must be assisted: Art and Numbers must unite their effort for a considerable length of time; a series of cases must be treated, with a constant view of the Investigation ... uninfluenced by Theory, Custom, or Authority. [And] Collaboration with other workers may even become indispensable to achieve these premises.*[67]

The most impressive feature in his second work in this series, the *Medical Reports on the Effects of Arsenic* (1786), was a table of all the 247 cases of ague in which the arsenic solution had been administered. Of these 247 cases, 144 patients had been cured without any relapse, and 27 had experienced relapses. In patients with fits, 51 had been totally controlled, 20 had been relieved, and only five not improved at all. Of the latter three groups, 45 patients were cured eventually by adding Peruvian bark. The 31 remaining patients were either described as "irregular" or were still under treatment. Fowler also quoted a letter from William Withering (see below, page 83), who had used the remedy in 48 patients. Thirty-three of them had been cured with the arsenic solution alone, and without complications; three had complained of side effects, which needed "a little soluble tartar", and only 12 patients received no benefit. Thus, Fowler claimed that in cases where the bitter tasting Peruvian bark was difficult to administer (for example, in children) or refused because of too many disagreeable "operational effects" (such as vomiting), arsenic was a valuable alternative.

It was a reasonable claim from *his* point of view, although his methods of observation appear *now* to have been inadequate for the assessment of a remedy for such a notoriously intermittent and relapsing disease.

Dr James' fever powder

Robert James, who had been conventionally educated at Oxford and Cambridge and was a Licentiate of the Royal College of Physicians, had taken out a patent for his anti-fever antimonial powder in 1746, a panacea that he also recommended against smallpox. From 1748 he was illustrating its value by describing his successful cases only in the numerous editions of his *Dissertation on Fevers*. In the seventh edition (1770) he forwarded as further proof the decreased overall mortality from 1751 to 1763, compared with that from 1738 to 1750, when his powder had not been generally available.

James' use of the official London bills of mortality (see above, page 16) was the same as that employed to investigate the effects of inoculation. But whereas 18th century authors on smallpox referred to that specific category (smallpox) within the bills, James cited only the overall figures of the bills.

Soon after publication of the seventh edition of James' *Dissertation on Fevers*, John Millar attacked the current use of antimonial preparations, especially his secret and much praised antimonial powder for fevers, in a paper read to the Medical Society of London in 1774. When analysing James' data, Millar (who was acquainted with the numerical approach to the smallpox question) first remarked that the inaccuracy of causes of death, as diagnosed by chambermaids, would be the same for both the 1738-1750 and the 1751-1763 periods.

Secondly, antimonials, albeit in another form, had already been used during James' earlier period, because of a strong recommendation by Huxham in his classic treatise of 1737. If a decrease of deaths from fever *alone* could be demonstrated, *"this"*, he said, *"will be most desirable evidence"*.[68] In fact it *had* decreased in absolute figures during the period mentioned by James; but in the ten years from 1764-1773, when his powder was even more extensively used, it had increased again. Millar therefore judged James' work valueless since it produced evidence directly opposed to that required if one accepted the facts as presented.

As in the case of scurvy, the Admiralty also ordered trials of treatments for fever, which is how James Lind came to test Dr James' Powder at Haslar. He was probably prejudiced against this patented panacea, because at about the same time as Millar and Lettsom, Lind had campaigned against the secrecy of medicines. He also thought that, considering the different kinds of fevers, one powder was unlikely to be universally effective. Yet Lind had to obey orders and give it at Haslar, in various cases, *"to above a thousand patients"*. He found it to be comparable to tartar emetic but admitted that he had continued his usual treatment *"as if no such powder had been given"*.[69] Obviously, Lind did not intend to make a case for the powder right from the start of his 'trial'!

Mercury

To conclude this long section, it is fitting to take a brief look at mercury, yet another traditional treatment on its way from being recommended as a specific to being regarded as a panacea – at least in the hands of some experienced practitioners. Recommended in various forms against syphilis for centuries (see below, page 107) it was now also being tried in fevers.

The most avid proponent of mercury in all acute diseases was Charles McLean, a Scotsman who had been with the East India Company for 14 years prior to becoming an Army surgeon in 1804. He departed after some years in this post, gained a Scottish MD, and settled in Liverpool. The history of the argument supporting his claim illustrates well the kind of difficulties – theoretical, empirical, social, ethical, and psychological – which the advocates of statistico-analytical evidence had to face in their struggle to gain acceptance for their argument against dogmatic evidence on the one side, and knowledge based on direct clinical observation in individuals on the other.

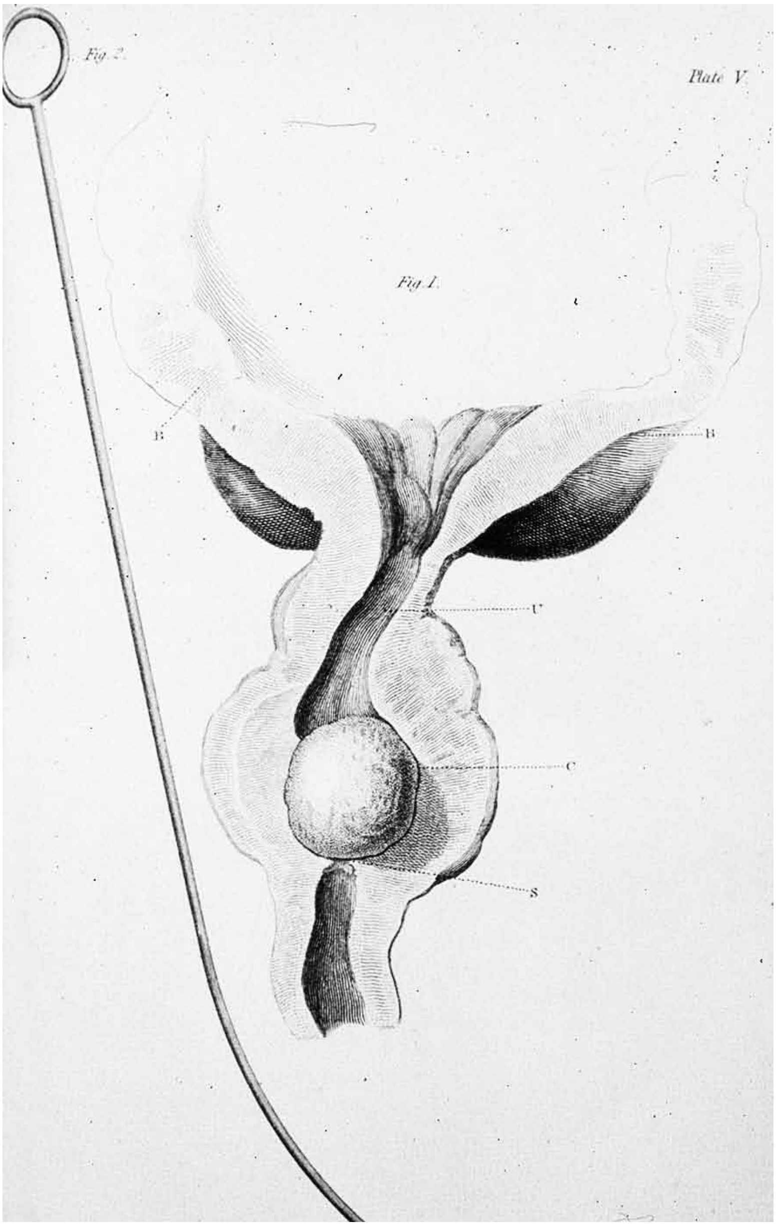
In the 1790s, McLean had started trying out mercury on himself for an intermittent fever. He found that *"the result was so satisfactory, that I resolved to continue the practice, in future, in every case of this disease and my expectations were not disappointed."*[70] By "analogical reasoning"[71] he extended its use to yellow fever in Jamaica, jaundice, ophthalmia, sunstroke, diarrhoea, dysentery, and typhus. In 1796 the results of his and a friend's "mercury wards" in the Calcutta General Hospital – stated only in general terms such as "unequivocal success" –were compared unfavourably with the mortality in other wards. He rejected the inferences against him by pointing out that his patients were generally in the last stages of hepatitis, dysentery, dropsy, etc., *"whilst those in the other wards consisted exclusively of young men from the European corps, seldom labouring under diseases severer in degree than gonorrhoea or slight intermittent [fever]"*. His proposal to compare his patients with those of his critics taken under similar circumstances of constitution and disease was apparently evaded:

> *... by pretending a reluctance to try experiments with the lives of men; as if it were not manifest, that my experiments, which were always tried upon myself, were capable of being conducted with perfect safety...*[72]

McLean's long attack on the practice of bloodletting and the kind of inconsistent evidence forwarded in its support was perfectly appropriate for the literature he chose to review. This gave him occasion for some methodological remarks: *"the days of miracles are past"*, he wrote; and even the influence of the Pope could no longer maintain an argument based on tradition, romantic tales, hearsay, personal experience, or the testimony of respectable gentlemen. Instead, he pleaded for *"principles which are deduced from numerous and undoubted facts, and which can be put to the test of experiment by all mankind."*[73]

Such a programme would have been an advance, but in its execution McLean fell into the same trap for which he reproached his opponents (those advocating bloodletting as a panacea). As justification for his view, as early as 1796, McLean had collected reports of "some of the cases" which he had treated successfully with calomel and opium. In 1818, in a privately printed volume entitled *Practical Illustrations of the Progress of Medical Improvement for the Last Thirty Years*, he published 70 selected cases, ranging from scurvy to pneumonia, all of which he had 'cured' with mercury. In contrast, there were nine cases of burns which had proved fatal, he claimed, because they were treated with bleeding and vomiting. It is always easier to see the faults with others than with oneself; and some of us have in-built psychological barriers to doing something new – even against better insight.

In conclusion, this section on the issue of fevers, as important and complex for contemporaries (and historians) as is that of cancer today, has painted a picture of the nature and culture of those who advocated a new type of evidence in therapeutics. In each of the following sections I will deal with more specific constituents of a critical approach.



Bladder stone

It all depends on age, sex, time, technique, and honesty: Removing bladder stones without killing patients

BLADDER stones used to be much more common than they are today, probablydue to a vicious circle of dietary habits and urinary infection, particularly in elderly men with hypertrophy of the prostate. Celsus described operations for stones in the first century AD. A rather harsh procedure, it was only possible when the stone was big so that it could be felt and pulled down *per rectum* into the perineum. Once localised under the skin in the previously dilated bulbous part of the urethra, a cut was made directly to the stone and it was extracted. For 1,500 years after Celsus wrote, no other method for lithotomy was described until two Renaissance surgeons published reports of two new techniques: Mariano Santo cut into the bladder through the prostate, Pierre Franco used a supra-pubic approach. From these two methods, the "new" practices of the 17th and 18th centuries evolved.

With the exception of Santo and Franco, the early lithotomists were self-trained wandering stone cutters. The persistent severe pain of the bladder stone, urinary obstruction, and the fact that a number of those submitting to surgery survived, might have made the sufferer willing to chance an operation. What the strolling 'specialists' who wanted to stay in business needed, therefore, was a reputation for success, and they used simple statistics describing their practice as a basis for their claims. Mortality was appreciable. For example, François Collot, one of a family of French court lithotomists who had given service over eight generations, reported seven deaths following 40 operations. Therefore, even before knowledge about lithotomy started to grow around 1700, numerical data were being used in publications and discussions about it.

With the appearance of Friar Jacques, an itinerant lithotomist, amongst the established surgeons in Paris in 1697, and William Cheselden in London, the operation acquired the semblance of a scientific procedure during the first third of the 18th century. Both Jacques and Cheselden demonstrated the fallacy of the Hippocratic belief that a wound in a "membraneous organ" (the bladder in this case) was necessarily fatal. They showed that cutting directly into the bladder was a much quicker, more convenient, and more successful way of extracting a stone than trying to pull it through an incision made in a painfully dilated urethra.

Friar Jacques used a lateral perineal incision for his operations, but his documented successes in Versailles, Aachen, Amsterdam and Strasbourg were insufficient to overcome his lack of prestige among the Paris professionals, who put him to the test by having him operate under scrutiny. Jealousies and the threat to their income may have been important. An English visitor to Paris in the summer of 1698 remarked:

> *Frère Jacques' reputation mightily slackens, for of 45 cut in the Hôtel-Dieu, but sixteen (!) survive; and of nineteen cut in La Charité only eleven survive: but I am sensible that he has got abundance of enemies, which makes me very often question what I hear; the surgeons have a great mind to shout down this man while they practise his method.*[74]

In London, William Cheselden adopted and developed the operation of "lateral" lithotomy, relying on statistics to guide changes in his techniques. In 1732 he first gave an account of his new results in an 'Appendix' to the fourth edition of his *Anatomy*:

> *The first twenty seven patients cut this way recovered, and I believe are all living at this time: Indeed I had cut thirty one who recovered before one died, having cut four more between the 28th was cut, and the time he died; but I scorn to use any fallacious way of representing my success. Some of these being cut in the hospital, and some privately, the truth of this account may be suspected by those who do not know me. I cannot take the liberty to mention the names of private patients, therefore I will give a detail of those only which I cut this way in the hospital, where the first twenty five recovered, to the truth of everyone of which I had above twenty witnesses, and I do believe these patients are all living at this time.*[75]

Considering the somewhat irregular past of lithotomy, one is impressed to see Cheselden going to considerable trouble to assure the truthfulness of his results. He gave a list of all these 46 patients, operated between March 1727 and July 1730, with their ages and dates of operation. Only two had died by 1732, even though "many" of the 32 or more children under 15 years had had smallpox during their recovery. Cheselden continued to keep accurate records of his public practice, for in the next edition of his *Anatomy* (1740) we read:

> *What success I have had in my private practice I have kept no account of, because I had no intention to publish it, that not being sufficiently witnessed. Publickly in St. Thomas's Hospital I have cut two hundred and thirteen; of the first fifty, only three died; of the second fifty, three; of the third fifty, eight, and of the last sixty-three, six ...*[76]

In order to evaluate and to advance lithotomy, Cheselden considered the ages of those who recovered and those who died. He grouped his 213 patients by age and gave the number of deaths for each age group in the text. I have drawn up the following table from Cheselden's figures:

Age in years	***10 or under***	***11-20***	***21-30***	***31-40***	***41-50***	***51-60***	***61-70***	***71-80***	***Total***
Cut	*105*	*62*	*12*	*10*	*10*	*7*	*5*	*2*	***213***
Dead	*3*	*4*	*3*	*2*	*2*	*4*	*1*	*1*	***20***

This list shows, again, that Cheselden's great success was in children. Almost half of his patients had been ten years or younger, with a mortality of 1 in 34. The mortality of the remainder had been 1 in 6.3. But this detail was not noticed while his overall results were taken as a standard for successful lithotomy for the rest of the 18th century.

In 1728, the operation was re-introduced in Paris (which had so severely censured its principal originator) by Sauveur-François Morand. Like Cheselden, Morand changed his technique several times. Convinced that every method had some good points and that a good surgeon could not only execute them, but should also choose the appropriate one, Morand wrote up descriptions of all of them. He started in 1728 with the supra-pubic method, much discussed since its revival by Cheselden and a handful of other British authors who had reported all their cases in some detail. In an attempt to show the advantages of this method, he compared the results obtained between 1720 and 1727 (131 patients, 5 deaths) with those obtained at the Hôtel-Dieu and La Charité during the same period with the established methods, analysing data from their administrative records (812 patients, 255 deaths). This was an unprecedented instance of comparison of data from a new method with a vast number of results from an older one (in today's terminology, a retrospective comparative study).

Morand set out next to assess the lateral operation. Having heard of Cheselden's discontinuation of the supra-pubic technique in order to test the lateral and then to compare them, Morand asked the Académie des Sciences to support a journey to England. In May 1729, he saw Cheselden operate on four patients, three of whom were cured. After questioning the patients and conversations with Cheselden, Morand felt this had given him *"the light which meditation might never have provided [him] and the courage to undertake this operation"*.

Morand kept on friendly terms with Cheselden, who wrote to him with detailed descriptions of his method, including his numerical results:[77]

March 1727 - June 1729:	*47 (hospital and private patients, 4 deaths)*
March 1727 - July 1730:	*46 (hospital only, 2 deaths)*
July 1730 - End 1730:	*20 (hospital only, 2 deaths)*

Impressed by Cheselden's figures, Morand and a colleague started operating in Paris during the spring of 1730. They reported two deaths out of 16 patients. Morand's superiors, and even the Académie des Sciences, who saw 11 of the cases, were pleased, especially as during the same period, five patients out of 12 had died at La Charité with the Mariano Santo method.

In early 1731, however, Morand suffered a similar misfortune to that which had ruined Jacques' reputation in Paris 30 years earlier: he lost two prominent patients. But Morand, as surgeon-in-chief at La Charité since 1730, and one of the founders of the Académie de Chirurgie in 1731, was well established in surgical circles and could therefore defend himself better than a newcomer and non-professional such as Friar Jacques had been able to. Autopsies also 'proved' that the deaths had been unrelated to the operation. In a '*Mémoire*' read before the Académie des Sciences in 1731, Morand was able to refute all allegations brought against him – especially the charge that he had selected easy cases for testing the new operation. The announcement of his results at La Charité was strong defence, but the trump card of his lecture was an account of Cheselden's statistical results, brought up to date:

> *Theory will furnish a great number [of motives for the re-introduction of this operation], but the sole ones capable of persuading are the facts. Examining the operations performed according to this method since the month of March 1727... everything must inspire us with confidence. I have just received Mr. Cheselden's list of patients cut since the one printed in his Appendix [1732] and I learn that he has [since] cut twenty, two of whom are dead.*

Morand rounded off his lecture with a set of precise figures:

> *If we join this list to his first and to ours, we find, once the calculations are made, altogether 82 persons were cut according to this method within four years, of whom only six have died and 76 have been perfectly cured.*[78]

This success was even greater than that of the supra-pubic method.

Thereupon, Morand became, as a lithotomist, a key figure in the dissemination of Cheselden's lateral technique, personally introducing it to at least 13 continental surgeons. He was proud to publish their results in 1772, one year before his death, as they had reported them to him. If we add up those testimonies, which are fairly precise, we obtain a total of more than 300 operations with only 30 deaths.

In the late 1720s, Morand had maintained that a surgeon's skill was of greater importance than the particular surgical method he employed. Yet it is clear that Morand himself had become convinced by statistical comparisons that different methods had different results, having taken over from Cheselden not only two operative techniques for trial, but also the practice of keeping notes, reporting comparative results and using them as a basis for argument. It is worth emphasising that this was a personal achievement of Cheselden and of some of his colleagues, since it was later testified repeatedly that there had been no official register of the operations performed at St. Thomas's Hospital in his time, nor, in fact, as late as 1819: The practice of maintaining registers and presenting quantitative data based on their contents did not die out during the rest of the 18th century, but neither did it evolve, based as it had been on the personal initiative of individual practitioners.

A further mid-18th century example of such personal initiative concerns Friar Cosme (Jean Baseilhac), who came from an old family of barber-surgeons in the Auvergne. Like Friar Jacques, he was an outsider to the Paris surgical world but found himself plunged into it because of his development of an instrument for use in lateral lithotomy. On entirely qualitative grounds, the Académie de Chirurgie judged his instrument to be useless. But Friar Cosme was an aware and self-critical man and, despite his claims of success with the lateral method (expressed in terms of mortality), he knew about its drawbacks, especially as urinary incontinence was often a consequence of incising the neck of the bladder in women. From 1758 onwards he operated on women, and after 1769 also on men, using a new procedure that did not require prior instillation of fluid into the bladder.

Friar Cosme's humility and his cautious attitude led him to wait 20 years before publishing the results of his new method. By then (1779), he was able to provide a detailed list of all the 46 women and 36 men on whom he had operated, and he continued keeping a register right up to his death (which his nephew published soon afterwards). *"The facts reported"*, wrote the friar, *"favourable or unfavourable, have been described immediately as they arrived"*.[79] Altogether he had operated on 100 cases, 59 women with nine deaths and 41 men with ten deaths. He was able to announce that all the 39 women included in his original report who had been classed as cured were not only alive, but continent. He thus considered he had achieved his main aim, at least in women.

Cosme's mortality of 15% was comparable to that of Cheselden's record for the lateral operation, and the publication of the results of all his cases, based on regular, prospectively assembled registers, reflected Cheselden's example in the 1720s. Cosme was exceptional, however, in registering cases prospectively from the moment that he launched his new operation.

It was far more common for lithotomists to use numerical evidence compiled in a more casual way, both by established surgeons, and some itinerant lithotomists, whose fantastic claims hung around like ghosts. Pajola, an Italian who operated in Vienna in 1804 was reported not to have lost one patient in 500 operations whereas another author claimed that only three of his "approximately 200 patients" had died. The figures of the established surgeons as published in secondary literature were often contradictory, too, as they were quoted from vague testimonies from memory. This prompted Jean François Deschamps of Paris to say, in 1796, that:

> *... a work that contains only the non-successes and the errors of the reputed practitioners would perhaps be one of the most instructive books; the art would gain one hundredfold what egotism [amour-propre] might lose.*[80]

An exception to this largely dismal picture was information collected and analysed at the Norfolk and Norwich Hospital. From the latter part of the 18th century, Norfolk enjoyed the unenviable reputation of having the highest incidence of bladder stone of any county in Great Britain, and as a result, a local tradition of surgical skill in the art of lithotomy had emerged. When the first general hospital in Norfolk was founded in 1771-1772, experienced local lithotomists were appointed to its surgical staff, as well as physicians interested in the medical aspects of bladder stone. The Norfolk and Norwich Hospital earned a European reputation for its standards of lithotomy, particularly because publications about the results of operations and clinical research there were based on registers that had been established at the time of the hospital's inception. As Alexander Marcet (see below, page 65) wrote in 1817, the Norfolk and Norwich Hospital stood *"in this and several other respects ... as a model of regularity and good management"*.[81]

Not only were complete registers of all operations kept (including the name of the surgeon, the technique used, and the outcome), but the Hospital also preserved all the bladder stones that were removed. Many a hospital at this time made a collection of its stones, as did individual surgeons, but the Norwich collection gained a special reputation, even in Paris. Both the registers and the stone collection have survived.

Apart from administrative needs, there were several specific roots of the exemplary patient registers in the Norfolk and Norwich Hospital. Norwich had civic records of bladder stone patients treated by lithotomy during the whole of the 17th century (and these survive today in the Mayor's Court Books of the City of Norwich). The writings of Sir Thomas Browne provided another source of information about stones in 17th century Norfolk. Furthermore, from at least 1704, Norwich had its own bills of mortality. Finally, Benjamin Gooch, who played an important role as medical consultant during the foundation of the Norfolk and Norwich Hospital, was a dedicated 'observationist'. His textbook (1758, 1767) has been considered one of the most important surgical works by a provincial surgeon of the 18th century.

The first investigator to make use of the records assembled at the Norfolk and Norwich Hospital was Matthew Dobson. He was trained in Edinburgh and settled in Liverpool around 1760. He was interested in the epidemiology of the stone, and used the admission lists of 15 provincial hospitals to study it (1779). He described his survey thus:

> *I have been at some trouble to collect a comparative view of the disposition to the stone in several parts of the kingdom. My design was, to ascertain the number of patients who had been cut for the stone, in several hospitals to which I applied, compared with the whole number of both in and out patients; and likewise*

> *whether there was any thing peculiar in the food, drink or situation of the inhabitants of the respective districts.*[82]

From the comparison of the figures obtained, Dobson showed the very variable geographic occurrence of lithiasis. But as to its pathophysiology, he considered his thoughts far from clear and conclusive. Rather, he concluded with a sentence typical of 'modern' scientists – a plea for further investigation:

> *Other physicians may make different comments, and draw different inferences from the above reports and a still more extensive collection of facts may produce also a more useful, satisfactory and decisive theory.*

The way to arrive at this was now obvious for him. Indeed, from his own experience, Dobson deplored the paucity of complete hospital records, which he rated as a major scientific tool. In 1779, he wrote:

> *I cannot conclude without expressing a wish, that the hospital reports throughout the kingdom, were drawn up in a more full and circumstantial manner. The sources and nature of endemics, and of some other diseases also ... might be thus more clearly ascertained, and a more successful method of cure consequently adopted.*[83]

Methodologically, Dobson's survey was an extension of the system of using a network of correspondents, which had been used by James Jurin in his investigations of the value of inoculation for smallpox and by Morand. What was new in Dobson's survey was his use of questionnaires. He calculated the *average* ratio of lithotomies to the total number of patients. These were 1:394 in the cider districts of Gloucestershire, Worcestershire, Herefordshire and Exeter; 1:420 in the North East of England; and 1:3,223 in North West England.

Dobson's type of research was taken up in enlarged form 40 years later, when a series of British statistical publications appeared at a rate of one per year between 1817 and 1823. The first of these writings was by Alexander Marcet, a Swiss-born, Edinburgh-trained physician, who had become a chemist at Guy's Hospital, London. The aim of his *Essay on the Chemical and Medical Treatment of Calculous Disorders* (1817) was:

> *... to describe, and illustrate ... the characters by which the different calculi may be distinguished; to indicate the easiest analytical methods by which their chemical nature may be ascertained; and to point out the modes of medical treatment which afford the best prospect of success.*[84]

Marcet felt there were good prospects for curing lithiasis medically in early cases (which could be diagnosed by chemical tests) and in girls and women, thus avoiding the pain and danger of lithotomy.

Although he had been a physician at Guy's Hospital since 1804, Marcet had been unable to find any regular records of cases of lithotomy in his own and the other large hospitals of London, such as St. Bartholomew's, St. Thomas's, and the London Hospital. He therefore travelled to Norwich and used statistics collected at the Norfolk and Norwich Hospital between 1772 and 1816 to analyse the deaths associated with lithotomy by sex and age at operation (quoting Cheselden's similar analysis), and presented them all in a table. The overall mortality among 506 cases was 70, or 1 in 7.25. Analyses by age showed that 12 boys out of 227 under 14 years had died (1 in 19) and 56 out of 251 men (1 in 45). The figures for girls and women were 1 in 8 and 1 in 20, respectively.

Marcet made a plea for compiling Norwich-like data to find out the relative frequency of lithiasis in various periods and geographical areas. For this he needed only the total number of admissions and lithotomies, not their results. For recent years, he was able to procure, or more often to infer or estimate, the number of admissions from metropolitan and provincial hospitals in Britain and on the continent. For earlier periods, he referred to Dobson's statistical inquiry of 1779. His work, conceived only as a commencement of a new type of investigation, allowed him nevertheless *"to draw results from a larger scale of observations than was perhaps ever furnished ... and to present a point of comparison to which other records of the same kind may in future be referred"*.[85]

Richard Smith, the remarkable senior surgeon at the Bristol Royal Infirmary, reacted to Marcet's outcry about the lamentable paucity and incompleteness of hospital records. He addressed a frank letter to every provincial hospital requesting information that would enable him to draw up statistical memoranda on the occurrence of lithiasis and the results of its surgical treatment. He received polite responses, giving the numbers of operations, from more than 30 charitable institutions for the poor all over Britain. In addition to Marcet's data from Norwich, Smith also included data on mortality from the returns of hospitals in Exeter, Birmingham, and Leeds.

Smith's most detailed account was of his own hospital, which had kept records since its opening in 1735 (a fact which had escaped Marcet). Large tables gave information not only about the geographical provenance of its patients and the relative occurrence of lithiasis in different periods, but also on mortality according to age and sex of the 354 patients admitted over a total period of 82 years.

The senior surgeon at the Norfolk and Norwich Hospital, Philip Martineau, also Edinburgh-trained, reacted against an imputation hidden in Marcet's and Smith's results, namely the high overall mortality of lithotomy (one in seven) at his hospital. One of the motivations for a paper he read to the London Medico-Chirurgical Society in May 1821 was clearly to show that *he* was not responsible for this, and that his colleagues were to blame. He attacked the introduction of the supra-pubic operation without evidence that it was better or technically easier. For his part, he provided a table containing names, ages, dates of operations, duration of recovery and weight of the stone for all 84 patients he had cut by his 'improved' lateral method from 1804 until 1820. Only two had died, he announced, and there had been no selection of patients *"as I never rejected anyone who was brought to the operation"*.[86] Although John Green Crosse, his assistant and later his successor, claimed exactly the contrary, Martineau's assertions were clearly successful, for Sir Astley Cooper, the famous London surgeon, said of him in 1835 that *"no surgeon in London, I am certain, can boast of similar success at lithotomy"*. And even Jean Civiale in Paris, who claimed that his lithotrity (intravesical crushing of the stone) was superior to lithotomy, called him *"le lithotomiste le plus éminent et le plus heureux de son époque"*.[87] [The most eminent and successful lithotomist of his time.]

In conclusion, quantitative comparisons of the results of lithotomy in British hospitals played a considerable role in the introduction of Cheselden's new surgical procedure for bladder stone therapy in the 1720s, and his statistics were recognised as the only reliable standards of success in Europe for a further hundred years. Around 1820, a new set of data was published, based chiefly on the records of the Norfolk and Norwich Hospital. These were in turn accepted even by leading French lithotomists *and* lithotritists.

The analysis of data such as those from Norwich was sophisticated. With the greater amount of data collected, it was possible to analyse operative mortality not only by the age and sex of the patients, as Cheselden had done, but also by the weight of the stone and the time between operation and recovery or death. Statistics assessing the results of treatment for bladder stones had thus been used not only to analyse personal case series individually and together, but also for institutions. It is worth noting that, in 1820, Smith declared himself greatly satisfied *"to lay before the public a proof that those [charitable] institutions are open to medical research upon proper application"*. He also pointedly expressed a hope that, in the future, there would also be contributions from the great London hospitals, which hitherto had *"set such an example of remissness in the non-preservation of chirurgical documents"*.[88] Such exhortations must be seen as the forerunners of Thomas Wakley's campaign of making publicly known, in medical journals like his *Lancet*, founded in 1823, what was going on in those hospitals.

This case study illustrates firstly how the notion of success is not absolute, but depends on age, sex and time. Secondly, and most strikingly, it shows that the *unbiased* compilation and use of simple but valuable statistics depended primarily on the operator not cheating to suit his own ends. The value of such statistics was thus as much dependent on individual temperament and moral integrity, qualities that in my opinion Cheselden particularly possessed, as it was on organisational skill and volume of data.

James Lind
1736-1812

Rationalist deduction and empirical trial: Abolishing scurvy in sailors

JAMES Lind dedicated his *Treatise on the Scurvy* (1753) to Admiral Lord Anson. This is significant, for it was the 1748 account of Anson's voyage around the world, documenting the extraordinary death rate from scurvy among sailors (at least 380 out of a crew of 510 died on one ship) that had prompted Lind to inquire more deeply into the subject and to publish his observations. When he consulted the existing literature, he found that the only descriptions of scurvy were by seamen and land-doctors, and that no physician conversant with this disease at sea had tried to throw light upon the subject. Lind wrote:

> *Legions of distempers … very different from the real and genuine scurvy, have been classed under its name: and because the most approved antiscorbutics fail to remove such diseases, hence we are told by authors (Boerhaave and many others) that it is the masterpiece of art to cure it … Before the subject could be set in clear and proper light, it was necessary to remove a great deal of rubbish.*[89]

Although there is no direct evidence that Lind was paraphrasing the philosopher – and physician – John Locke, who had represented himself as *"an under-labourer in clearing the ground a little, and removing some of the rubbish that lies in the way to knowledge"*, it can fairly be said that Lind wrote in Locke's spirit.[90] Locke's "master-builders" were his friends Boyle, Sydenham, and Newton, all of whom worked by way of observation and generalisation from facts, the very methods Lind proposed for advancing an understanding of ways to prevent and treat scurvy.

Lind stressed in his *Treatise* that, because facts were *"the surest and most necessary guides"*, his work was to be founded *"on attested facts and observations, without suffering the illusions of theory to influence and pervert the judgement"*.[91] The standard opinion of the time, deduced from theory, which had been promoted by Boerhaave and adopted by people of influence such as Lind's former chief, William Cockburn, attributed scurvy to bad air, congenital laziness and indigestible food. Lind also believed that indigestion and the seasons had something to do with the disease,but he set out, in his own way, to minimise the influence of theories on his investigations.

What did Lind mean when he referred in the *Treatise* to pure ("theoryless") facts? These facts were based upon his own observations while on board the "Guernsey" and the "Salisbury", augmented by letters to him from members of the Society of Naval Surgeons and accounts of past voyages. He had made his longest cruises on the "Salisbury" as part of the Channel Fleet during the War of the Austrian Succession in 1746-1747: 80 out of 350 sailors died from scurvy during this ten week absence from shore. A similar cruise of 13 weeks with the Channel Fleet in 1747 had led John Huxham to recommend fruit as a prophylactic and cure for scurvy, and Lind quoted him and solicited his collaboration by letter.

Lind's descriptions of aetiology, symptomatology and diagnosis were mostly qualitative, although there was a quantitative element in some of his examples. Thus, he illustrated the untenability of the current 'bad-air' aetiological hypothesis by noting that 70 sailors were cured of scurvy even though they had been isolated in the store-room of the "Guernsey", *"where there is generally worse air than in any other part of the ship"*.[92] This, as well as many other passages in his book, especially the famous experiment on which he based his views on the prophylaxis and therapy of scurvy, shows how Lind relied on his recorded observations to investigate both aetiology and the means of prevention and treatment.

A CONTROLLED CLINICAL TRIAL

Lind's celebrated experiment began on 20 May 1747. He gathered together 12 sailors with scurvy, *"as similar as I could have them"*, who all received the same basic diet.[93] Over a fortnight, five groups of two patients each received cider, elixir of vitriol, vinegar, salt water, or an electuary of garlic, mustard, horseradish, balsam and gum myrrh. The remaining two patients received two oranges and one lemon daily for six days only, because the quantity that could be spared had by then been consumed. The short 'treatment' with the latter remedy was sufficient to render one of the two men fit for duty.

Next to fruit, cider appeared to have the best effect, as had also been recommended by the Plymouth practitioner John Huxham (see above, page 24) on the basis of a comparative trial on a large scale and involving several ships. The elixir of vitriol and the other remedies appeared to be useless. The six experimental groups were compared at the end of the fortnight with a vaguely described group of *"others who had taken nothing but a little lenitive electuary ... in order to keep their belly open; or a gentle pectoral in the evening, for relief of their breast"*, in other words 'no medicine whatever'.[94] Possibly the course of scurvy without treatment was too well known for anyone to feel a need for a group without treatment.

Lind judged this small number of observations, reported in detail, as convincing, because the sailors in the orange and lemon group compared so favourably with those in the other groups. In fact, Lind 'confirmed' his own findings using selected observations made by others, although the latter were not as reliable as his own results, nor were they quantified.

The results of Lind's therapeutic trial made little impact on medical opinion in Britain, and requests for supplies of fruit juice were actually rejected by the Navy's Sick and Hurt Board the year after the publication of the *Treatise*. But this "man of observation", as his disciple Trotter called him, proved to be a most influential guide for future work in naval medicine: in the three editions of the *Treatise* (1753; reprinted 1754, 1757, 1772) Lind stressed the use of the experimental approach in clinical conditions. This message was important in itself and Lind was successful in promoting comparative clinical trials, possibly even within the Sick and Hurt Board, whose lethargy has often been criticised: Besides the trials with antiscorbutics related below, the Board later ordered others, including trials of drugs against fevers (see above, page 53).

The history of scurvy after the publication of the first two editions of Lind's *Treatise* affords a good example of the scientific status of British naval medicine in the second half of the 18th century. In hindsight, the slow reception of Lind's work – which entailed a lag of 42 years between his clearly described and experimentally demonstrated cure and its actual introduction by the relevant authorities – seems, as many historians have noted, one of the most foolish episodes in the whole history of medical science and practice. But, if one looks at the contemporary context, it becomes understandable. There was competition both in the medical approach and in the way one argued about the 'right kind' of evidence.

The fact that Lind's 1757 *Essay on the Most Effectual Means of Preserving the Health of Seamen* was republished in 1762 by the Admiralty (as an honour because of his recommendation of a simple method of obtaining drinkable water by distillation of sea water) suggests that his writings were not unknown to the authorities. Moreover, during the first 30 years after publication of the *Treatise*, the Sick and Hurt Board did not act unreasonably with respect to scurvy either. One must recognise that Lind's was only one of a great number of treatises on the subject; and that as a naval surgeon his status was lower than that, say, of a learned Oxonian compiler of 'facts' or a friend of the influential James Pringle. The Board was also inundated with suggestions concerning scurvy; and the proposal that lemon juice was a cure was by no means novel (a fact of which Lind was perfectly aware).

It is worth noting that Lind's experiment was not designed on the basis of theory, but rather was 'controlled empiricism'. In fact, Lind made a mistake of some consequence. Aware of the problems of storing adequate amounts of fresh fruit or fruit juice during long sea voyages, he recommended preparing a condensate (called "rob") by evaporating over several hours a dilution of fresh fruit juice in nearly boiling water. Unfortunately, as we now know, heat destroys much of the ascorbic acid of fresh juice, and the condensate's relative ineffectiveness was noticed by subsequent observers. That, together with Lind's recommendation of a list of other vegetables whose antiscorbutic potential was uncertain, was at odds with his rejection of unwarranted speculation and his professed reliance on carefully observed facts. His theory of scurvy, too, was traditionally speculative. It could lead away from fruit juice, as we shall see in the following section which considers the work of David Macbride.

LABORATORY GENERATED PATHOPHYSIOLOGY

David Macbride, in whose views the Admiralty became chiefly interested, was actually an admirer (and perhaps imitator) of Lind. His *in vitro* experiments embodied the hypothesis of William Cullen, the famous Edinburgh professor, which accorded with the prevailing theory that scurvy was due to a lack of digestive fermentation in the absence of fresh vegetables. From these experiments he derived the idea that malt, with its potential for fermentation, might be an ideal cure.

This was not unscientific by 18th century standards; on the contrary, it was completely rational. *In vitro* experiments were actually a feature of 18th century British pharmacology. By these means Macbride, a little known Dublin physician looking out for a stronghold in London, impressed professional and administrative authorities far more than did the empirical observations of Lind (who had initially explained the mechanism of the action of his fruit juices on the basis of the same theory).

Macbride was ten years Lind's junior. They had both been on active sea duty as ship's mates and later as surgeons during the War of the Austrian Succession. After 1748, both studied for a time in Edinburgh, Macbride also in London. Lind remained in Scotland until his appointment to Haslar in 1758, whilst Macbride settled in his homeland of Ireland. In 1756 Macbride was, with George Cleghorn, one of the founding members of the Dublin Medico-Philosophical Society. It was to this forum that he first presented, in the early 1760s, the results of his *in vitro* experiments on fermentation and putrefaction, which were considered sequels to those of the Edinburgh men, above all of Pringle, who was knighted in 1766 and already highly regarded in London (see above, page 25).

Fermentation was seen as one specific expression of the cementing principle of life, its absence leading to disintegration and putrefaction. Autopsies of scurvy corpses had shown a great deal of disintegration and putrefaction in many organs, so Lind also considered scurvy a "putrid" disease, before making his own observations (1757). A method for its prevention or cure therefore had to counteract putrefaction and/or restore the cementing principle.

For Lind the antiscorbutic action of fresh fruit and vegetables was also explained by their acidescent quality (as opposed to the alkalescent or putrescent nature of animal substance), i.e. to their good digestibility. Vegetables worked through their *"saponaceous, attenuating and resolving virtue"* (note the laboratory jargon!) *and* their fermentative quality, which made them resist putrefaction (in contrast to flesh and animal substances, which tended to promote it). This fermentative quality stimulated digestion, that is, the setting free of a subtle imperceptible gas, transforming food into chyle and blood. Such were the "*chief and most essentially requisite"* qualities, mixed together from several sources, for an antiscorbutic mixture.[95]

For Macbride, and here they disagreed, it was the capacity of fermentation alone of vegetables, when mixed *in vitro* with animal substance and placed in the proper degree of heat, which explained their effect. In the course of fermentation the fresh vegetables *"throw off an elastic vapour, or spirit [i.e. new air] of surprising activity endured with a power of restoring sweetness to putrid animal fluids."*[96] Unfermented malt (called also "the wort") had this quality, too, and as a substitute for fresh fruit it had obvious practical and economical advantages: it was easily obtainable, storable and cheap; and it might operate also in other putrid diseases, such as fevers or ulcers. Thus, despite the repeated anti-theory stance of both Lind and Macbride, speculation was an important feature of their work. Their theories would now be tested by others.

CLINICAL OUTCOME OBSERVATIONS

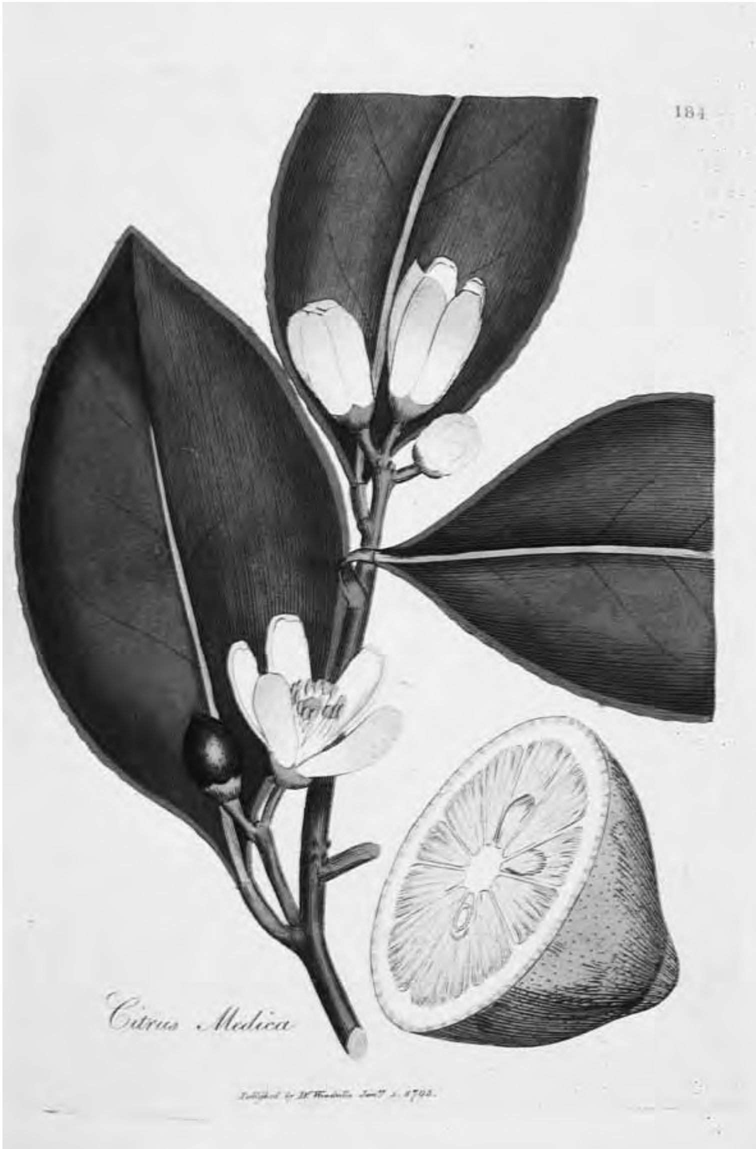
In 1762, the Admiralty became interested in Macbride's work, as a result of a recommendation made by George Cleghorn to William Hunter, the well-known London physician and a Commissioner of the Navy Sick and Hurt Board. The Board ordered a trial of the malt in the naval hospitals of Portsmouth (Lind's hospital!) and Plymouth. The trial was envisaged methodically:

> *It was absolutely necessary, in order to determine the genuine effects of the remedy proposed, that the patients should, during the time of trial, be entirely debarred from any sort of recent vegetable. [But this restriction] … looked so like retarding men's cures for the sake of experiment, that it occasioned a murmur and disgust.*

Thus the trial had to be stopped and the Admiralty ordered it to be taken up at sea *"where it was expected that patients would cheerfully submit"*.[97]

Yet until 1766, the Admiralty was unable to forward Macbride any reports in consequence of its order. He could only quote a letter he had received from Sir John Pringle in May 1764 confirming Macbride's *theoretical* view – also Pringle's own – of the *modus operandi* for a cure of scurvy. The Admiralty, strengthened in its views by Pringle, was keen on having the trial finally implemented according to its orders of 1762. It therefore directed that it should be carried out on the ships of Samuel Wallis and Philip Carteret during their circumnavigations, starting in August 1766.

Macbride finally received a first report (dated April 1767) while the second edition of his *Experimental Essays* was being printed and was able to add excerpts from it as a 'Postscript'. The report was by the surgeon of HMS "Jason" (which was



Citrus medica

commanded by Macbride's own brother). The surgeon reported in great detail four cases of patients who had been put on the wort the same day and had received the same vegetable-free diet. After nearly two months, two of the patients returned to duty while still at sea, one had no specific complaints (it is mentioned that one of the four patients had a *lues venerea*) and the fourth was "mending" but slowly. Macbride himself did not consider these cases as *"altogether conclusive with respect to the antiscorbutic virtue of the Wort,"* but at least they had shown that the preparation could be taken in large doses, in opposition to Huxham's claims.[98]

In Macbride's eyes, it was the journal of Mr Badenach, a surgeon of the Honorable East India Company (transmitted to him by William Hunter), which *"put the Matter beyond all Dispute"*. There had been enough malt only for six cases, related in detail, in which the disease was more or less checked (in three cases there were relapses!) until they landed, when all were cured in five days by the use of fresh fruits and vegetable soups. Although Badenach contradicted himself, saying that one of the three relapsing cases and *"the rest of the [forty] scorbutics were but very little better when they were landed …"*, the Admiralty seems to have been pleased by these results.[99] This was defendable on three grounds at least:

(1) On superficial reading, the evidence brought forward so far by Lind and Macbride was similar when it came to the cases actually observed and described.

(2) Their pathophysiological theories of scurvy and their explanations of the *modi operandi* of the acknowledged antiscorbutics were not too divergent.

(3) The wort was much easier to handle and cheaper than the rob of fruit juices.

Thus, in July 1768, with Wallis and Carteret still at sea, the Admiralty sent Captain James Cook precise orders for another trial during his first voyage of exploration, with explicit reference to Macbride's *Account*, a copy of which was sent with the orders. Cook was also expected to try other antiscorbutics such as fresh fruit and to keep exact accounts. Also in 1768, John Clark (see above, page 43) used the wort during a voyage to the East Indies. He was aware that the proposals of the *"ingenious Dr Lind"*, advancing the preparation of a rob of fruits and berries, had *"been found to answer best upon experiment"*. However, he said, of late:

> *… no proposal has inspired greater hopes of success than the malt infusion recommended by Dr Macbride. His theory … is founded upon the most plausible principles, and is supported by seemingly conclusive experiments made out of the body"* [that is, *in vitro*].[100]

But what were the facts reported from the three voyages by Wallis and Carteret, Cook, and Clark? On Wallis' "Dolphin", three among the sailors with scurvy selected for the experiment with the infusion of malt were showing severe symptoms: they *"either boiled their bread or fruit [!] in it, and after fifteen days fell in some island with plenty of fresh vegetables and cocoa nuts …"*. Carteret's "Swallow" was less fortunate, with 18 people were affected. Details of five were given, two of whom had died, *"notwithstanding they were fully supplied not only with the wort, but also with a variety of fresh vegetables ... which were procured from time to time at different islands*".[101] This surgeon believed that the wort did not actually cure, but retarded the progress of scurvy. He also wondered about the quality of his malt, it being somewhat damaged by insects, a view also expressed by Carteret in the report submitted after his return in 1769.

It is highly to Macbride's credit that he did not conceal the reports of Wallis' and Carteret's surgeon in the Appendix to his new book, *A Methodical Introduction to the Theory and Practice of Physic* (1772) (translated into Latin, French, Spanish, and German), in which he gathered all the evidence known by then on the value of wort in scurvy. His final, but as became apparent, most important evidence, was based on extracts from the journal of Cook's surgeon, Perry.

Cook's "Endeavour" had returned to England in July 1771 without one loss from scurvy. Perry's was a confused and contradictory piece of work, but, nevertheless, contained a firm conclusion which was quoted fully by Macbride. After listing the antiscorbutics used – sauerkraut, mustard, vinegar, inspissated orange and lemon juice, sugar, molasses vegetables, etc. – Perry said that *"these were of such infinite service to the people in preserving them from a scorbutic taint that the use of the Malt was, with respect to necessity, almost entirely precluded"*. It was used in four cases of scurvy in March and April 1769, apparently with all the good effects that could be wished, and from then on:

> *... while at Sea the Wort became part of our diet, so that, excepting five cases ... not a Man suffer'd any inconvenience from this distemper. In the cases I have mentioned, a trial was made of the Robs (of orange and lemon) and attended with success. It is impossible for me to say what was the most conclusive to our preservation from Scurvy, so many being the preventives used: but from what I have seen the wort perform, from its mode of operation, from Mr Macbride's reasoning I shall not hesitate a moment to declare my opinion, viz. That the Malt is the best medicine I know, the inspissated Orange and Lemon juices not even excepted.*[102]

This statement by a decent young man was intended to avoid contradicting the views of his superiors in the Navy Board and in professional circles, and Perry's conclusion, despite its weak basis, seems to have been adopted, even outside Britain.

Let us turn now to the facts presented by John Clark after his journey to the East Indies. His *Observations* were first published in 1773. He reported on four cases in great detail. These patients had received the wort for a maximum of three weeks, but as the scorbutic symptoms constantly increased, they were also all given fruit and vegetables. In two other cases, the symptoms had worsened so quickly that the wort had to be discontinued earlier. From another of the Company's ships that had been at sea in 1770, two similar cases were described in detail and four were mentioned briefly. All were totally cured only after they came on shore.

Clark thought himself *"wanting in duty to the public"* if he concealed these cases. However, as the malt infusion had been supported by very strong instances, namely the cases related in Macbride's *History*, he suggested cautiously that *"it may still seem to merit some further trial"*.[103] For this purpose he recommended a comparative trial, as Lind had carried out: could not the beneficial effect reported by Macbride on the "Jason" have been due to the nourishing diet seasoned with garlic, currants, rice and sago given to all four patients in addition to the wort? Had two of them been put on this regimen without, and two with the wort, the latter's effects might have been more precisely ascertained.

Thus the first clinical trials of the wort set the balance officially in favour of this remedy on the basis of well intentioned trials, but which, in practice, could not be called scientific, even by the standards of the time. This fact was clearly recognised by an independent-minded observer such as John Clark. It is of particular interest, therefore, to analyse the attitude James Lind took to them, nearly 20 years after his first publication on scurvy.

PURE ("THEORYLESS") FACTS REVISITED

In 1772 Lind published the third edition of his *Treatise*, including the substance of four volumes of observations, daily and carefully made at Haslar Hospital. Lind had kept records of all his patients: during the first two years of his activity there he saw 1,146 cases of scurvy among 5,743 patients. During the Seven Years' War (1756-63) he said he had frequently visited 300 or 400 scorbutic patients a day. What use did he make of this unique opportunity?

Again, Lind did not publish lists of his cases, nor numerical *results* of his therapeutic trials or autopsies. But there had been a change in his theory on scurvy and he became reluctant to assert that scurvy was a 'putrid' disease – which he now thought anyway was an inappropriate designation. This was important, for it shook the rationale for the malt therapy. Apart from this, Lind's view of the disease had not changed very much during the 15 years spent at Haslar. Justifying his change of view concerning putrefaction, he said:

> *... some doubtful theoretical doctrines remained unaltered, as resting on the faith and dissections of other authors, and as being agreeable to the present theories of physic ... but the theory of ... [scurvy] as well as of many other diseases, is in general merely conjectural, and is always the most exceptional part of a medical performance ... it is indeed not probable, that a remedy for the scurvy will ever be discovered, from a preconceived hypothesis; or by speculative men in the closet, who have never seen the disease, or ... at most, only a few cases of it.*[104]

These clear remarks against rationalism were probably aimed less at Macbride than at some other contemporary British authors writing from their 'closets'. It was also self-critical if one considers his earlier theoretical deliberations (see above, page 69). Lind's new clinical experiences were summarised in the 'Postscript' to the third edition of his *Treatise*. Several experiences of "some thousand", "several thousand", "above two thousand", "some hundreds", and of 10 or 12 "out of the number of 100 scorbutic patients" were hinted at.[105] As to the cure of scurvy, he inserted letters from four naval surgeons relating a total of 232 scorbutic patients cured with fruit juices during the Seven Years' War. He said that the wort had not produced "any considerable effect" in the trials during Wallis' and Carteret's circumnavigations, although he quoted the testimony of one of Carteret's soldiers who had assured him personally that he had been restored to health by it.[106]

When reporting his own trials, Lind also had a good word for the wort. Whether he knew already of Perry's report, approved by Cook and the Admiralty, is uncertain: The Admiralty had received this report, dated 12 July 1771, before the 2nd August 1771, and Lind's manuscript was finished on the 30th August. Macbride's infusion of malt was the only omission from Lind's list of *"all the medicines and methods of cure that have been recommended for this disease"* – that is, scorbutic juices, scurvy-grass juice, Peruvian bark in large quantities, infusions of guaiac wood – of which he had made it his *"study for some years, with unvaried diligence, to observe the effects by putting them to the fairest trials"*. Nor was the wort dealt with in the main text, but only mentioned in a footnote:

> *I put 130 scorbutic patients under a course of it for fourteen days ... it has the advantages, when newly made, to be extremely palatable, the patients were very fond of it, and there was not one instance of its occasioning sickness, gripes, or purging. On the whole, it is a very nourishing liquor, well adapted for scorbutic patients.*[107]

It was a cautious, non-committal statement, but considering Lind's popular position among his naval colleagues by 1772, it might well have been interpreted as evidence in favour of the wort.

Lind's had been controlled studies, the patients were confined in special wards, strictly watched and *"debarred from eating any green vegetable, fruits or roots whatever, though many of them had not tasted anything of that sort for several months; they were not even permitted to taste the hospital broth"*; and their state was followed daily.[108] Comparative effects of different fruits and vegetables had been assessed likewise. These experimental conditions had impressed colleagues working on scurvy, such as John Clark. Thus Lind had changed his theory of scurvy according to his own observations, a fact which is well worth stressing in view of recently expressed doubts of his practising experimental science.

Yet in terms of therapeutic recommendations, he cannot be credited with any major advance. Despite his repeated assertions to the contrary, with hindsight it may cautiously be suggested that Lind, like his counterpart in the Army, John Pringle, was both a clinical observer and a theoretician working in the speculative framework of his time. In addition, however, Lind undertook to test (or rather to verify) one of his hypotheses. And, with respect to the therapy of scurvy, he may have been more objective an observer than previously thought, for many of his scurvy patients probably suffered from a mixed deficiency of both vitamins B and C, and the wort *was* rich in vitamin B complex. One of his conclusions in 1772 was therefore not only very correct but also farsighted:

> *A work, indeed, more perfect, and remedies more absolutely certain might perhaps have been expected from an inspection of several thousand scorbutic patients, from a perusal of every book published on the subject, and from an extensive correspondence with most parts of the world … but, though a few partial facts and observations may for a little, flatter with hopes of greater success, yet more enlarged experience must ever evince the fallacy of all positive assertions in the healing art. Est modus in rebus, sunt certi denique fines.*[109] [The ways are many, but only the end is certain.]

THE EVIDENCE FROM ARMY AND NAVY RETURNS

Meanwhile, the War of American Independence had begun in 1774 and was to become general in 1778. The official British Navy policy for the prevention of scurvy derived from Cook's recommendations: the Sick and Hurt Board allowed the wort, sauerkraut and potable soup. The rob of fruit juice was considered ineffective and too expensive, although some naval surgeons looked on it as a medicament that they might occasionally provide from their own purse.

During this War, nosological tables, which included for the first time the results of different treatments for scurvy, were compiled and published. To his great credit, Robert Robertson, whom we encountered in the chapter on fevers (see above, page 39), initiated this practice in the Navy during active duty. Before entering the Navy in September 1760 he had kept a journal while serving as a surgeon in the Greenland whale fishery, and he continued keeping daily records during his whole practice afloat until 1783. But more than that, he continually summarised his records in *"pathological and comparative tables to show the efficacy of different modes of practice"*.[110] As he served in Africa, the West Indies, North America and the Channel Fleet, good accounts of naval medicine during the American War became available from these theatres. Gilbert Blane, who became physician to the West Indies Fleet in 1780, wrote *Observations on the Diseases Incident to Seamen*, which appeared soon after the end of the War in 1785 (and was re-issued in 1789 and 1799). These three books illustrated not only their authors' passion for statistics, but also their ability to draw succinct conclusions from the elaborate nosological tables that they loved to compile.

Robertson listed 30 patients with scurvy in his *Journal* (1777), none of whom had died on board. He had used Lind's method of cure, to which, in his opinion, nothing needed to be added. Blane, having read Lind and Cook, wisely limited himself in his instructions in 1780 to merely stating both their opinions, and recommending both malt and lemon. The Board, which referred to the testimony of Cook and his surgeon, refused his application in 1781 for a stock of lemon juice. Scurvy promptly broke out once more. Blane, as physician to the fleet, did not hesitate to present his findings in the form of '*Memorials*' to the Sick and Hurt Board during his first leave to Europe in October 1781 and again in 1782.

It is from this time onwards that the Board may be blamed for its hesitant attitude. From the statistical evidence it became clear that scurvy was not being kept under control. The letters of surgeons asking for a more liberal supply of preventives increased. Furthermore, Robertson's and Blane's tables gave for the first time regular statistical information on the nosology of both scurvy and fevers. Scurvy appeared to be a worse scourge than typhus in the West Indies; both were associated with cold latitudes; but whereas continuous fevers (typhus?) disappeared with the sun, scurvy continued if the ships remained long at sea. For instance, Blane reported that by May 1781 no fresh vegetables had been taken on board since January of the same year and that there were 1,077 cases of scurvy compared with 678 in April and 543 in June, when supplies became available again. The superior efficacy of fresh lemons as compared with the rob was also noticed. Blane called the native juices of lemons and oranges *"real specifics in that disease, if anything deserves that name"* (although he recognised a certain value of sauerkraut, molasses and malt). It could also be stated precisely that scurvy was not infectious, and that it was not due to a defect of digestion, but to a defect of diet. Furthermore, it was realised that it was not the land *air* which was curative, but the *diet* ashore.[111]

Thus the deliberate use of quantitative methods during the American War yielded a clearer description of the aetiology of scurvy, and a more precise assessment of the remedies that could be employed was gained by the mid-1780s.

Unfortunately, the books reporting this evidence, especially those containing many figures, were sometimes considered a new kind of dull literature and were despised by many. However, they must have proved more convincing in the long run (even to the authorities) than the conjectural arguments of men like William Renwick who, in 1792, claimed that scurvy was *"not occasioned by diet to which it is so generally attributed, but … [by] mephitic exhalation, by which the animal fluids are very differently affected"*.[112] Renwick therefore claimed that the distribution of lemons and oranges had been less favourable to sustaining the vital powers than would have been as many pinches of snuff – and this in a fleet for which precise returns existed. It was perhaps luck that the 'right' side fought with better arms, for with statistics one could prove many things, as outlined in the earlier section on 'fevers'.

THE CONQUEST OF SCURVY, 1795

By the 1780s there remained still the task to impress upon the Admiralty the utility of the fruit juices. The final approval by the Sick and Hurt Board was apparently accidental. Part of the story says that in 1793, upon Blane's advice to a friend appointed to the East India Company, a fleet well supplied with lemon juice (kept with alcohol) reached Madras scurvy-free after 19 weeks without touching at any port. This remarkable demonstration of the effectiveness of lemon juice enabled Blane, now himself a commissioner of the Board, to persuade the Admiralty in 1795 to sanction the issue of lemon juice on a far more generous scale than ever before, although a number of naval surgeons claimed credit for its introduction into the fleets under their responsibility without a general order.

This is perhaps of less concern to us than the fact that the consequences were easily expressed numerically. For instance, it is said that when in 1797 the First Lord of the Admiralty asked to see a case of scurvy when visiting Haslar Hospital, no such patient could be found. Although such cases continued to be frequently reported, nearly all could now be cured on board. Thomas Trotter, the physician to the Channel Fleet from 1794 who had asked for and received lemons and oranges before sailing in April 1795, was able to state that *"upon comparing notes and remarks from the reports of the surgeons … not less than three thousand cases, unfit for duty had been cured, on board"*.[113] In 1815 Gilbert Blane showed that the scurvy had almost disappeared from the fleet: according to the figures sent to him by Dr John Lind, the son and successor of James at Haslar, only two cases had been sent to his hospital in the last four years of the Napoleonic Wars.

In summary, the history of scurvy in the British Navy during the second half of the 18th century shows how comparative empirical clinical trials were well described by Lind and Clark, yet imperfectly set into practice on a very small scale. Simultaneously the rationalist pathophysiological explanation of scurvy, based partly on the interpretation of fashionable *in vitro* experiments and partly on mere reasoning, brought about the episode of Macbride's wort. Yet, due to an interplay of accurate observation and simple numerical records from individual ships and whole fleets in wartime kept by Robertson and Blane, both the clinical features of scurvy and the effectiveness of means of prevention and therapy became better understood and were better assessed. This was rational empiricism carrying the day. It led ultimately to a change of opinion in favour of fruit juice amongst the authorities, both professional and political, directing the naval service, and thus to the conquest of scurvy.

Digitalis purpurea

From "ordinary experience" to "ordered experience": Adopting a folk remedy for dropsy

ONE of the most outstanding and lasting contributions to the 18th century pharmacopeia was digitalis, and William Withering's *Account of the Foxglove and some of its Medical Uses with Practical Remarks on Dropsy and Other Diseases* (1785) is a medico-historical 'classic'. An Englishman born in the Midlands, Withering studied medicine in Edinburgh and then settled in Stafford in 1767. Having little to do in his practice at first, he occupied himself with botanical studies, eventually becoming a celebrated botanist. He also kept a climatological journal. In 1772, a hospital was founded in Stafford, to which he was appointed physician, but three years later he moved to Birmingham, where he became chief physician to the General Hospital when it was opened in 1778. He was also a member of a local society for the abolition of the slave trade.

Lettsom was keen to have Withering as a corresponding member of the Medical Society of London after reading his *Account of the Foxglove* in 1787. By then, Withering had already been a Fellow of the Royal Society for three years. A friend of Percival since their Edinburgh days, they continued correspondence, and Withering also knew Thomas Fowler (see above, page 53). An old countrywoman had recommended foxglove to Withering as "her" remedy against 'dropsy' (oedema). He obviously believed her, but not uncritically: he undertook a prospective study, and collected data for 15 years before he was prepared to publish his findings.

Withering's systematic study of the effects of the foxglove in dropsy was based almost entirely on patients seen in private practice. Of the 163 cases he had collected by 1785, only seven had come from the Birmingham Hospital. He introduced the description of his cases as follows:

> *It would have been an easy task to have given select cases, whose successful treatment would have spoken strongly in favour of the medicine, and perhaps been flattering to my own reputation. But Truth and Science would condemn the procedure. I have therefore mentioned every case ... proper or improper, successful or otherwise.*[114]

This approach may be one reason why he succeeded in deciding which types of dropsy patients would benefit from digitalis, all the more remarkable as virtually nothing was known then about the pathology of different kinds of oedema. In assessing the value of his treatment Withering relied upon the clinical methods available: close observation of the patient, assisted by counting the pulse and measuring the urinary output as an objective check of the validity of subjective improvement. He thought a case most promising:

> *... if the pulse be feeble or intermitting, the countenance pale, and the lips livid, the skin cold, the swollen belly soft and fluctuating, or the anasarcous [oedematous] limbs readily pitting under the pressure of the finger, [for then] we may expect the diuretic effects to follow in a kindly manner.*[115]

He compared these parameters with the patient's previous condition and sometimes observed relapses on discontinuing the drug. Considering the clinical methods at his disposal, he could only be cautious in drawing conclusions from an inquiry as objective as his attempted to be:

> *No general deductions, decisive upon the failure or success of the medicine, can be drawn from the cases I now present ... [for they] must be considered as the most hopeless and deplorable that exist ... lost to the common run of practice.*[116]

He defended his decision to limit his descriptions to his own cases. Although he admitted that people might doubt the impartiality of his account, he reasoned that, had he reported the cases sent to him by fellow physicians, his book would have been seemingly free from any preselection. He was concerned that the critics then:

> *... would ... close the book, with much higher notions of the efficacy of the plant than what they would have learnt from me ... [for] the cases [I have received] are, with some exceptions much too selected.*[117]

Withering thus dismissed the common practice of increasing the number of observations by adding the experiences of others, which would be misleading if the latter did not give all the details of their whole practice, successes and failures alike. As a careful observer and thinker, he realised a fundamental truth that has been reflected throughout the history of medicine:

> *It is much easier to write upon disease than upon a remedy. The former is in the hands of nature, and a faithful observer, with an eye of tolerable judgment, cannot fail to delineate a likeness. The latter will ever be subject to the whims, the inaccuracies, and the blunders of mankind.*[118]

Withering's indirect successor at Stafford and an acquaintance of his was Thomas Fowler, whose *Medical Reports on the Effects of Tobacco* (1785, 1788) presented data according to exactly these principles, reporting the incidences of "operational [side] effects" such as sensation of heat, vertigo, nausea and diarrhoea among

400 cases.[119] In the same report, Fowler referred to 79 cases of dropsy, among whom 28 were cured (particularly those with oedema of the legs), 32 relieved, and 19 not relieved.

Withering's *Account of the Foxglove* aroused widespread interest and reaction among others, as well. In *Medical Histories and Reflections on Dropsy* (1792), John Ferriar (see above, page 17) also emphasised the importance of reporting clinical data without allowing "personal considerations" to intrude, stressing the importance of reporting unsuccessful cases. In his opinion, keeping and periodically analysing a journal recording indications for and success of treatment was fundamental for any physician who wished to avoid false conclusions based on memory alone and who wanted to *"do justice to his patients"*.[120]

On the treatment of dropsy, Ferriar wrote: *"I do not remember, to have seen any comparison instituted among the various methods of reducing the swelling by increasing the quantity of urine in this disorder"*.[121] Accordingly he presented 47 cases: 24 treated with digitalis, ten with cream of tartar, eight with calomel, the others with various remedies. He presented the results in a table presenting both the overall results and data relating to the four categories of 'dropsy' (anasarca, ascites, hydrothorax and combined cases), showing the numbers of patients cured, relieved, not relieved and dead. He concluded from this analysis that digitalis was the most favourable agent in general, and that cream of tartar represented the best treatment for hydrothorax (admittedly, based on only four cases).

Ferriar pursued a research programme on dropsy well into the 19th century. His cumulated experience was reported in the second volume of his *Medical Histories* (1795), and he published an *Essay on the Medical Properties of the Digitalis Purpurea* in 1799, in which he recommended the use of digitalis combined with cream of tartar. In 1813, he reported on a new remedy for dropsy (Extract of Elaterium), with which he had treated 20 selected "desperate cases". He reported a "nearly uniform successful" result, but noted that the observation was insecure because he had used another active diuretic with it![122]

This case illustrates some of the criteria to be fulfilled in undertaking the step from Bacon's "ordinary experience", based on more or less fortuitous observation and therefore largely subjective, towards his "ordered experience", built on planned observation using pre-established, measurable criteria and aiming at objectivity (see above, page 1). I have shown the same phenomenon with James Currie's cold water bathing against fevers (see above, page 51) and it holds also for another time-honoured therapy: taking the waters for various chronic ailments, as I shall describe in the next section.

William Falconer
1744-1824

Towards objectivity in a commercial environment: Bath waters and other things for palsies and rheumatic diseases

THE General Infirmary at Bath was opened in 1742. It was a specialised institution admitting only poor patients who came from outside the city upon medical recommendation. From its outset, this charity was thus doubly committed to promoting the utility of spa treatment – to its lay supporters as well as to the medical profession. Its physicians therefore laid great emphasis on numerical evaluation of the results of treatment, prompted in part by the "balneological war", a prolonged argument over the uses and abuses of Bath waters during the 18th century. In 1770, Rice Charleton, an Oxford MD who was honorary physician to this establishment, asked a recurring question:

> *Whose opinion is to be trusted if, after experience of ages, the question of usefulness or detriment of a remedy still persists, if for instance, the most eminent physicians of the last and the present centuries, are dramatically opposed?*

His answer was that *"the most respectable authority must give way to the force of Facts"* (and it is worth noticing his use of typography to emphasise Facts rather than authority).[123]

In his *Inquiry into the Efficacy of Warm Bathing in Palsies* (1770) Charleton set out to resolve the dispute using precisely kept records of all patients seen between May 1751 and May 1764. He summarised his findings in a table categorising the 1,053 patients admitted under the general diagnosis of palsy into 12 sub-categories: 45 general palsies, 283 hemiplegias, 144 palsies of the lower limbs, 3 dead palsies, 5 shaking palsies, 247 palsies from cider … and 183 without diagnosis. For each of these he presented the number of patients cured or benefited (813), and the number not improved (240). The latter group was further subdivided into patients "improper" for treatment, those who were discharged "for misbehaviour" or at their own request, and those who had "eloped". He commented that the benefit of the Bath waters was so great *"that, it is almost unnecessary to take notice of an error in this calculation tending to their disadvantage"*, namely that the last four groups had not had the trial of the waters.[124]

Charleton also used arithmetic to resolve other questions. For instance, *"The evidence which the table of Paralytics affords"* would, he hoped, best determine the question as to whether warm bathing would result in a recurrence of stroke in patients with hemiplegias, as was often presumed. This Charleton did by deducing the mortality rates, which were 1 in 22 for all his patients, and 1 in 21 in the hemiplegic, some of whom had actually died of smallpox. Therefore the cure at Bath was "preventive" rather than an accelerating agent for the return of strokes, for "*more might have died of apoplexy without bathing"*.[125] The formulation of a hypothesis, then testing it by analysis of the records, was a genuine feature of research done at Bath.

In this case, the method of determining the probability of a cure being effective, albeit defective in its lack of appropriate controls, was nevertheless remarkable in its use of simple arithmetic. It is reminiscent of Jurin's demonstration in the first half of the 18th century that the probability of death from inoculation smallpox was very much less than that of natural smallpox.

In 1784, William Falconer became honorary physician to the General Infirmary at Bath. Born in Chester, Falconer had studied in Edinburgh and Leyden and, before his appointment in Bath, had been a physician at the Chester Infirmary (where John Haygarth had been a colleague). Falconer continued and elaborated Charleton's numerical analyses based on the register that had been kept at the Bath Infirmary since 1772, and in 1790 he published his findings in a *Practical Dissertation on the Medicinal Effects of the Bath Waters*. This contained a comparison of Charleton's statistics for 1751-1769 with those for 1775-1785. Falconer introduced his report by referring to the mischievous influence of preconceived theories and concealment of unsuccessful cases and the consequent need for mass observation. For instance, he declared that if the mineral waters were *"described as doing good only without power of doing harm, we may be satisfied either that the account is misrepresented, or that their qualities are too insignificant to merit notice"*.[126]

Falconer then indicated the probability of the success of the waters by giving the simple ratios of those who had benefited to those admitted and those who had not benefited. The latter ratio could be enormous (63,877 to 1 for "chronic rheumatism" and 3,175 to 1 for "ischiatic complaints of the hip") or small (5 to 1 for "white swelling of the knee"). The total numbers of cases of palsies, chronic rheumatism, ischiatic complaints of the hip, white swelling of the knee and leprosy were 730, 362, 167, 12 and 196 respectively. In other diseases, where there were presumably not enough cases, as no numerical accounts were given. A table of the age-distribution of idiopathic palsies and a list of conditions that were not amenable to treatment with the Bath waters completed this notable *Dissertation*, which was in its third edition by 1807.

Having 'established' the success of the waters in some conditions, Falconer used the registers of the whole hospital practice (not only of his own practice) for two even more elaborate studies. These concerned *Rheumatic Cases* (1795) and the closely related topic of *Ischias; or the Disease of the Hip Joint* (1805).

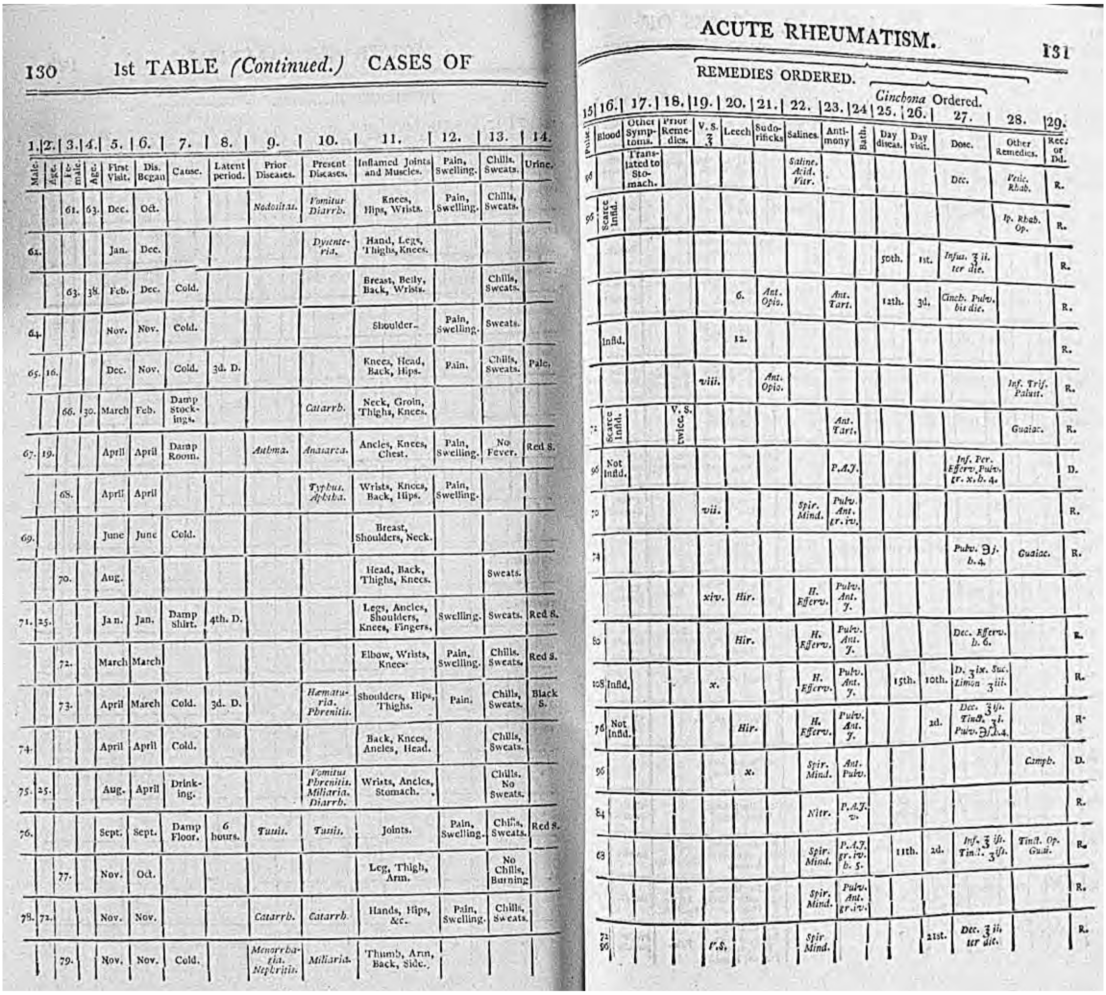
The first study analysed 444 patients treated between 1785 and 1793. They were divided into 154 “cured”, 167 “much better”, 65 “better”, 53 “no better” and five dead (including one of smallpox, one of intestinal disorder), each category being well defined. After excluding 38 patients who had had no real trial of the waters, 406 remained. For each of the five categories the average duration of stay was calculated. They were also grouped according to those who could have been described as benefiting or not benefiting. The proportions in each sex and age group were presented in detailed tables for each of the five categories, as well as their distribution according to the month of the year and the average stay of the patients admitted in each month and each season.

Comparison with Charleton’s earlier account (1770) showed that Falconer’s registers gave “a full and decisive testimony”, independent of the period chosen, because the ratios of patients “cured”, “much better” or “benefited” to the whole were *“nearly on a level”*: 1 to 2·7532 as compared with 1 to 2·818, 1 to 2·5381 with 1 to 2·4864, and 1 to 1·0984 with 1 to 1·1438, respectively. (These were Falconer’s own calculations!)

Numerical analysis of the records also served to challenge the commonly held belief that the disease was no more frequent in women than in men. On the contrary, the proportion of men to women was 1·9041 to 1. By adjusting the sex ratio by a simple “rule of three”, Falconer demonstrated that the successful results were rather in favour of the men: If the success rate (the proportion of “admitted” to “benefited”) was the same in men as it was in women, namely as 146 to 130, it should be 278 to 247·53 in men. But the real number of men benefited was 256. Thus there was a small difference, the proportional advantage being only as 31 to 30, in other words, favouring one case in 30 admitted.

Falconer’s analyses are probably the most detailed published attempt during the 18th century to quantify what ‘success’ and ‘difference of success’ meant. His analysis of 556 patients with ischias admitted between 1785 and 1801 was very similar. It included a numerical comparison with the results obtained between 1761 and 1773 in the same establishment and published by Charleton. However, it is important to note that the cure at Bath consisted of many elements, traditionally including measures such as bleeding, vomiting (antimonials) and blistering, as well as warm bathing and drinking the waters. It follows that the effect of the waters *per se* was difficult to evaluate. Both Charleton and Falconer tried to circumvent this by showing in their case histories how medical treatment prior to the cure at Bath had often been ineffective.

Finally, it is worth mentioning that Falconer, who corresponded with Lettsom on various issues, was a regular contributor to the *Memoirs* of the Medical Society of London. In 1787 he had been the first winner of an annual award sponsored by Lettsom, and a numerical study on palsy, based on 100 consecutive cases from the register at Bath, was published soon after (the findings being presented as percentages). In 1792, Falconer was listed as a corresponding member of the Society, and in 1802 he won another of its awards reserved for non-fellows.



130 1st TABLE (*Continued.*) CASES OF

1. Male.	2. Age.	3. Female.	4. Age.	5. First Visit.	6. Dis. Began	7. Cause.	8. Latent period.	9. Prior Diseases.	10. Present Diseases.	11. Inflamed Joints and Muscles.	12. Pain, Swelling.	13. Chills, Sweats.	14. Urine.
		61.	63.	Dec.	Oct.			*Nodositas.*	*Vomitur Diarrh.*	Knees, Hips, Wrists.	Pain, Swelling.	Chills, Sweats.	
62.				Jan.	Dec.				*Dysenteria.*	Hand, Legs, Thighs, Knees.			
		63.	38.	Feb.	Dec.	Cold.				Breast, Belly, Back, Wrists.		Chills, Sweats.	
64.				Nov.	Nov.	Cold.				Shoulder.	Pain, Swelling.	Sweats.	
65.	16.			Dec.	Nov.	Cold.	3d. D.			Knees, Head, Back, Hips.	Pain.	Chills, Sweats.	Pale.
		66.	30.	March	Feb.	Damp Stockings.			*Catarrh.*	Neck, Groin, Thighs, Knees.			
67.	19.			April	April	Damp Room.		*Asthma.*	*Anasarca.*	Ancles, Knees, Chest.	Pain, Swelling.	No Fever.	Red S.
		68.		April	April				*Typhus. Aphtha.*	Wrists, Knees, Back, Hips.	Pain, Swelling.		
69.				June	June	Cold.				Breast, Shoulders, Neck.			
		70.		Aug.						Head, Back, Thighs, Knees.		Sweats.	
71.	25.			Jan.	Jan.	Damp Shirt.	4th. D.			Legs, Ancles, Shoulders, Knees, Fingers,	Swelling.	Sweats.	Red S.
		72.		March	March					Elbow, Wrists, Knees.	Pain, Swelling.	Chills. Sweats.	Red S.
		73.		April	March	Cold.	3d. D.		*Hæmaturia. Phrenitis.*	Shoulders, Hips, Thighs.	Pain.	Chills, Sweats.	Black S.
74.				April	April	Cold.				Back, Knees, Ancles, Head.		Chills, Sweats.	
75.	25.			Aug.	April	Drinking.			*Vomitus Phrenitis. Miliaria. Diarrh.*	Wrists, Ancles, Stomach.		Chills, No Sweats.	
76.				Sept.	Sept.	Damp Floor.	6 hours.	*Tussis.*	*Tussis.*	Joints.	Pain, Swelling.	Chills, Sweats.	Red S.
		77.		Nov.	Oct.					Leg, Thigh, Arm.		No Chills, Burning	
78.	72.			Nov.	Nov.			*Catarrh.*	*Catarrh.*	Hands, Hips, &c.	Pain, Swelling.	Chills, Sweats.	
		79.		Nov.	Nov.	Cold.		*Menorrhagia. Nephritis.*	*Miliaria.*	Thumb, Arm, Back, Side.			

ACUTE RHEUMATISM. 131

REMEDIES ORDERED. *Cinchona* Ordered.

15. Pulse.	16. Blood	17. Other Symptoms.	18. Prior Remedies.	19. V. S. ℥	20. Leech	21. Sudorificks	22. Salines.	23. Antimony	24. Bath.	25. Day diseas.	26. Day visit.	27. Dose.	28. Other Remedies.	29. Rec. or Dd.
96		Translated to Stomach.					*Saline. Acid. Vitr.*					Dec.	*Pulv. Rhab.*	R.
96	Scarce Infld.												*Ip. Rhab. Op.*	R.
										50th.	1st.	*Infus.* ℥ *ii. ter die.*		R.
					6.	*Ant. Opio.*		*Ant. Tart.*		12th.	3d.	*Cinch. Pulv. bis die.*		R.
	Infld.				12.									R.
				viii.		*Ant. Opio.*							*Inf. Trif. Palust.*	R.
72	Scarce Infld.		V. S. twice.					*Ant. Tart.*					*Guaiac.*	R.
96	Not Infld.							*P.A.J.*				*Inf. Per. Efferv. Pulv. gr. x. h. 4.*		D.
70				*vii.*			*Spir. Mind.*	*Pulv. Ant. gr. iv.*						R.
74												*Pulv.* ℈*j. h. 4.*	*Guaiac.*	R.
				xiv.	*Hir.*		*H. Efferv.*	*Pulv. Ant. J.*						
80					*Hir.*		*H. Efferv.*	*Pulv. Ant. J.*				*Dec. Efferv. h. 6.*		R.
108	Infld.			*x.*			*H. Efferv.*	*Pulv. Ant. J.*		15th.	10th.	*D.* ʒ *ix. Suc. Limon* ʒ *iii.*		R.
76	Not Infld.				*Hir.*		*H. Efferv.*	*Pulv. Ant. J.*			2d.	*Dec.* ℥ *iß. Tinct.* ʒ *i. Pulv.* ℈ *j. h. 4.*		R.
96					*x.*		*Spir. Mind.*	*Ant. Pulv.*					*Camph.*	D.
84							*Nitr.*	*P.A.J. v.*						R.
63							*Spir. Mind.*	*P.A.J. gr. iv. h. 5.*		11th.	2d.	*Inf.* ℥ *iß. Tinct.* ʒ *iß.*	*Tinct. Op. Guai.*	R.
							Spir. Mind.	*Pulv. Ant. gr. iv.*						R.
72 96				*r.s.*			*Spir Mind.*				21st.	*Dec.* ℥ *ii. ter die.*		R.

Table 1 from John Haygarth's Clinical History (1805)

In addition to the analyses of the hospital records at Bath to assess treatments for rheumatic diseases, Thomas Fowler (see above, page 53) delved into the nearly 5,000 cases of different diseases he had recorded during his ten years' practice at Stafford to analyse about 500 cases of both chronic and acute rheumatism.

He published his findings in 1795 in the *Effects of Blood-letting, Sudorifics, and Blistering in the Cure of the Acute and Chronic Rheumatism*, declaring that he had undertaken it *"for the purpose of illustrating on a more enlarged scale than in his former specimens the plan of the celebrated Lord Bacon for the improvement of physic"*. He also hoped to convince those who were suffering because of their blind belief in the healing power of nature, that there was value in the art of medicine. Fowler pointed out that although the three remedies mentioned in the title of the book were by no means new, it had not been possible hitherto to discriminate their effects from the efforts of nature, their side effects from their curative effects, and the effects of one remedy from another. This required the prescription of only *one* at a time, possibly in one dose and one form, *"a vastly ignored fact"*.[127]

An examination of his 109 detailed cases (with four different treatments for acute rheumatism and six for chronic rheumatism) reveals that despite this rational programme the groups were not strictly separated, many patients receiving one or more medicines. Fowler broke down his overall results into six categories, namely: patients cured by one particular method only; patients cured "chiefly" by one particular method; and cases that were "much relieved", "moderately relieved", "only slightly relieved" and "not at all relieved". He used a table of 78 cases to support his conclusion that bleeding was only an auxiliary treatment in acute rheumatism, and even less likely to be helpful in chronic cases. An analysis of 81 cases supported his scepticism about the effects of blistering, and scrutiny of 180 cases strengthened his recommendation of sudorifics – other than Dr James' powder! (See above, page 55.)

In his studious endeavour *"to render his hospital practice subservient to medical improvement"*, Fowler went a step further by using his numerical notes for clinical research to produce a clearer distinction between acute and chronic rheumatism.[128] He gave precise proportional data for 87 cases of acute rheumatism and 401 cases of chronic rheumatism, in particular lumbago, concerning the duration of marked pain and fatalities, analysed by age, sex and season; and also noted the occurrence of concomitant affections of the brain and sense organs. Fowler concluded that a quarter of the acute cases (that is, accompanied by fever) had, in fact, had a semi-acute onset and that three quarters of the chronic cases were related to exposure to cold or incomplete cure of acute rheumatism.

John Haygarth published precisely the same type of study, but on acute rheumatism, ten years later. Haygarth retired to Bath in 1798 and decided to work up notes on 10,549 patients which he had collected over 32 years during his practice in Chester. He had used a concise method of recording in Latin, which had been published in 1784. Interestingly, Haygarth's study was based on his private patients only, as due to lack of time, he had not yet dealt with the even larger number of patients he had seen at Chester Infirmary. Even so, he had managed to assemble 271 cases of herpetic or scorbutic eruption, 383 of dyspepsia, 827 of syphilis, 914 of hypochondriasis and 470 of rheumatisms (with the exclusion of sciatica, lumbago, "*tic douloureux*" and nodosities of small joints).

It was on the 170 cases of acute rheumatism that Haygarth wrote the first of a planned series of *Clinical Histories* (1805). Abstracts of all these cases were drawn up in a table with 27 columns, 11 of which concerned remedies (three of the columns dealt with the administration of bark alone) and their outcomes (recovery or dead). Analysis of this table permitted a clear numerical comparison of the proportional success of treatment, with or without bark, as a replacement for bleeding, including details of all 12 unsuccessful cases. The clinical history of the disease and its distinctive symptomatology could be similarly described. Several tables gave the proportional occurrences of the disease according to sex, age, seasonal distributions, and "cause" (as diagnosed by the patients themselves). The cause was mostly exposure to cold or moisture. The average period that elapsed before the appearance of the first symptoms could be fixed at between 48 and 72 hours. Concomitant diseases were listed in order of frequency, as were the joints and/or muscles inflamed and the pulse-ranges. The occurrence of pain and swelling (alone or together) of chills and sweat (alone or together) and their localisation in joints and muscles (alone or in both) were also given.

A second example drawn from Haygarth's records concerns the "nodosity of joints", in which he described and differentiated for the first time what is now known as *arthritis deformans*. This second treatise showed exactly the same methodological features as the first, with the exception of the giant 27 column table which was now dropped, for its printing had been *"so tedious and troublesome a business ... that ... no more shall be published"*.[129]

Thus Haygarth used the numerical method both for a better clinical differentiation of diseases and for the evaluation of therapy. He had also started to do such numerical research on phthisis (probably tuberculosis) in 1777. In 1805 he wrote: *"But after I had made considerable progress in this inquiry, I found the subject too melancholy, and could not assume resolution to proceed in this investigation"*.[130] Nevertheless, he was able to indicate the age and sex distributions and some of the 'causes' of phthisis numerically.

Haygarth was afraid that his array of factual detail might seem superfluous to many readers; but he felt that as the material was taken from nature it would perform the important and much-needed task of verifying the opinions of others, writing that: *"The altar of truth should be built with unhewn stone"*.

A truly remarkable feature of Haygarth's work was his realisation that the results of his inquiries were based on probabilities, which he attempted to calculate (or rather, to estimate). In fact he had already used simple calculation of probabilities in 1784 in his *Inquiry how to Prevent the Small-Pox (sic)*, and in 1801 for deciding on the mode of propagation of fevers.

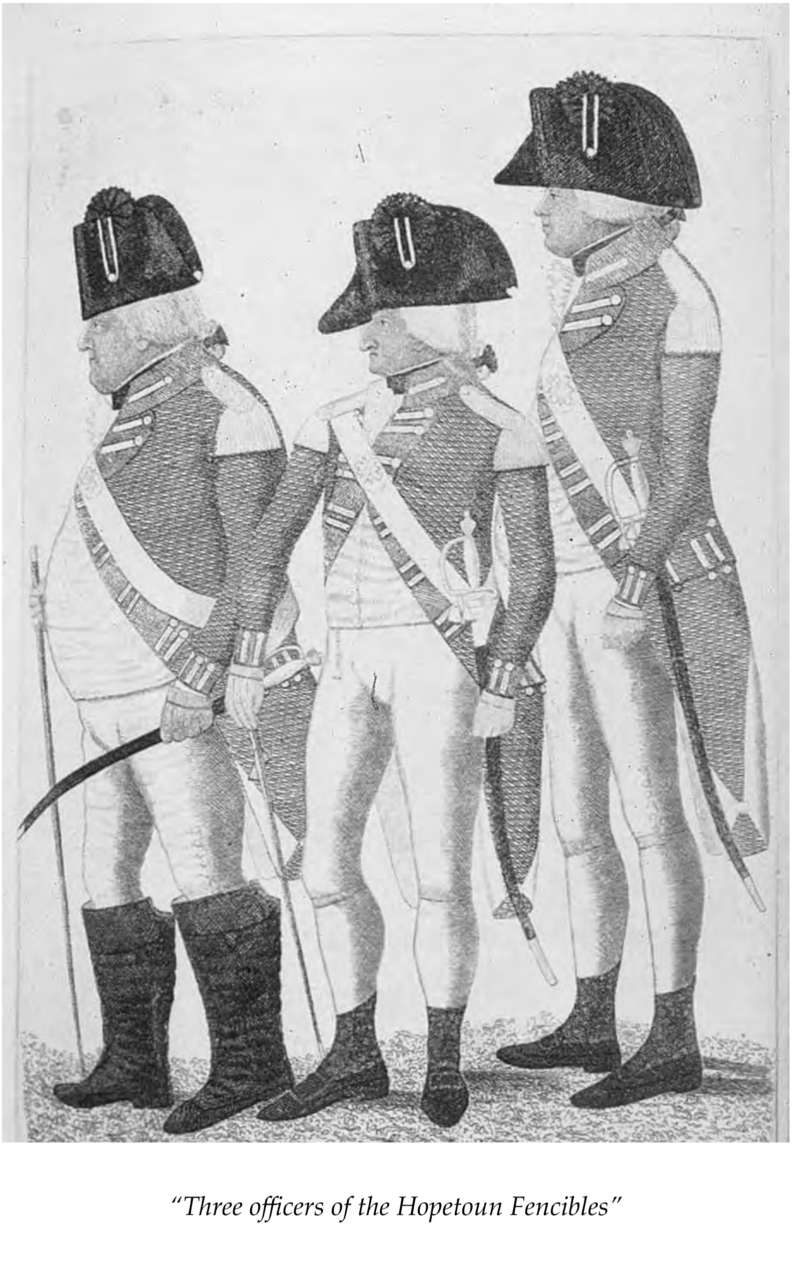
Haygarth brought still another aspect into the discussion of the evaluation of therapy with his writing on the *Imagination as a Cause and as a Cure of Disorders of the Body* (1800). It was dedicated to Falconer *"as a memorial of a mutual, cordial and constant friendship for thirty-six years"* and described a trial of "Perkins metallic tractors".[131] The "tractors" were metallic rods supposed to cure a great variety of diseases, including rheumatism, by some electrical or magnetic influence (a treatment that was one of the legacies of the supposed phenomenon of "animal magnetism" described by Franz Anton Mesmer in 1779). Distinguished doctors recommended this treatment and an "Institute of Perkinism" had been founded in London.

In Haygarth's trial, wooden imitation tractors were first used on five patients without their knowledge, and all but one were relieved. The next day, with genuine tractors, the same result was obtained. The results of this (in our terminology) single-blind placebo trial prompted him to quote Lind's comment on fictitious scurvy remedies: "*An important lesson in physic is here to be learnt, viz. The wonderful and powerful influence of the passions of the mind upon the state and disorders of the body. This is too often overlooked in the cure of diseases…"*.[132]

Here, as in every subject he touched, Haygarth increased the accuracy and reliability of his statements by clear experimental design and numerical expression of the results. As with his approach to smallpox, fever and rheumatism he thereby shed new light upon a socially important question of the time. This time it was the fight against quackery, which was on the programme of medical and social reformers. This had been an influence in the writings of Lettsom, Millar and Fowler, and the regulations of the Medical Society of London stated that no proprietor of a secret medicine could become a member. Other writers, like James Makittrick Adair, wrote popularly at great length against quackery and secret remedies. A combative Scottish graduate of Edinburgh, Adair settled in Bath and undertook, with Falconer, a series of laboratory experiments to disclose the nullity of a certain *nostrum* (a patented secret remedy).

Adair explained the flourishing of quackery by outlining the difficulties of attaining certainty in medical knowledge. Yet he did not show a way out of these difficulties. Haygarth did so with much persistence and success, as is attested by the reviews of his works in the contemporary literature (see below, page 123).

The trend towards making objective assessments of nosography and therapy described in this section may well have been triggered in Bath by the need for admission criteria for selecting from among referred cases, and commercial considerations. In the long run, an objective approach would guarantee the success of the institution. Nevertheless, it is greatly to the credit of the Bath physicians that they did not yield to any temptation to 'cook the books', despite their clear vested interests in promoting the taking of the waters in the Bath General Infirmary to patients from outside the city. This has been demonstrated in a recent comparison of the surviving original admission register with the Charity's published *Annual Reports*.



"Three officers of the Hopetoun Fencibles"

The reasons for (not) doing prospective trials:
Innovations in coping with injured limbs in war and peace

THE 17th and early 18th centuries were the great period of amputating limbs, especially after the introduction of the tourniquet. This device to interrupt the blood flow in limbs replaced cautery to check haemorrhage. French surgeons availed themselves so quickly of the advantages of the tourniquet to increase the frequency of amputation for gunshot wounds and gangrene that even Louis XIV was aware of the popular belief that his soldiers were as much in danger from the operative ardour of the surgeons as they had ever been from enemy action. But was amputation effective compared to more conservative treatment?

This fundamental question tended to be set aside by people addressing secondary questions concerning the timing and techniques of amputation. A French military surgeon, Henri François Le Dran, advocated immediate amputation in cases of severe crush fractures and crushed joints, and when a limb had been completely shot off. He gave a quantitative estimate of his experience in his *Observations de Chirurgie* (1731): *"The cutting of the limb must not be deferred, and experience teaches that for one patient whom a triumphant nature will have saved without amputation, ten will perish if one retards it."* [133]

Le Dran's policy of immediate amputation, presented in a clear style and originating from a man with status due to his book on military surgery, had a powerful influence over the opinions and practice of his contemporaries and younger surgeons in Britain. John Ranby, the leading British military surgeon of the time, endorsed Le Dran's approach in his *Methods of Treating Gun-Shot Wounds* (1744), but without Le Dran's relative precision. In 1737, using statistics from the Edinburgh Infirmary, Alexander Monro *primus* (see above, page 8) underpinned his own special method of amputation and after-care. In 1752 he listed 99 amputations of large extremities with only eight deaths (these encouraging results were still being published unaltered by his son, Alexander Monro *secundus*, in 1781!).

In spite of Le Dran's influence on practice, doubts about the value of amputation were kept alive in the minds of many practitioners by the frequent deaths following amputation and also by recovery in cases that had seemed at first to require amputation, but in which it had not been performed. These doubts found expression in the aftermath of the War of Austrian Succession (1742-1748), in which Le Dran's principles had first been applied on a large scale.

At least ten memoirs were published on the question in the following decade. A formal discussion on the value of amputation and of some of its technical aspects began in Paris, the leading surgical school of that time, and particularly in its unique Académie Royale de Chirurgie. Significantly, the question for the Academy's annual prize for 1754 was:

> *Amputation being absolutely necessary in wounds complicated by shattered bones especially those arising from fire-arms; determine the cases in which amputation should be done immediately, and those in whom it is convenient to defer it, and give all the reasons.*[134]

The prize was given to a *'Mémoire'* by J.F. Faure, a French military surgeon, and was eventually published by the Académie in 1759. Faure favoured delayed surgery on the basis of a trial in which he had purposely delayed amputation in ten wounded Englishmen after the Battle of Fontenoy in 1745, and compared their favourable outcomes with the overall mortality of soldiers who had received immediate amputation. Adducing further testimonies and numbers, he calculated the chance of healing after immediate amputation as between one in ten and one in three; whereas it amounted to nine in ten after delayed operation in patients of the same constitution, with the same surgeon, and in the same circumstances.

The decision of the Académie to award the prize to Faure made delayed amputation respectable, but the question of immediate versus delayed amputation continued to be debated throughout the next 100 years.

Even though the indiscriminate use of amputation had come under attack, it is noteworthy that the main issue considered by the Académie was not the primary question of whether amputation should be done at all in a given type of case, but whether the *timing* of the operation was important. The primary question was restated vigorously and cogently in 1761 by the Swiss, Johann Ulrich Bilguer, one of the three surgeons-general in the Army of Frederick the Great of Prussia. Horrified by the mutilations resulting from barely trained craftsmen-surgeons, Bilguer wrote an MD thesis (in Latin) during the winter war-break, in which he threw down the gauntlet to those promoting the orthodox practice of his time. He declared amputation needless in most cases, presenting statistics showing results of conservative treatment carried out on a large scale during the Seven Years' War.

Bilguer made clear that he placed greater value on a practice confirmed by repeated experience than on one conforming to whatever happened to pass for "sound reason". At one time in the Seven Years' War he had 6,618 wounded soldiers in a military hospital, all of whom were treated according to his directions. He reported that 5,557 recovered sufficiently to endure all the fatigues of service; 195 returned to garrison duties; 213 remained incapable of any labour, civil or military; and 653 died. Bilguer's thesis, soon published as a booklet, caused a sensation throughout Europe. In a century dominated by French surgery it was the first German surgical text since 1718 to be translated into a foreign language. The 1761 German edition was followed by English and French editions in 1764, Italian and Dutch translations in 1771, and a Spanish edition in 1773.

Why was Bilguer's booklet so successful? His style had nothing of the elegance of the French '*Mémoires*' of the 1750s. But he was concise: instead of relating cases over hundreds of pages, he explained his practice simply and condensed the results into one page of impressive statistics. Moreover, his mood was aggressive. This was especially so in the French translation by the well known Swiss Professor, Simon André Tissot, from which the English translation (dedicated to Sir John Pringle) was made. The original, more subtle, Latin title was rendered bluntly as *Dissertation on the Inutility of Amputation of the Limbs*.

Neither the enthusiastic approvals – Frederick the Great forbade amputation in his Army except in fully developed gangrene – nor the equally harsh condemnations of this book, include any comment on Bilguer's extensive statistics. One may conclude that it was the strident tone that caused most reaction.

In London, Percival Pott of St. Bartholomew's Hospital took exception to Bilguer's *"indecent as well as untrue reflections on the profession in general and those who have the care of hospitals in particular"*, and suggested that *"The boast of … means whereby chirurgical operations may be rendered totally unnecessary is the language of quackery, and not of science"*.[135] Pott refuted repeatedly Bilguer's claims that amputation was unnecessary in the five indications the latter had identified, but did not provide any statistics describing the results of his own practice. In other words, despite Bilguer's results he continued to reason exactly as Le Dran had done some 50 years earlier.

There was opposition in Edinburgh, too, where Benjamin Bell strongly recommended amputation for compound fractures after gunshot wounds. The only numerical indications he adduced concerned the dangers of the operation, which he said had greatly decreased: *"In the present improved state of the operation I do not imagine that one death will happen in twenty cases"* in hospital and private practice.[136] Given the wide distribution of his *System of Surgery*, this view may well have promoted continued wide use of amputation all over Europe.

In Dublin, the most distinguished Irish surgeon, experimentalist and historian of the 18th century, Sylvester O'Halloran, agreed with Bilguer's criticism of the frequent abuse of amputation. Amputation, he said, was sanctioned by tradition, even if the patient died; whereas the ignorant public would not accept death after conservative treatment. O'Halloran set the question of indications for the operation above all others in surgery: *"The clearing up of this single point alone is unquestionably of the greatest service to mankind, particularly to the military"*.[137] Significantly, however, his investigations did not address this primary question, concentrating instead on how the operation could be improved technically.

One of O'Halloran's achievements was the revival of the flap-technique for amputations. In 1770, his friend Charles White in Manchester (see above, page 17), published a table showing eight cases treated with O'Halloran's method, with only one death. Apart from the Edinburgh report by Alexander Monro *primus*, White's table, which gives name, age, date of admission and discharge, is the first comprehensive report of a practice that I have found in the history of amputation – and the first presented in tabular form. White notes in his book that it was written with the *"only aim to represent facts as they really were, not as they would tell the best"*, and calls for *"men in every science"* to *"... divest themselves of that illiberal spirit of prejudice and jealousy which is too apt to prevent the mutual assistance which they owe to one another, and to the public"*.[138]

Another friend who propagated O'Halloran's method in London was Sir William Bromfield. The account that this fashionable surgeon published in his 1773 *Surgical Observations and Cases* is rather typical of the later 18th century ambivalent adherence to authority and the presentation of factual observations and experience:

> *I have such authority in my possession, as induces me to believe, that Mr O'Halloran's method deserves preference to that I have recommended [myself] ... and I shall not ever be ashamed to retract my methods ... by adapting a practice recommended by others, which, experience in repeated instances, has proved successful ... The many idle reports that have been spread, relative to the disadvantages from this new method of amputating, and the conclusions drawn from false facts determined me to make enquiry, as to the success in general, from those who had performed the operation repeatedly with the flap. I shall not trouble the public at present with the authorities in my possession, by way of answer to the objections I have heard made by some, who have never performed the operation themselves in this manner, nor even seen it performed by others ... But ... if we give credit to the cases related by Mr White, we shall find that ... [these objections are] ill grounded.*[139]

A surgeon in Liverpool, Edward Alanson, took operative methods for amputation a stage further by combining the flap technique with the immediate postoperative union of the skin edges by apposition, thus hoping to achieve true healing by first intention. Alanson had been around at the time of a Liverpool medical shake-up when, within a few years of 1770, all six consultant posts at the Infirmary (three surgical and three medical) fell vacant. As a result, six young men with original and enquiring minds were appointed, some of them interested in statistical recording. There was also teamwork, the consultants helping each other in their many research projects.

It was in this atmosphere that Alanson described frankly his method of numerical comparison, its deficiencies, and his results in the 'Preface' to his influential *Practical Observations on Amputations* (1779):

> *When we attempt to introduce any new and important deviations from the common mode of practice into general use, and, particularly ... in the mode of performing and after-treating one of the principal operations of surgery, the public have a right to be fully acquainted with the author's reasons and motives ... and such trials should likewise previously have been made, as are sufficient to demonstrate that the doctrine recommended will bear the test of general experience ... Had I been aware of the utility of such an attention, I would not have omitted taking an accurate history of every amputation at which I have been present. However, the following heads of success [evidence] may be relied upon, and I hope will answer my present purpose.*[140]

Prior to his "improved" plan Alanson had been present at 46 amputations and observed the postoperative treatment. Ten of these patients had died, and he numerically listed the causes of death, as well as the complications. In more or less all surviving cases, violent symptomatic fevers and exfoliation of the bone were reported to have occurred. Alanson compared the statistical results of his new method of amputation with those he had previously achieved using the old technique (a study using 'historical controls', as we would call it today).

Alanson's report shows that he was conscious of possible sources of 'selection bias' (to continue in present day terminology). He noted that he had *"never refused to operate upon any case that has presented, where a single person in consultation has thought such operation adviseable"*. Since he began his new method he had *"operated in thirty-five cases, such as promiscuously occurred at the Liverpool Infirmary, without the loss of a single patient"*.[141] Symptomatic fever and other complications had in all of these been slight, and, with one exception, there had been no haemorrhage. After one month the wounds had either healed or become smaller than a sixpenny piece, and all patients had ultimately been cured.

It is noteworthy that these early statistical reports of the results of amputations came from two sources – foreign military surgeons, and a group of surgeons who knew each other and worked at British provincial hospitals where other consultants with an interest in quantification were also active. In contrast, the statements by the representatives of the large hospitals in London, such as Percival Pott, were based on opinion unsupported by statistical evidence.

At the onset of the Napoleonic Wars in 1792, there was still uncertainty about when and how to use amputation for gunshot wounds. In his *Discourses on the Nature and Cure of Wounds* (1798), John Bell, the Edinburgh anatomist, wisely left the question of indication undecided, noting that all the surgeons of Europe with their collected experience had left it so. Indeed, data from operations performed in the 1740s could no longer be used for comparison as the operations were not the same, technically, nor were the circumstances. What was needed as a basis for judgement, Bell noted, was a large series of observations comprising all cases of amputations, successful and unsuccessful alike, in well-described, comparable circumstances.

In this respect, naval surgeons led the way. Gilbert Blane, whom we encountered in the sections on fevers and scurvy (see above, pages 36 and 79), analysed information in books recording the surgical operations at Haslar Naval Hospital, to *"serve as a subject of comparison to those who perform amputations on board of ships at sea"*.[142] In his *Observations* (1799), Blane included the results of amputations done between 1772 and 1778: 4 thighs with 1 death; 27 legs with 10 deaths; 2 forearms with no deaths; and 7 arms with 2 deaths. Total: 40 amputations with 13 deaths. He also provided the long term results of 28 primary amputations specifically for gunshot wounds, which had been done on board ship during an action in 1778: 7 thighs with 1 death; 5 legs with 2 deaths; 14 arms with 5 deaths; and 2 forearms with no deaths. Total: 28 amputations with 8 deaths.

John Rollo, the surgeon-general of the Army's Department of the Ordnance and surgeon-in-chief at its hospital at Woolwich, also kept exact records of his operations. In 1801, he published a summary of the results of his first five years' practice: 27 simple or compound fractures had occurred, for which 22 amputations had been performed, with three deaths. Blane's and Rollo's analyses showed the way that British military surgeons, led by Wellington's surgeon-general James McGrigor, would to try to elucidate the still unanswered question of the timing of amputation. McGrigor, yet another Edinburgh-trained Scot, had predicted the scientific value of statistical returns, and this was now clearly shown by the contribution of one of his deputy inspectors, George Guthrie.

Guthrie was the most brilliant of the active British surgeons of the Peninsular War, and he later became a major figure in English hospital medicine (Surgeon at Westminster Hospital, and President of the Royal College of Surgeons from 1834 till 1842). In his book *On Gun-Shot Wounds of the Extremities* (1815), Guthrie laid out his experience of the Peninsular campaigns according to the new statistical standards established by McGrigor. He claimed to have stated nothing but facts, and made clear that he trusted *"... in no part to theory or opinion of authors not supported by actual experience"*.[144] He went on to discuss the importance of concurrent comparisons of early and delayed operation:

> *It is not sufficient to perform twenty amputations on the field of battle, and contrast them with as many cases of amputation, done at a later period. The twenty cases for delayed operation must be selected on the field of battle, and their result compared at the end of three months with that of the others when the value of the two modes will be duly estimated.*

This was truly a programme for what we would call today a prospective study, and it was better and more objective than anything published earlier in this field.

However, Guthrie immediately set out to explain that he had never actually done this:

> *... because I had ascertained the safety of immediate amputation in all cases that required it, after the first battles of Rolica and Vimiera in 1808; and when circumstances would have enabled me to have done so, I did not feel myself authorised to commit murder for the sake of experiment.*[145]

In the four tables in his report, Guthrie presented data that he acknowledged were insufficient, as they resulted from retrospective analysis. Two tables comprising returns from June to December 1813 compared secondary with primary operation. 551 secondary operations (after three to six weeks) in hospitals were compared with 291 primary amputations (within 48 hours). These groups were further subdivided into amputations of the upper and the lower extremities. The numbers of patients dead, cured and still under treatment were given, with the latter considered cured for the purposes of further calculations. These showed that *"the comparative loss, in secondary ... and primary ... operations is as follows":*

	Secondary		*Primary*
Upper extremities:	*12*	*to*	*1*
Lower extremities:	*3*	*to*	*1*

The two other tables made the same type of comparison between 48 early operations and 51 delayed amputations following the battle of Toulouse in 1814. According to Guthrie's reports, the survival rate of primary amputation for the upper limb was 95%, compared to 75% after the secondary operation. (I calculated 80% and 50% respectively for the lower limb.)[146]

Guthrie also described an interesting trial done after the battle of Toulouse in 1814 concerning indications for amputation of the thigh. Forty-three of the "best" fractures of the thigh had been treated conservatively, because there were good hospital facilities within a short distance. After three months, 13 had died; 12 had undergone a secondary amputation and 7 of these had died; and 18 had retained their limbs. Among those who had retained their limbs, 7 were cured, and 11 wished that they had had amputations as they were now only likely to recover as invalids. Guthrie concluded that:

> *... if the thirty-six of the forty-three who died and have only partially recovered [in this trial], would had been amputated on the first day, the country would have had at least twenty-five [i.e. 72%] stout men, able, for the most part, to support themselves by their labour, instead of five, or at most ten ...*[147]

Since primary amputations of the upper extremities had given him up to 95% success, the case for a wide range of indications for amputation, and for primary amputation, appeared settled.

Illustration from George Guthrie's 1827 "Treatise on Gun-shot Wounds, on inflammation, Erysipelas, and mortification, on injuries of nerves and on wounds of the extremities requiring the different operations of amputation; in which The various Methods of performing these Operations are shown, together with their After-Treatment; and containing an account of The Author's successful Case of Amputation at the Hip-Joint".

Guthrie's figures may easily be criticised, especially for considering all patients still under treatment as cured. Yet even if one takes into account that some of them must have died later and that the secondary operations were not done on the same type of case as the primary ones, Guthrie's precepts stood methodologically on much firmer ground than those advanced by the celebrated French surgeon, Baron Dominique-Jean Larrey, who had previously arrived at the same conclusions on the basis of clinical impressions. Guthrie's study of 43 fractures of the thigh shows that in 1814, when French surgeons would have used amputation in such cases, Guthrie was still busy ascertaining the value of this risky operation. Indeed, when the Peninsula War ended in 1814, he expressed his regret that *"we had not had another battle in the South of France, to enable me to decide two or three points in surgery that were doubtful"!*[148]

In the event, the battle of Waterloo (18 June 1815) *"afforded the desired opportunity"* for this further research.[149] Although, medically speaking, this battle was a disaster due to over-hurried preparation of the medical services, Guthrie, who volunteered to work in the Hospital of Brussels for five weeks, managed again to collect detailed records of all the operations performed there between 16 June and 31 July. He distinguished accurately between 146 primary and 225 secondary amputations, further grouping them according to six anatomical localisations, with the proportion of deaths calculated for each category. Although this was the most complete and informative table published so far, Guthrie himself warned that it was an approximation of the truth, as it did not include those operated on who died on the battlefield of Waterloo and those who were transferred to the hospitals of Antwerp. But, as the *Edinburgh Journal* declared in 1816 in praising Guthrie's work, the proper time to amputate *"seems now finally decided by the experience of military surgeons in favour of early and immediate amputations when the limb cannot be saved"*.[150]

In summary, Guthrie had taken the recorded experience of many years, completed, revised and shaped it, *"with the support of all [his] junior medical officers, the approbation of all seniors under whom... [he] had served, ... and the esteem and recommendation of most of ... [his] equals"*, and taken full advantage of the military conditions with their opportunities to study great numbers of cases for the elucidation of his question.[151] One commentator considered the resulting report *"much more minute, accurate and useful than any to be found on the record of military surgery"*.[152]

On such grounds Guthrie found it easy to defend his views even against famous civilian surgeons such as John Hunter or John Bell. Hunter, he asserted, had written:

> *... from his knowledge of principles... unbiased by any particular theory and from having had some opportunity of practice [during six weeks in 1761, whereas Bell who] had no practice of his own and little opportunity of enquiry into that of*

> *others ... [reasoned] from theory, probably on an individual case, and not from actual observation made on many.*[153]

The indication of primary amputation for severe gunshot wounds being quite unanimously approved of by military surgeons after 25 years of warfare, there remained some doubt about what "primary" really meant in practice. Should the amputation be delayed for some hours after the accident to allow the constitution to recover from *"the shock of the injury as to bear the additional one of the operation"*, as Guthrie advocated for the practice in the Army?[154] Or was it to be performed as soon as possible after the injury, as had been the practice for 40 years aboard the ships of the Navy?

The naval surgeon Alexander Copland Hutchison decided to settle this question when a British naval expedition to North Africa culminated in a battle before Algiers on 27 August 1816. Hutchison had not himself participated, but sent off a circular letter on 29 October to all surgeons of the 11 ships then engaged, asking them four questions:

(1) What was the number and nature of wounds needing amputation?

(2) Was amputation performed during action or was it slightly delayed?

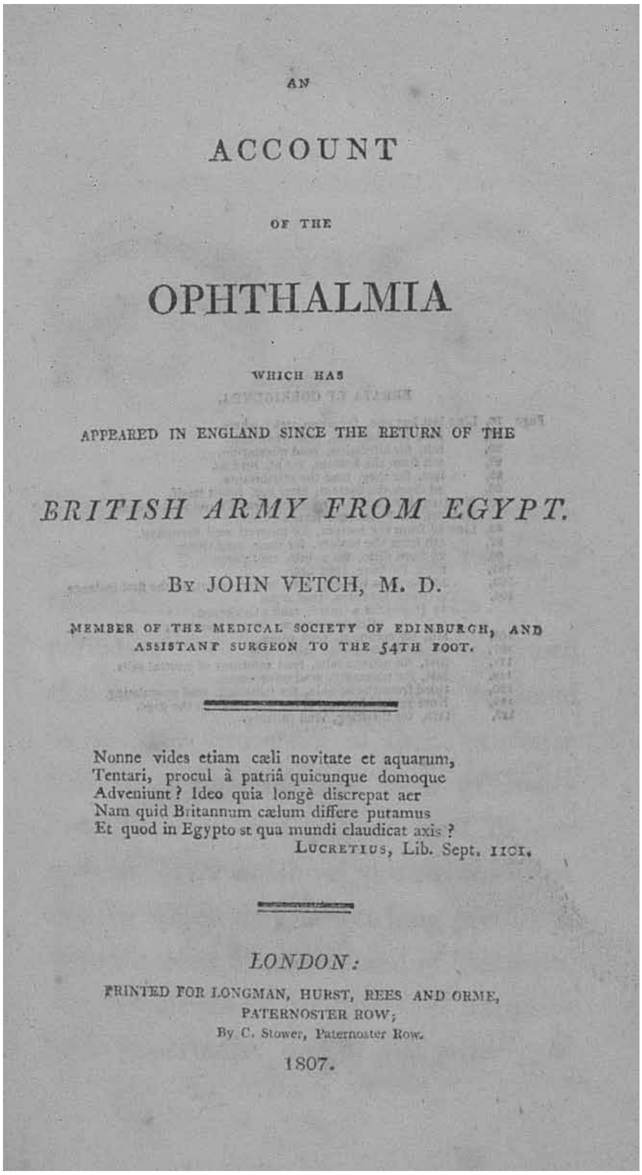
(3) At what exact time after injury were amputations performed?

(4) What were the numbers of recoveries and deaths, and the exact timing of the latter?

By 18 November 1816, Hutchison had received returns from all but one ship (still at service abroad) – an excellent collaboration! He published abstracts of all these returns, showing that the ship on which amputations had usually been done after several hours delay had lost nine out of 11 patients, whereas the two ships on which immediate amputation had been practised had lost only four out of 19 men. Although he did not summarise these data in a table, he concluded that from the results of *"the contrasted practice ... so amply adduced, ... the question will now be considered by the profession as fully illustrated and finally settled ... Magna est veritas et praevalebit."*[155] [Truth is great and will prevail.]

Clearly, James McGrigor, as the surgeon-general of the British Army in the Peninsula, had been aware of the scientific potential of statistics to elucidate clinical problems. He required regular returns amidst all the difficulties and unstable wartime circumstances, analysed some of them himself, and encouraged others to do so. As with lithotomy, a number of new parameters, such as the anatomical localisation of the lesion, and the age and way of life of the patient, were now taken into consideration. In addition, around 1750, the need for prospective comparative trials was recognised. In this section, I have outlined the intellectual, structural and also ethical reasons for performing (or not performing) prospective trials as they were formulated by the 18th and early 19th century surgeons, and the alternatives used.

After the end of the Napoleonic wars, the clear-cut statistical results of the military surgeons, contradictory as they sometimes were, laid open questions for further investigation. The equally clear-cut conclusions some of them drew impressed and challenged the view of their civilian counterparts after the Wars, with the result that by 1830 it was admitted that most of the questions were unresolved. Meanwhile, questions in fields old and new triggered critical and numerical evaluation of therapies, particularly when the state had to pay. In the concluding section of this chapter, I shall sketch the state of the art in quantitative evaluation of therapy in early 19th century Britain.



AN

ACCOUNT

OF THE

OPHTHALMIA

WHICH HAS

APPEARED IN ENGLAND SINCE THE RETURN OF THE

BRITISH ARMY FROM EGYPT.

BY JOHN VETCH, M. D.

MEMBER OF THE MEDICAL SOCIETY OF EDINBURGH, AND
ASSISTANT SURGEON TO THE 54TH FOOT.

Nonne vides etiam cæli novitate et aquarum,
Tentari, procul à patriâ quicunque domoque
Adveniunt? Ideo quia longè discrepat aer
Nam quid Britannum cælum differe putamus
Et quod in Egypto st qua mundi claudicat axis ?
LUCRETIUS, Lib. Sept. IICI.

LONDON:

PRINTED FOR LONGMAN, HURST, REES AND ORME,
PATERNOSTER ROW;
By C. Stower, Paternoster Row.

1807.

The state of the art in the early 19th century: Controlling syphilis and ophthalmia in soldiers after the Napoleonic wars

A LOOK at the approaches used to tackle new phenomena is an appropriate way to gain an impression of the state of the art in numerical analysis applied to therapeutic questions. One might, however, easily clamour 'selection bias' about my choosing as test cases the introduction of a new cure for an old disease, syphilis, and the management of a new disease, Egyptian ophthalmia in the Army, given the generally favourable climate for quantification in the military and the examples described in the earlier sections of this chapter. If, on the other hand, I was to take examples from among famous London consultants, their emphasis would be on the superior value of direct clinical observation and their own subjective experience derived therefrom. Such examples would not allow us to explore problems that some people perceived as implicated in the numero-comparative approach to providing an objective account of experience.

In considering 18th century 'syphilis' today, we must take into account issues of retrospective diagnosis (see above, page 24). For the present purpose, which is to show how a proposed new therapy was handled by leading British military doctors, I shall take the diagnosis for granted (although some of them were perfectly aware of diagnostic uncertainty).

Syphilis had long been a special domain of military surgeons. As was the case for fevers, John Pringle had contributed to it in the 1750s, when several papers were published in the *London Medical Observations and Enquiries* (1757-84) concerning the use of mercury to treat syphilis. In one of these, Pringle described how he had collected results by correspondence with six Army surgeons during the winter of 1756/57, and then a year later to confirm the duration of the cures. The results were stated in terms such as: "35 cases without failure nor relapse"; "approximately 60" with two failures; "35 new cases cured without relapse except two; seven and eight cases without relapse"; but also imprecise reference to "many" cases.[156]

The generally accepted therapy for syphilis at the end of the 18th century was still systemic mercury, although some doctors and patients feared the side effects of this treatment as much as the complications of the disease itself. When British military surgeons arrived in Portugal during the Peninsular War, they were astonished to find that the disease was treated there without using this potentially dangerous drug; instead simple topical remedies and washings were used. William Fergusson, who was head of the medical department of the Portuguese auxiliary forces, drew the attention of the medical community at home to this fact in a paper read to the Medico-Chirurgical Society of London on 24 January 1812, supporting his case with a numerical example.

On the same day, two further papers were read on the subject before the same society. The first, by Thomas Rose, an Oxford graduate and surgeon to the Coldstream Guards in London, reported his observations among his own soldiers. After trying Fergusson's recommendations with success in two cases, he had adopted conservative treatment, which consisted mainly of clean dressings, cinchona bark and/or antimony as an emetic given systemically. The new regimen had proved successful in all cases (which were admittedly not all venereal), and he reported 28 of them in detail. He reported that the patients had been followed up long enough to be certain that they had been cured.

Thomas Rose had also referred to successful results in more than 60 patients who had been observed by a colleague of his, and George Guthrie (see above, page 100) presented a detailed analysis of these. As in other military establishments, Guthrie and his colleagues at Chelsea Hospital had been treating all types of ulcers of the penis using simple, mild means. Not all of their patients could be followed up, but out of "nearly a hundred" who had been, all had healed without mercury.

Three questions remained: Would the new cure be quicker? Would there be a larger, smaller or an equal incidence of secondary symptoms? And how severe would those secondary symptoms be? In a preliminary attempt to address these questions, Guthrie compared the incidence of secondary symptoms after the new treatment (as reported numerically from his own and the military establishments at Dover, Chatham, Edinburgh and various regiments in Britain and abroad) with his earlier recollections of prognosis from Spain, France and Britain, where nearly all the cases had received mercury. Although less than 10% developed secondary symptoms after the new regimen, this compared with an estimate of *"between two or one in seventy-five"* after systemic treatment with mercury.

Guthrie's conclusion from these data (probably gathered with the help of his chief, James McGrigor: see above, pages 5, 49 and 100) was that although mercury could often be dispensed with, in severe cases it was the only reliable remedy. He admitted that much more satisfactory information was still needed, and that investigation was necessary to compare alternative treatments, with and without mercury, *"before we can arrive at any fair conclusion on a subject of* *such great importance"*.[157] As McGrigor had already given a great deal of attention to this issue, Guthrie had every reason to think that much *would* be done in the course of the next few years. He pointed out, as had military surgeons before him, that if well directed, they all possessed:

> *... advantages as to ascertain facts which are not to be met with in any other walk in life. The persons affected are completely under [the surgeon's] control ... he can do what pleases with them under observation for a number of years, certain that they cannot have a change of opinion, and act contrary to his wishes.*[158]

Accordingly, clinical trials were conducted at the military hospital in Edinburgh Castle, supervised by the surgeon-in-chief, John Thomson, who was also professor of military surgery at the University (see above, page 20). Thomson published the results together with those of a planned controlled study on 54 patients with gonorrhoea. The patients with syphilis had been distributed into three groups: 15 'controls' were treated with *"rest and abstinence"*; 20 received localised treatment with silver nitrate injections; and 19 received three different internal medicines. All patients were "cured", the first (control) group after an average of 8½ days, and the second after 17 days. Among those receiving systemic treatment, only the eight patients who had taken a plant extract had been discharged earlier (after an average of 5 days) than the controls.

Similar investigations were encouraged by John Hennen, another Edinburgh-trained veteran of the Peninsular War, who had been appointed by McGrigor as inspector of the Scottish military hospitals in 1815. He reported the cases from only one regiment, expressing concern that he had not yet collected sufficient data. Had he had sufficient time, he would have liked to present a "multiplicity of details and calculations" allowing comparisons based on data from all hospitals he superintended.

One can understand this remark when one considers his "analytical view" of cases extracted from a casebook *"kept with praiseworthy minuteness"*. It consisted of eight tables presenting data on 105 primary and 11 secondary infections treated without mercury. These were analysed by subgroups and their clinical features (that is, ulcers only, and buboes succeeding ulcers). The time until cure was tabulated for each subgroup, and a special set of tables gave the maximum, minimum and average for each subgroup (that is, the arithmetical means of all values of a subgroup expressed to two decimal places). For the secondary cases, the type of complication and the interval until its onset were also given. Like Guthrie, Hennen concluded his report by calling for more research.[159]

At this stage, McGrigor, by then Head of the Army Medical Service, again stepped in actively. In December 1818 he sent a circular letter to all regimental surgeons with a series of queries concerning their experiences during the years 1816-1818, making it clear that he expected numerical answers. By April 1819, with the help of an assistant, he had analysed 2,827 cases treated with mercury and 1,940 without, and sent the results out to the surgeons who had contributed the data. In the routine mercury group, all patients had been cured, the time necessary being longer than in the non-mercury group. For reasons he was able to classify precisely, mercury had ultimately been given to 65 of 1,940 patients from whom it had initially been withheld. Secondary symptoms were rarer, but more severe than in the non-mercury group (in 51 out of 2,827 cases with mercury and in 96 out of 1,940 cases without mercury).

McGrigor warned against the possible fallacy of such comparative estimations, as they were only averages, covering great differences within single regiments. He, too, stressed the need to continue the inquiry, announcing that additional data would be sought at the beginning of the following year. In reply to criticism from a London physician, Charles Bell, that British soldiers had been used *"for experimental purposes"*, McGrigor emphasised the value of the military statistics presented so far, and held that his investigation was an unprejudiced enquiry after truth, quite uninfluenced by either ambition for innovation or any particular doctrine (see above, page 5).

He recommended keeping a particularly watchful eye on those patients treated without mercury, just as he made it absolutely clear that he did not enforce the non-mercurial treatment – a remarkable instance of moral behaviour, respecting the patients' views, in contrast to Guthrie's concept of control and coercion for the sake of obtaining valuable evidence.

McGrigor's analysis was included in an American compilation on the treatment of syphilis in 1830, and John Hennen, too, included it in his *Principles of Military Surgery* published in 1829. In the section on syphilis he pointed out that the results of comparative trials conducted during the same six months of 1818 and 1819 at the Edinburgh Castle Hospital had yielded contrasting results. Hennen commented on this fact as follows:

> *A prudent and unprejudiced practitioner knowing that mercury will agree with one set of patients, and disagree with another though their symptoms may be alike, and even contracted from the same source, will not draw hastily conclusions from either, but will wait patiently until, in the progress of events, the respective merits of those plans become more fully developed. Indeed, the numbers subjected to comparison are too limited to deduce from them any positive or fixed corollaries.*[160] [There had been 47 patients without and 18 with mercury in one trial, and 16 and 18 respectively in the other.]

In 1820, Hennen became principal medical officer of the Mediterranean Fleet and he now analysed the results from all the hospitals he had superintended in Scotland, from June 1812 to December 1819, which covered a total of 407 primary and 46 secondary infections treated without mercury. On this basis he favoured non-mercurial treatment as 'first-line' therapy choice, a choice he felt rested on really reliable evidence, for *"few men could have been more fortunate in their opportunities, and I assuredly am not conscious of having either abused or perverted them"*.[161]

This short and necessarily selective survey shows that, in the 1810s and 1820s, leading British military doctors used statistics to investigate both the course and the therapy of syphilis. Conscious of the importance of mass observation, they took advantage of the available opportunities, and were not deterred by stringent organisational requirements. In their evaluation of therapy, they seem to have appreciated the necessity of comparing comparable cases, and the value of a 'control' group and a long enough period of observation. They calculated averages, yet they were also aware of potential fallacies of inferences based on these. It is clear that they believed that the use of numbers would increase objectivity. Indeed, for these doctors the numerical method seemed not only the best, but also the normal way of proceeding. In contrast to the soul-searching debates that were to occur in Paris in the mid-1830s about Pierre-Charles-Alexandre Louis' *méthode numérique*, this approach seemed to be uncontentious to these British medical investigators. As Hennen wrote in 1818:

> *The care of syphilis without mercury is now under investigation in the military hospitals ... with the same spirit of candid inquiry as the cures of any other disease by any new remedy proposed on respectable authority*.[162]

Because of the intended objectivity of his approach, Hennen thought that his work would be profitable to medical science, although its specific results might, in time, be superseded. Whether it was profitable to the patients is, for many reasons, difficult to determine. What can be said is that it helped to change the therapy many of them received, as had been the case when bloodletting had been re-launched for the therapy of fevers ten years earlier, even though with uncontrolled case series, rather than comparative statistics, as was the case for syphilis.

While the example of syphilis in the Army exhibits quite a strong methodological consciousness, both theoretical and practical, research on Egyptian ophthalmia was rather weak in this respect. Ophthalmia was new to the Army when it set out on the Egyptian campaign against Napoleon in 1801, yet within a short time it became one of the most distressing and widespread diseases affecting soldiers. It was highly contagious and was regarded as an especially malignant type of inflammation. Beginning with purulent conjunctivitis, it could lead to pan-ophthalmitis, suppuration of the eyeball and total blindness in more than 10% of cases. This obliged the state to pay pensions to severe sufferers of the disease, and, since even after the return from Egypt ophthalmia continued to recur and spread (partly through self-infliction) to units which had never been to Egypt, the Army Medical Board took steps intended to limit the spread of infection, and the accompanying costs, and to ensure the best available cure. Were they numerical, as one might expect?

One of these measures was the concentration of all cases upon arrival in England in a specialised "depot" hospital at Selsea, near Bognor Regis in Sussex. John Vetch,

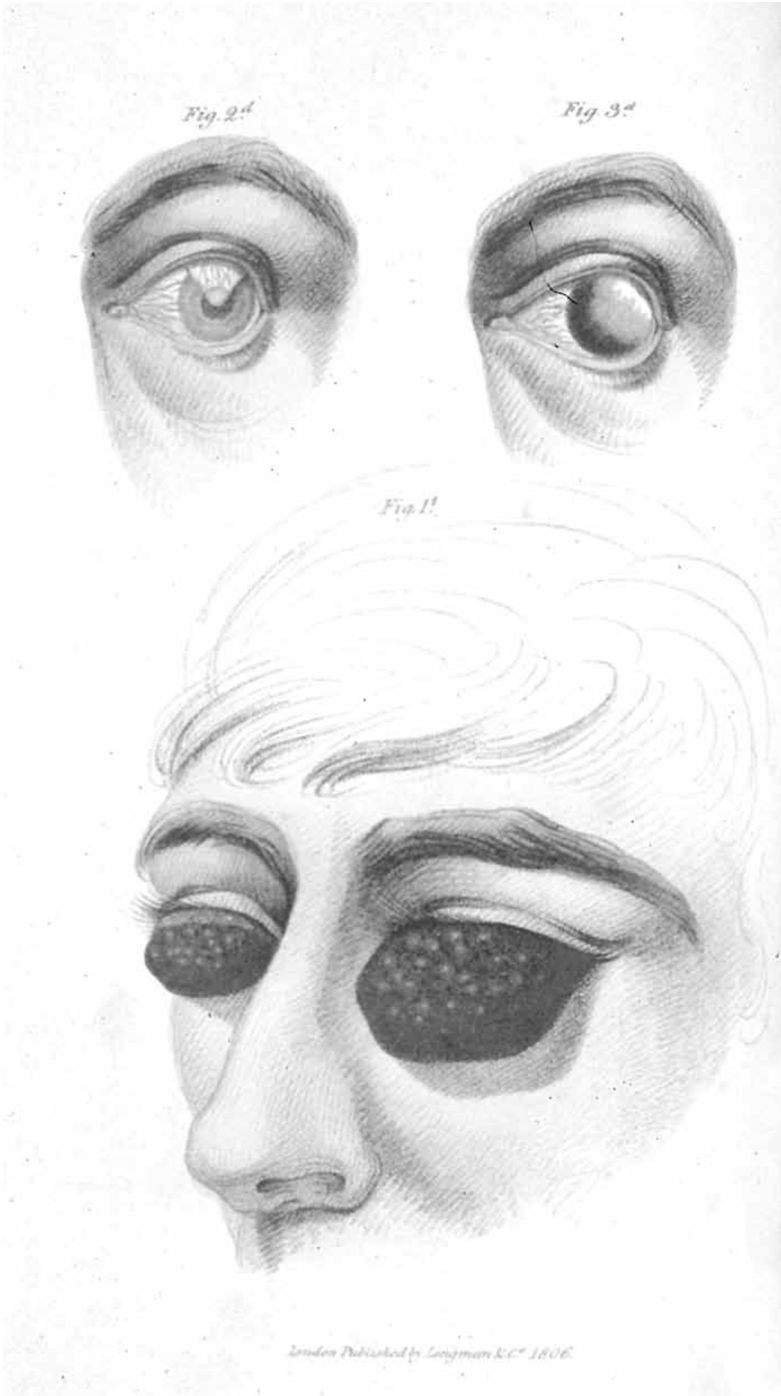
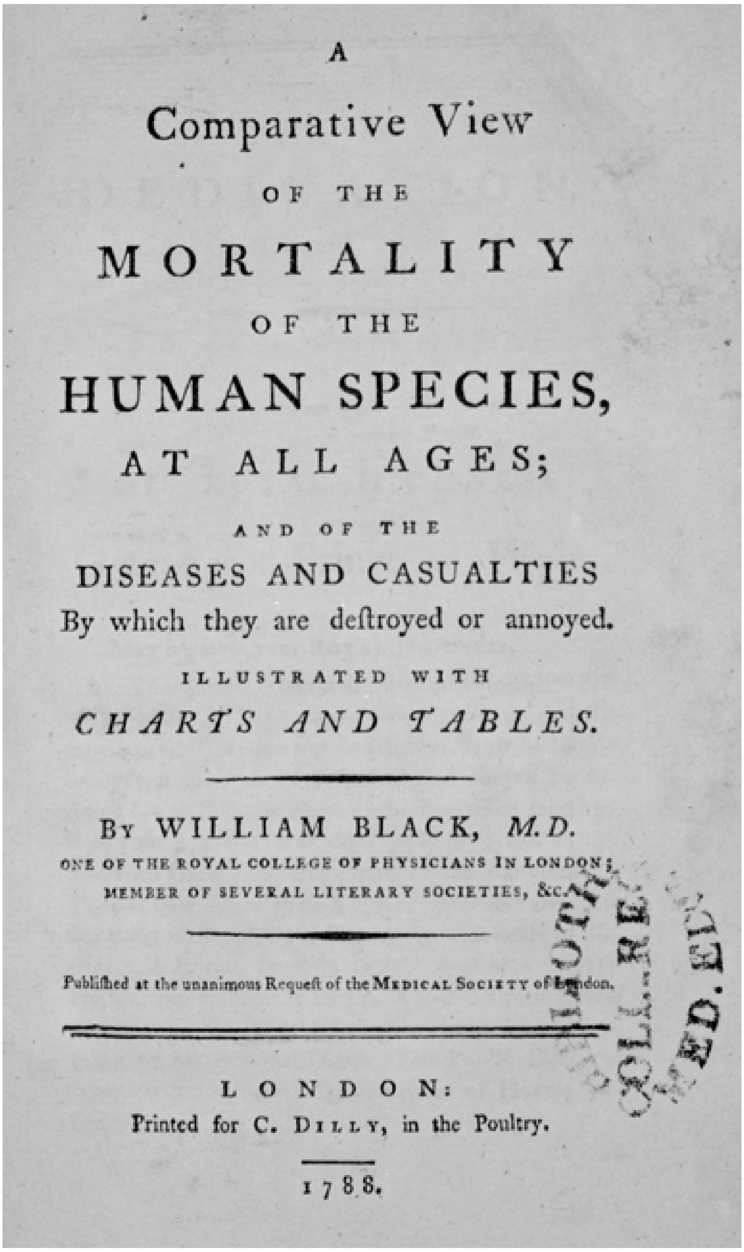


Illustration from John Vetch's "Account of the Ophthalmia which has appeared in England since the return of the British Army from Egypt" yet another Edinburgh-trained Scot, was in charge of this facility, and treated around 3,000 patients in this hospital between 1807 and 1812. Vetch published detailed statistics on the 536 patients admitted with vision already impaired.

Together with the civilian oculist William Adams, Vetch was involved in studies to assess which treatments should be given priority. Again, statistics were the basis of the discussions. These had been collected for largely administrative purposes, and in the hope that they would support the case for an increased allocation of resources by parliament.

In fact, the treatments on offer hardly differed. Although Vetch began by copious bleeding and Adams believed in promoting violent vomiting using tartar emetic, the subsequent irrigations, local instillations, cold compresses, and surgical procedures were much the same. Not unsurprisingly, however, McGrigor refuted the alleged successes of these regimens because of the lack of convincing proof upon later re-examination of the patients.

Obviously, in the early 19th century, when doctors – at least those having certain functions with official responsibility – were aware of the troublesome task of searching for the best available evidence, and when there was a culture of a critical approach by way of statistical analysis of aggregated data from groups of patients, the results of attempts to produce such data could be very different – just as today. Equally different were the reactions to the perception of some moral issues linked to this new method, such as freedom of choice of therapeutic alternatives by patients compared to doctors forcing them into a given treatment group. However, the morality of older methods – that is, dogmatic evidence and subjective experience derived respectively from theory and clinical observation – was not addressed in the context of syphilis and ophthalmia.



A

Comparative View

OF THE

MORTALITY

OF THE

HUMAN SPECIES,

AT ALL AGES;

AND OF THE

DISEASES AND CASUALTIES

By which they are deſtroyed or annoyed.

ILLUSTRATED WITH

CHARTS AND TABLES.

By WILLIAM BLACK, *M.D.*

ONE OF THE ROYAL COLLEGE OF PHYSICIANS IN LONDON;
MEMBER OF SEVERAL LITERARY SOCIETIES, &c.

Publiſhed at the unanimous Requeſt of the MEDICAL SOCIETY of London.

LONDON:
Printed for C. DILLY, in the Poultry.

1788.

Black's "Comparative View of the Mortality of the Human Species at all Ages, and of Diseases and Casualties" (1788) was withdrawn shortly after publication. The revised second edition "An Arithmetic and Medical Analysis of the Diseases and Mortality of the Human Species" was published in 1789.

REFLECTIONS

"Medical arithmetick as a guide and compass through the labyrinth of therapeutick"

What was achieved?

IN the second half of the 18th century, a number of British doctors, civilian and military, perceived the need for adequate empirical evaluation of existing and proposed new remedies. They saw extensive, comparative trials, with results expressed by numbers, as the only way to achieve this end. This approach had been used earlier in the century to assess the effects of smallpox inoculation, but, around 1780, some doctors saw the application of arithmetic as an answer to contemporary discussions on certainty and probability in clinical medicine. They indeed spoke of "medical arithmetic". They also stressed, in the prevailing spirit of the Edinburgh school of rational empiricism, the primacy of observation of facts over deduction from pathophysiological theories, even over those derived from *in vitro* laboratory experiments. They considered such deductions as rationalist speculation and worthless unless underpinned by factual observations as tested by trials. I have previously referred to these men and their younger pupils as "arithmetic observationists" but, because of the clinical trials some of them performed, the designation "arithmetic observationists and experimentalists" is more appropriate.

The arithmetic observationists and experimentalists distinguished themselves further from those who advocated the value of direct clinical observation in individual patients: They wished to base clinical medicine on elementary numerical analysis of compilations of observations made on distinct *groups* of patients. They saw themselves also as departing from the traditional methods of reporting, especially from the authoritarian aphorisms of Boerhaave (who had died in 1738) and, to a lesser extent, from those of Hippocrates in Antiquity and Sydenham in the 17th century, who had both made their own factual observations, by now considered outdated. In short, they were consciously acting in the spirit of Francis Bacon's "ordered experience" and emancipating themselves from tradition and prejudice, as urged by John Locke.

In 1777, John Millar answered a question often asked in the period: "What is the way out of the maze of observations opposed to observations, facts to facts?" His response was that *"detached cases, however numerous and well attested, are insufficient to support general conclusions … The test of arithmetical calculation [ought not to be] evaded"*.[163] In therapeutics, this involved calculating sums, arithmetic means and sometimes success-to-failure ratios – expressed, if possible, in tabular form, as the authors of such reports realised that this was the only concise way to include all cases that had occurred during a given time. They stressed the importance of documenting the experience of all cases that met particular nosological criteria over a given time, and of not omitting information about treatment 'failures.'

By the end of the 18th century, observational and experimental methods – according to Bacon's distinction between "ordinary" and "ordered" experience – were being used to evaluate treatment in Britain. Observational analyses, using mortality statistics, administrative returns or personal case series, included studies of one clinician's experience with patients receiving a particular treatment, as well as compiled statistics describing the experience of several clinicians. Historical and concurrent (though unplanned) controls were used, and some analyses attempted to take account of the influence of confounding variables, such as the age and sex distribution of patients, the severity of their disease, or the anatomical location of an injury.

Experimental – that is, planned prospective – studies were designed, implemented and reported. These compared, for example, the effects of immediate versus deferred treatments, surgical versus medical treatments, and different drugs. In these studies either concurrent controls, or successive periods of comparison, were used, sometimes with efforts to match the comparison groups. In addition, some of these studies used masking of observers, and there is at least one example of the use of a placebo treatment. At the height of their activities, around 1780, the pioneers stressed the novelty of these methodological steps and the need to adopt medical arithmetic. After 1800, their methods were more or less taken for granted, albeit not always in their entirety, as 'standard' techniques by civilian and military doctors.

William Black, an Irish physician attached to a midwifery dispensary in London and a friend of all the London arithmetic observationists, wrote a comprehensive account of their movement in 1789 entitled *Arithmetic and Medical Analysis of the Diseases and Mortality of the Human Species,* (see above, page 114). He saw the "science of medical arithmetic" as the dawn of a new era in medicine. It marked a rejection of unquestioning reverence for great authorities, and for the unsupported opinions of lesser individuals. Black asserted that "... *however it may be slighted as an heretical innovation, I would strenuously recommend Medical Arithmetick, as a guide and compass through the labyrinth of therapeutick."*[164]

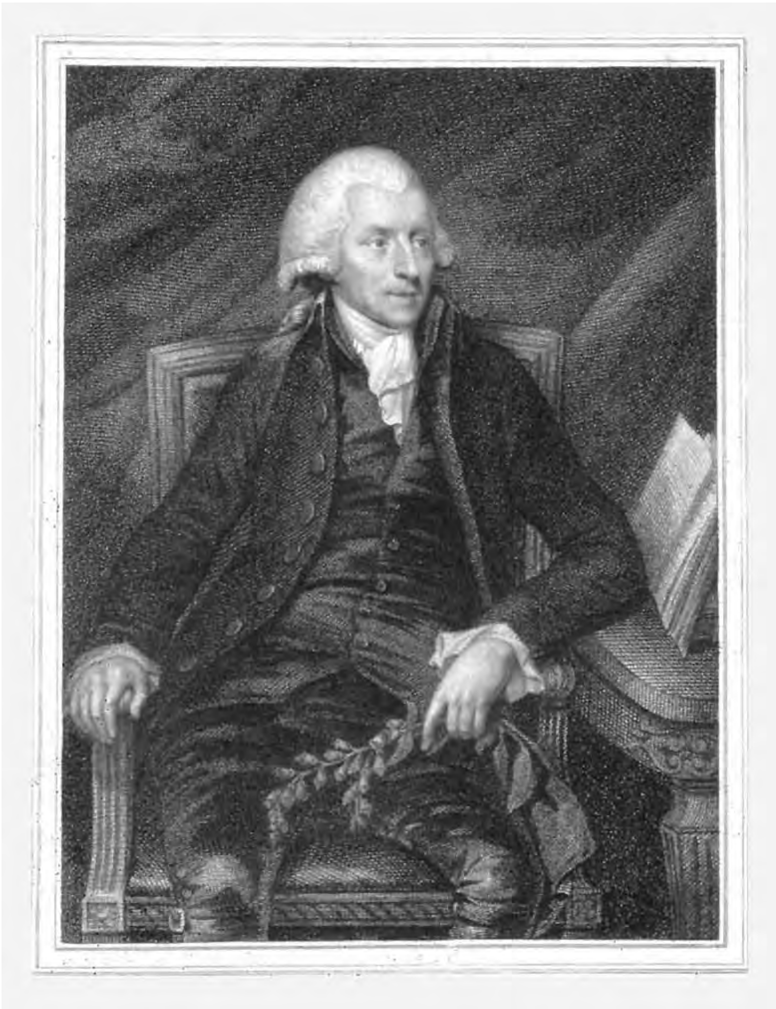
For Millar, too, arithmetic was the candle that could save the investigator from groping in the dark, and Robert Robertson deemed Millar to merit the title of *"the Sydenham of his age"*.[165] Robertson made no secret of using his position in the Navy for large scale therapeutic trials, thereby enabling medical practice to become a science like any other. James Currie and Charles McLean, too, would speak of "test" by "experiment" (see above, pages 52 and 56).

Opposition to open publication of the results of hospital treatment from around 1780 until the 1820s suggests that contemporaries realised the distinctiveness of the method. But despite this opposition, it spread steadily. Indeed, its early propagators were not isolated workers, but knew each other personally. Two influential groups, the Medical Society of London and "The Warrington Group", promoted each other's work, orally and by including reports in their publications. Furthermore, around 1800, adoption of the quantitative method became the norm among scientifically interested doctors in the Army, Navy and the Honourable East India Company. After 1815, there was not a head of a medical department who had not championed or used it.

Who achieved it?

Who exactly were the men who pioneered these developments? The fact that the early arithmetic observationists and experimentalists knew each other – or at least knew of each other – raises the question of whether they had common social roots, which might also partly account for their common social and professional aims. Although I am not able to give here a full social history of the men involved in the movement I have described, I can draw a picture that seems to emerge quite clearly.

The 'typical' representative was either a Scot or a man of English provincial stock. His family background would allow him to be apprenticed to a local doctor or to study for some time at Edinburgh. He had often entered the Army, the Navy, or, if he was lucky, the Honourable East India Company, with the rather low status of 'surgeon'. There, he met with a number of colleagues who would hardly have been trained at all. After some years' service (at the settlement of a peace for instance), he would set up in private civilian practice anywhere except in London (unless he had an MD degree). Alternatively, he might choose to go into private practice in Scotland or the provinces straight away, but the quality of his professional colleagues might still leave a lot to be desired.



William Withering
1741-1799

Without the prestige of an appointment in a large London teaching hospital, for which publications were helpful, getting a practice off the ground was not easy, either in the provinces or in London. Charity practice among the poor, in a new dispensary or one of the smaller or provincial hospitals, could provide a valuable beginning and was much sought after, offering opportunities for treating many cases – and for making contacts with wealthy hospital governors. Such opportunities could also be found in the military hospitals. None of these institutions forbade their medical staff from undertaking private practice, thus a professionally and socially satisfying career was possible, even if one did not hold an appointment at one of the large London hospitals. Such a career was even more interesting for those who took an active part in the foundation and activities of one of the new medical and literary-philosophical societies.

As was true of most doctors, none of the arithmetical observationists was born into landed society. All started as relatively insignificant, or indeed 'marginal', men. Provincial doctors around 1800 were indeed marginal twice over, for they were striving for both individual status, and for membership of a profession still in the making. The men featured in this book must have had strong ambitions to move upwards socially, and distinguished themselves from the majority of ordinary practitioners and Army and Navy surgeons by their scientific work, all of which was completely voluntary.

The arithmetic observationist method required particular organisational skill and constancy of will simply to compile the raw data. Not surprisingly, some of its promoters were perhaps more important as medical organisers than as medical discoverers or scientists in the conventional use of these terms. In this respect, it is noteworthy that they recognised, as early as the 1750s, that hospitals, dispensaries and military conditions afforded opportunities for clinical observations and experiments.

Another aspect of the marginality of the early arithmetic observationists and experimentalists is shown by their involvement in the lives of their own (medical) societies, which were open to surgeons and physicians alike. This was particularly important in London, where Fellowship of the Royal College of Physicians was restricted to graduates of Oxford and Cambridge alone. Instead, the arithmetic observationists and experimentalists taught at their hospitals and dispensaries, and delivered private lectures in their houses, creating a variety of facilities for discussion, training, education and publishing outside the more established avenues such as the Royal Society, the Royal College of Physicians, and the Surgeons' Company.

Furthermore, being Scots, Quakers or Unitarians, most of these men were dissenters in one form or another. They illustrate the general observation that dissenters, by their very exclusion from established centres of influence and power in 18th century Britain, made a distinctive contribution to the nation's educational, scientific, industrial and commercial progress. Indeed, the idea of 'reform' or 'change' was probably the strongest shared root among those who led the arithmetic observationist movement in clinical medicine. This included reform of medical care for the poor, reform of traditional and introduction of new treatments, reform of the professional organisation of medicine, and the elimination of quacks. The laborious task of compiling statistics was always undertaken initially with a definite aim related to these objectives, even if it was sometimes encouraged by the hope of some pecuniary reward.

For John Millar, for example, medicine was just one of many fields in which reform was necessary. This is illustrated by the title of his collected works (1802-1803): *Observations on the Change of Public Opinion, in Religion, Politics, and Medicine; on the Conduct of the War; on the Prevailing Diseases in Great Britain; and on Medical Arrangements in the Army and Navy*. His use of the new term 'public opinion' is typical of the time. The demand for information about public affairs was increasing, and with improved industrial processes for papermaking and printing newspapers, the capacity to meet it was being created. Such demand for information applied to medicine as well as to politics. Just as 'proprietary politics' came under attack, so too did the 'proprietary medicine' of secret remedies and patented *nostrums*, and sometimes the confused state of scholarly medicine as a whole.

Arithmetic observationists and experimentalists, by publishing the results of their practice, aimed to pre-empt both types of criticism. Just as 'shop arithmetic' (or bookkeeping) offered the tradesman a clearer view of his business, and 'political arithmetic' made possible the collection and interpretation of mass observations for the guidance of the statesman, so 'medical arithmetic' would enable the doctor to elevate medicine to a higher level. Debates were occurring about increasing trade, political and social reform and there was a growing awareness of public opinion on economic affairs. It was therefore no coincidence that the term 'medical arithmetic', created by William Black (1789), now followed the earlier introduction of the term 'political arithmetic' by Sir William Petty over 100 years earlier (see above, page 16).

Finally, besides all this evidence and self-asserting rhetoric that an altruistic spirit of reform fostered the use of figures in clinical medicine, we should not forget the place of these men in society, which many of them must also have had in view. There was the question of getting on in the world, after all; and because 18th century British society was dynamic and open, there was always the possibility of advancement, provided one had achieved something with which to impress a potential patron. There was a strong case for a more extensive meritocracy to counter the dominance of patronage and nepotism. One opportunity for advancement as a doctor was to demonstrate, using numbers, one's success in curing disease. Given the challenging spirit of the time and the evidence presented in earlier chapters, it seems very likely that the clear-cut presentation of the results of a doctor's work was relevant to his promotion. And, as shown by the subsequent careers of the early arithmetic observationists and experimentalists, a number of them did indeed make their way up the ladder in military and civilian life.

Both the pursuit of ideals and the prospect of a career may therefore explain why paying for their publications out of their own pockets was considered worthwhile by quite a few of these pioneers. What resources other than quantification would these men, who were relatively uninfluential in social terms, have had? As it was, it seems that this was the trump card. This brings me to the significance of arithmetic observation and experimentation, its causes and hindrances.

What's the significance – then and now?

How can we assess the importance of the ideas and changes brought about by these men? My evidence for the impact of the movement in the 18th century is limited. As mentioned in the third chapter, I have found no direct reference to the development of a critical approach in the lectures of William Cullen in Edinburgh, nor mention of it in the published writings of important figures of the London establishment. Complaints about the absence of accurate record keeping in the large London hospitals, confirmed by a parliamentary inquiry of 1818, and criticised contemporaneously in the *Lancet* and the *Edinburgh Medical and Surgical Journal*, lead one to conclude that the physicians at these institutions were not particularly interested in arithmetical observation and experiment. *Medical and Philosophical Commentaries* (continued as *Annals of Medicine*), the forerunner of the *Edinburgh Medical and Surgical Journal*, was the most important British review journal of medical literature between 1773 and 1804, and was published in several editions, simultaneously in London, Edinburgh and Dublin. It is therefore worthwhile screening this journal for comments, positive and negative, on 'arithmetic observations', although I have obviously not been able to consider all the authors whose works were reviewed.

The selection of books reviewed in the *Commentaries*, and occasional editorial remarks, provide an impression of the impact created by the publications of contributors to the movement. Lind's and Millar's books were not reviewed, but John Clark's were included twice, the second time with some very flattering remarks. Percival's and Lettsom's work on mortality in and around Manchester and at the Aldersgate Dispensary was reviewed equally well, as were Matthew Dobson's on fixed air and William Black's on smallpox. However, there were no specific remarks on their methodology, although a section of Dobson's numerical work was reprinted in the review.

By contrast, Fowler's and Withering's works were the subject of repeated methodological comments. Upon reading Fowler's first book on tobacco, the reviewer thought that his manner of introducing this new medicine *"may justly be considered as a discovery of very great utility"*. He agreed with the author that still more facts were necessary, but concluded that whatever further work might discover, Fowler was *"still entitled to much praise as a faithful and industrious observer"*. Withering's *Account of the Foxglove* earned similar appreciation.[166] Both authors were again quoted in relation to Fowler's second and third *Medical*

Ex Libris

THE

EDINBURGH

Bibliotheca

MEDICAL AND SURGICAL

JOURNAL:

Colleg. Regii

EXHIBITING

Medicor. Edinburgi

A CONCISE VIEW

OF THE LATEST AND MOST IMPORTANT

DISCOVERIES IN MEDICINE, SURGERY, AND PHARMACY.

1805.

VOLUME FIRST.

EDINBURGH:

PRINTED FOR ARCH. CONSTABLE & COMPANY, EDINBURGH; AND LONGMAN, HURST, REES, & ORME, AND JOHN MURRAY, LONDON.

1805.

Reports. Fowler received a rare and favourable comment: *"We cannot too highly applaud the industrious zeal with which he has endeavoured to render hospital practice subservient to medical improvement"*.[167] Gilbert Blane's *Observations on the Diseases Incident to Seamen* (first edition, 1785) received an even longer plaudit concerning the necessity for mass observation. This 70-page review reprinted in full Blane's recommendations for numerical evaluation of clinical practice. Haygarth received high praise for his calculus of probabilities concerning the contagiousness of typhus, which was also reprinted.

However, this favourable reception for the medical observationists and experimentalists should not be overstated, for both the *Commentaries* and the *Edinburgh Medical and Surgical Journal* were largely the product of two men: Andrew Duncan senior and, later, his son. As they wrote most reviews, their periodicals illustrated a particular perspective, namely their criteria for 'sorting the wheat from the chaff'.

A further clue to the impact of the movement is provided in the *London Medical Review* (1799-1802,1808-1812), which included an analysis of the third edition of Blane's *Observations* (1799). His method was seen as having set an example worthy of imitation, and its principles were again fully reprinted. The rest of the valuable contents of the book were presumed by the reviewer to be familiar to most of his readers in the medical profession.

It is tempting to conclude from this limited evidence that 18th century doctors must have been aware, or made aware, of arithmetical observation and experimentation. With the exception of the opposition mentioned by Millar and Black themselves, it seems to have been appreciated in therapeutics as well as in nosography. This inference may be supported by consultation of the more explicit early 19th century review literature. From 1805, the *Edinburgh Medical and Surgical Journal* continued the policy of its forerunners in printing critical book reviews. It described James Currie's *Medical Reports* as *"one of the most valuable [books] which has ever been published ... the style and manner should be imitated"*.[168] Haygarth's *Clinical Histories* was seen as one of the too rare exceptions where a doctor, possessing extensive opportunities for observation, did not simply hurry from patient to patient, write fashionable prescriptions, receive his fees and forget about the patient and his disease. Haygarth had taken the trouble to record his observations and, having a sufficient number, to arrange and then reduce them to a tabular state, intelligible to others; and finally to generalise the facts, uninfluenced by hypothetical opinions.

The impact of William Black's work is revealed in the *Journal*'s comment on his short *Dissertation on Insanity* (1810):

> *We are glad to hear that he has not abandoned his plan, to exhibit the births of the human species, and the mortality of all ages over the globe; then the diseases and accidents by which they are swept away; and to reduce the whole, together with the remedies and modes of cure and prevention to arithmetical proof.*[169]

On the other hand, Clutterbuck's *Inquiry into the Seat and Nature of Fever* (1807), which contained no statistics, despite the evidence collected and the spirit of investigation evinced rhetorically, failed *"to excite a general conviction of its truth among his reader"*. The reviewer felt that one would believe Clutterbuck, if one did not know about different interpretations: *"We should be well pleased if he could decidedly show that fever is always connected with inflammation in any viscus"*.[170] (Clutterbuck advocated a rationalistic approach in the bloodletting revolution described in the previous chapter: see page 47.)

It would seem that it had become unacceptable to defend any method as *"generally successful without any discrimination of circumstances"*.[171] Even a new edition of Ferriar's first three volumes of *Medical Histories* (1810) and a fourth volume in this series (1813) were criticised for lacking the additional evidence which the first editions had seemed to promise. On the other hand, Guthrie's experimentally-derived answer to the question of the timing of amputation, and McGrigor's and Blane's later works of 1815 (see above, page 81) attracted praise.

From this evidence a more or less tacit acknowledgement of the utility– and even necessity – of numerical observations in clinical medicine can be recognised in the first decades of the 19th century. However, this did not preclude a critical attitude to the method from the beginning, both by reviewers and by the promoters themselves. It was a valuable method, but it could also become treacherous and valueless if the data were observed, arranged, or interpreted in a narrow-minded or prejudiced fashion. Thus arithmetic observationism marked a shift away from reliance upon authority, both scientific and social, towards the assertion of the individual himself. This quest for a new basis for knowledge in medicine and for a new meritocracy put increased personal responsibility on the investigator; for to use the method credibly, he was required (as he or she still is) to observe stringent moral standards, both in the conduct of the research and in the interpretation of the results. This was recognised in Percival's *Medical Ethics* (1801).

Yet, with the availability of more and more such trials, the importance of possible confounding factors was realised, as numbers sometimes stood against numbers. In the midst of the struggle about the utility of bloodletting for treating fever, statistics were widely used on both sides. In 1813, the *Edinburgh Medical and Surgical Journal*, after stating its assumption that the numbers were correct and the authors honest, wrote:

> *There is something painful and perplexing to the mind. For we are compelled to admit that there must be some … grievous misconception of the phenomena of the diseases in question, and of the operation of the medicines administered … on the part of those who maintain the one or the other of these opposite opinions: and the practical consequences … appear to be of most fatal import.*[172]

The *Journal* commented further, in a way that would have been rare if not impossible before the dawn of rational empiricism, that it actually raised the possibility that none of the therapeutic alternatives in contention was useful:

> *... if we admit of another alternative, the dilemma is still more painful, namely that neither of the methods of treatment have had any material influence upon the progress of the diseases in question ...*[173]

This latter inference was explained away by the reviewer because of the powerful nature of the agents used by both parties in fevers. Thus, he humbly conceded that other explanations had to be found: Was it perhaps that under different external or internal conditions of the animal economy, similar diseases did not require similar remedies? Significantly, this writer saw the way out of the maze by means of "extensive comparative experiments". And indeed, soon after, Alexander Hamilton reported a sophisticated trial in his Edinburgh thesis (see above, page 49). Because Hamilton lived a scandalous life, his biographer judged this account to be *"a fabrication, made up for the purpose of obtaining a degree and impressing his readers."*[174] However, numerous examples have shown that *"scandalous lives are not incompatible with worthwhile research"*.[175] Although we may never know whether Hamilton really conducted a comparative experiment showing the adverse effect of bloodletting in continuous fevers during the Peninsular War, the fact that he chose to describe it in the way he did is significant. If one considers that he did so to impress his readers and judges, it suggests that the importance of arithmetic observation and experimentation was recognised at least in Edinburgh and in Army medical circles.

Besides its influence on thinking, what impact did the movement have on clinical practice? Based as they are on what people wrote rather than on evidence of what they did, my answers must be tentative and ambiguous; therefore I shall be brief.

As we have seen in earlier chapters, the impact of numerical evaluation on practice varied. The history of scurvy in the British Navy was probably shortened by the numerical method, which showed that malt was not an effective alternative to fruit juice. The lateral and supra-pubic approaches for lithotomy were new techniques introduced and propagated on numerical grounds, and this probably won them adherents, each according to the school and temperament of the individual surgeon. The same was probably true for the British improvements in amputation technique.

The generally adopted therapy for continuous fevers is said to have changed at least twice during this period – bloodletting and purging were replaced in the 1770s and 1780s by hygienic measures, Peruvian bark and other stimulants, but reintroduced at the beginning of the 19th century, only to be attacked again by the 1820s. On the one hand, the 18th century empiricists had initially no particular opinion to defend. The studies of the value of Peruvian bark for continuous fevers were quite empirical in this sense, as they went outspokenly against the prevailing theoretical framework. The same holds for the examination of 'new' drugs, such as tobacco, arsenic, and even foxglove. The extent to which a practitioner was also persuaded by the changing theoretical and pathophysiological explanations of these fevers must remain open, since the former were often published to support the latter. On the other hand, it has become clear that the theory of disease alone could be influential, without there being any empirical evidence to support it. For example, Clutterbuck's influential book (1807), which reopened the period of bloodletting, contained no statistics, thus showing that a theoretical dogmatic basis for medical practice was alive and well.

For the same reasons, the use and timing of amputation also remained contentious. In spite of calculations suggesting strongly that the operation was grossly overused and that delaying it might improve the outcome in certain circumstances, these issues remained matters of dispute throughout the Napoleonic Wars. The results of controlled clinical experiments conducted during the wars influenced a future generation of British military surgeons, although it should be noted that French military surgical practice moved in the same direction based on the authority of its legendary leader, the Baron Larrey, without published experiments or statistics.

In 1833, John Bostock, a teacher at Guy's Hospital Medical School, after noting that rational empiricism had become especially characteristic of Britain in the late 18th century, stated that it had:

> *... produced a most beneficial influence on the general state of medical practice. If it has, on some occasions, produced fluctuation of opinion, and in others indecision or inertness, it has tended to sweep away much error, and to purify the science from many of the antiquated doctrines and practices that still maintain their ground among our continental brethren.*[176]

Arithmetic observation and experimentation had indeed become acceptable methods. Around 1830, both the holder of the chair of the Institutes of Medicine at Edinburgh, William Poulteney Alison, and a physician at the Westminster Dispensary chosen as the Gulstonian Lecturer at the Royal College of Physicians of London, Francis Bisset Hawkins, looked back on the movement described in this book (and their biographies qualify them as competent analysts). While Alison perceived the particular merit of the early comparative statistical enquiries into community diseases, Hawkins stated dryly:

> *Statistics has become the key to several sciences ... And there is reason to believe that a careful cultivation of it, in reference to the natural history of man in health and disease, would materially assist the completion of a philosophy of medicine ... Medical statistics affords the most convincing proofs of the efficacy of medicine.*

and went on to specify:

> *If we form a statistical comparison of fever treated by art, with the results of fever consigned to the care of nature, we shall derive an indisputable conclusion in favour of our profession.*[177]

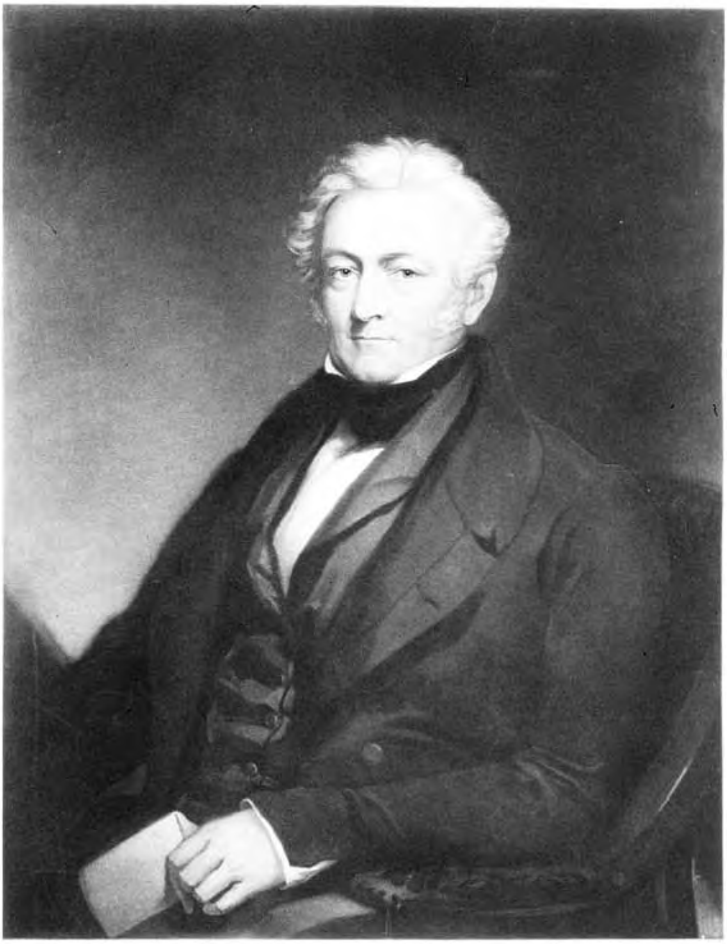
If the word *"statistical"* were replaced by *"arithmetic"* in the above sentence, it might well have been written 50 years earlier by the first physician at the Westminster Dispensary, John Millar; or 150 years later by yet another Scot, Archie Cochrane! Indeed, most if not all of the themes and issues addressed by 18th century British doctors continued to be discussed throughout the 19th century and are again widely debated today.

In order to understand why this is so and, above all, to get a fuller picture of the significance of 18th century arithmetic observation and experimentation, it is essential to see also the arguments against quantification in clinical medicine.

Some reflected seemingly straightforward technical issues, for example that the printing of statistical tables was too *"tedious and troublesome a business"*. Statistics were also considered *"dull literature, despised by many"*.[178] Lack of time to collect data was also pleaded as an excuse for not assembling statistics. But was the writing and reading of pages and pages of single case reports not equally time consuming and tedious? It is true that these excuses were not real arguments against statistics, for they were also used by numerically-minded doctors. The qualification of statistics as *"dry, insipid … altogether useless"*[179] hints at a deeper-rooted opposition, as do ethical issues and a link to politics, when a clinical statistician was decried as a *"Jacobin* [a French pro-revolutionary] *leveller, republican, democrat"*,[180] in other words, a most radical political opponent to the existing political order in Britain.

Quantification can indeed be considered useless in the context of particular concepts, for example, the subjective, the individualistic, and the rational pathophysiological. In the last of these, the logically deduced therapy must be the only and the certain one. It therefore needs no empirical evaluation or justification, which can in any case yield only probable results. On the contrary, this would have signified that the doctor admitted some uncertainty. In this view, to proceed by trial and error was a matter for quacks and mountebanks, not for the learned physician. His distinctive label was that he *knew*. Thus to be against numerical evaluation did not necessarily mean that one would ignore it, but it could signify that the point of view was different. This was the case, for instance, for some advocates of bloodletting during the "bloodletting revolution" of the early 1800s, where the traditional pathophysiological 'culture' prevailed once more.

Indeed, renouncing or opposing arithmetic observation and experimentation could also mean a respectable attempt to deal with the unique nature of disease in an individual patient, which was yet another time-honoured 'culture' in medicine, and not necessarily regarded as inferior to that based on group evaluation. The insistence by advocates of the latter that there should be objectification and standardisation, and that its own observed 'facts' should be analysed with the neutral instrument of arithmetic, thus represented a new culture within medicine



George Guthrie
1785-1856

twice over. As with the others, it had its own specific advantages and benefits, but also its disadvantages and risks, which could be used against it.

An important example of the latter were the ethical issues linked with well controlled human experimentation as required by clinical trials. Some Army surgeons saw no problem in allocating soldiers to experimental groups during a battle, while others hesitated. Faure and Alexander Hamilton, for instance, apparently belonged to the former group; James Lind and George Guthrie to the latter. Despite his theoretical insight into the necessity of conducting prospective comparative trials and the unique opportunities a commanding military surgeon had to enforce them, when it came to carrying out a study of delayed versus immediate amputation, Guthrie had scruples after the "success" he deemed to have seen with immediate intervention, and he felt himself not *"authorised to commit murder for the sake of experiment"*[181] (see above, page 101). He renounced the trial and relied on retrospective analysis of his casebooks and of returns sent in by colleagues, both containing records of operations used on an *ad hoc* basis – in today's terminology, in what amounted to poorly controlled human experimentation.

One author, Charles McLean, realised in 1818 the ethical double-standard involved in this pretended *"reluctance to try experiments with the lives of men ... as if the practice of medicine, in its conjectural state, were anything else, than a continued series of experiments, upon the lives of our fellow creatures."*[182] This reflection on the morality of acting according to evidence gathered in traditional ways remained isolated, however, while Guthrie's argument represented the widespread opinion that those participating in research *"should benefit from a trial and must not be put in danger for the sake of scientific curiosity"*.[183] Indeed, 50 years earlier, Lind had reacted in such a way to a trial ordered by the Admiralty, but the case ended quite differently. When starting a trial of the wort, Lind acknowledged the "murmur and disgust" when withholding vegetables from scurvy patients at Haslar (despite the knowledge that they would improve their condition) and stopped the experiment. But the Admiralty ordered it to be taken up at sea *"where it was expected that patients would cheerfully submit"*[184] (see above, page 73). Although there was a climate of "ethical awareness", consent was obviously not a major issue. The influence of power was thus central in this and other trials, particularly in the Navy, but also in the Army and probably in civilian institutions.

There was another way to circumvent the risks involved in a trial with a new method. Because he felt *"it would be unjustifiable to neglect for the sake of experiment any means of safety"*,[185] James Currie in 1804 "superadded" his cold water bathing to the traditional fever treatment – in other words, he used today's 'add-on design'. This implied, of course, that he considered the traditional bleeding as safe (on what evidence we do not know) – with fatal consequences for himself (see above, page 29). But this was precisely the point being contested by Millar and his colleagues.

These discussions of risk, even sacrifice *"for the sake of experiment"*, and of safety, illustrate the ambiguity of the notion of experiment. Many 18th century doctors understood its everyday meaning, that is, a straightforward trial with unknown (yet sometimes hoped for) results. Some, like James McGrigor, meant by it an intervention under well-controlled conditions and circumstances with respect to the selection of patients, the treatment(s) given *and* the particular care with which the patients were attended (see above, page 110). Finally, Charles McLean did not see much difference between an "experiment" and routine clinical practice based on "conjectural", in other words, inferior, evidence.

Cheating was a further ethical problem recognised among 18th century investigators. More mildly put, the quantification of prejudice – as encountered for instance in the bloodletting revolution – was an argument used against numerical analysis. A number of contemporary medical authors used a rhetoric of candid enquiry and honest reports. In his book *Medical Ethics* (1803), Thomas Percival recommended the devising and subsequent trial of new remedies and new surgical methods in public hospitals as being "for the public good", provided they were scrupulously and conscientiously carried out.[186] Clearly, stringent and specific moral standards were required for the proper use of statistical methods, both in the conduct of the research and in the interpretation of the results; but apart from the specifics, the same issues applied to the pathophysiological and the individual clinical approaches.

This brings me to the 'hidden agendas' behind arithmetic observation and experimentation. I have quoted above the political arguments that, to a limited extent, were used against it. While arithmetic observation and experimentation insisted on objectification, public comprehensibility and transparency of results; pathophysiological and individualising clinical 'cultures' stressed the power of the individual doctor. In this context, the introduction of a critical approach could be seen as an attempt to subvert the traditional order of things. Although the pathophysiological, individual clinical, and statistical strategies have all three been important in the making of the modern medical profession, their respective protagonists have often fought each other in changing alliances, sometimes claiming exclusive credit for medical advance. Which of the three types of evidence carried the day, however, has always depended on socio-cultural factors.

Having said that, and without denying the changed social and political circumstances, there are striking parallels between some aspects of the developments in the late 18th and early 19th centuries and those in the second half of the 20th and the early 21st centuries in Britain. This is not to suggest that these similarities have existed throughout the past 200 years: on the contrary, the features that these periods share are very different to the situation that prevailed during most of the intervening 19th and early 20th centuries. To mention just a few:

First, now as then, there is an intense discourse about how best to assemble reliable evidence about the effects of health care.

Second, the two periods are characterised by an emphasis going beyond the treatment of individual patients, which demands an evaluation of what 'science' has delivered. This is reflected today, for example, in the development of clinical guidelines, a concept that was certainly in the minds of military doctors concerned to improve the care of sailors and soldiers, and their civilian colleagues serving the urban poor in the 18th century.

Third, as we have been reminded recently by editorials in both the *Lancet* and the *New England Journal of Medicine*,[187] vested commercial interests are causing concern, just like Dr James' poorly documented claims of the success of his patented powder did, over 200 years ago. Evaluation of spa therapy at Bath, however, showed how legitimate economic interests could be dealt with honestly.

Fourth, the relatively high cost of fruit to prevent scurvy and Peruvian bark to treat fever shows that, in the 18th century as today, decisions about how to allocate limited funds had to be taken. Also as today, there emerged a premium on statistical evidence as the best available guide to decisions about the cost-effectiveness of care.

Fifth, both eras are characterised by an array of medical innovations that are advocated on purely rational grounds, but which also trigger a demand for valid comparisons with existing remedies and procedures.

And sixth, empirical testing of medical interventions and publication of the results in a form intelligible for everyone, vigorously advanced – and equally vigorously opposed – in the 18th century, are recognised features of consumerism in modern democracies.

In other words, critical statistical evaluation of medical interventions, whether termed "medical arithmetic and experimentation" in late 18th century Britain, the "numerical method" in the 1830s Paris of Pierre-Charles-Alexandre Louis, or "clinical epidemiology" and "evidence-based medicine" in our era, depends on an appropriate climate to grow and become credible. I hope that this book has shed some light on the favourable climate prevailing in the 18th century and has helped to show why, how, and with what effect British, and particularly Scottish, pioneers took advantage of it *"to improve the evidence of medicine"*.

REFERENCES

1. Silverman W.A. (1998), *Where's the Evidence?* Oxford, Oxford University Press.
2. Johnson Th. (1678), *The works of that famous surgeon Ambroise Paré*, London, Mary Clark.
3. *Pharmacopoeia Collegii Regii Medicorum Edinburgensis*, (1699). Edinburgh, Royal College of Physicians of Edinburgh.
4. Lind J. (1757), *A treatise on the scurvy*..., 2nd ed., London, Millar, pp. 50, 149.
5. Quoted by Desruelles H.M.J. (1830), *Memoir of the treatment of venereal disease without mercury*, Philadelphia, Carey and Lea, pp. 202-3.
6. Fordyce G. (1793), 'An attempt to improve the evidence of medicine', *Trans. Soc. Impr. Med. Chir. Knowl.* **1**; 243.
7. Black W. (1789), *An arithmetical and medical analysis of the diseases and mortality of the human species*..., London, Dilly, pp. vii-viii.
8. *Ibid.*
9. Haygarth J. (1805), *A clinical history of diseases*, London, Cadell and Davies, p. 182.
10. *Medical Observations and Inquiries*, (1757), **1**; p. vi.
11. Quoted by Cassedy J.H. (1974), 'Medicine and the rise of statistics', in: Debus A.G. (ed.), *Medicine in seventeenth century England*, Berkeley-Los Angeles-London, Univ. California Press, p. 291.
12. Davenant C. (1771), as quoted by Borsay A. (2000), 'An example of political arithmetic: The evaluation of spa therapy at the Georgian Bath Infirmary', *Medical History*, **45:** 149-72, p. 149.
13. Quoted by Newman G. (1932), *The rise of preventive medicine*, Oxford, Oxford University Press, p. 171.
14. Ferriar J. (1792), *Medical histories and reflexions*, Vol. 1, [quoted from a later ed. 1810], London, Cadell and Davies, pp. xvii-xxix.
15. *Ibid.*
16. *Ibid*, pp. xxiv-xxv.
17. Millar J. (1783), *Observations on the management of diseases in the Army and Navy*, London, for the Author, p. 3.
18. Quoted by Sienger D.W. (1949-50), 'Sir John Pringle and his circle', *Annals of Science*, **6:** 127-80, 229-61, p.154.
19. Gregory J. (1805), *Lectures on the duties and qualifications of a physician*, 1772, revised and corrected ed. by J. Gregory (son), Edinburgh-London, Creech and Cadell, p. 150.
20. Quoted by King L.S. (1971), *The medical world of the eighteenth century*. Huntingdon, N.Y., Krieger, p. 141.
21. I owe this and the following two paragraphs to Irvine London.
22. Lind J. (1763), *Two papers on fevers and infection*, London, Wilson, p. 228.
23. Quoted by Lloyd C. and Coulter J.L.S. (1961), *Medicine and the Navy*, Edinburgh, Livingstone, Vol. 3, p. 335.
24. Lind J. (1763), as note 22 above, p. 73.
25. *Ibid*, pp. 71-2, 79.
26. *Ibid*, pp. 71-2.
27. Lind J. (1768), *An essay on diseases incidental to Europeans in hot climates*, London, Beckett and de Hondt, pp. 291, 313-5.

28. *Ibid*, pp. 316-7.
29. Lettsom J.C. (1772), *On the general treatment and cure of fevers*, London, Cornish, 11.
30. *Ibid*, p. 343.
31. Millar J. (1777), *Observations on the practice in the Medical Department of the Westminster General Dispensary*, London, by Order of the Governors, p. 2.
32. *Ibid*, pp. 4-5.
33. *Ibid*, pp. 7-8.
34. Millar J. (1778-1779), as note 17 above, London, for the author, p. 2.
35. *Ibid*, pp. 103-4.
36. *Ibid*, pp. 104-5.
37. *Ibid*, pp. 107, 110-2, 128-41, 150-2, 158, 175-6.
38. Quoted by Millar J. (1798), *Observations on the prevailing diseases in Great Britain*, 2nd. ed., London, for the author, p. 75.
39. Millar J. (1783), as note 17 above, p. 41.
40. Millar J. (1798), as note 38 above, pp. 8-11, 63-73.
41. *Ibid*, p. 80.
42. *Ibid*, p. 76.
43. Robertston, R. (1777), *A physical journal kept on board His Majesty's Ship Rainbow*... London, Dilly, pp. vii-viii, 22, 120.
44. Robertson R. (1790), *An essay on fevers*, London, for the author, p. 5.
45. Robertson R. (1783), *Observations on the jail, hospital or ship fever*, London, Murray, pp. vi-vii.
46. *Ibid*, pp. 228-9, Tables II and III.
47. *Ibid*, p. 237.
48. *Ibid*, p. 312.
49. *Ibid* (1789), 2nd ed., London, for the author, pp. xviii, 471, 473.
50. As note 44 above, pp. 1-3.
51. Clark, J. (1780), *Observations on fever, especially those of the continued type,* London, Cadell, pp. 189-96.
52. Reide T.D. (1793), *A view of the diseases of the army in Great Britain, America, the West Indies and on board of King's ships*..., from the beginning of the late war to the present time, toogether with monthly and annual returns of the sick..., London, Johnson, pp. xi, xiii.
53. Millar J. (1798), *Observations on the prevailing diseases in Great Britain*, 2nd. ed., London, for the author, pp. 17-24, 81-4.
54. Rowley W. (1788), *The causes of the great number of deaths amongst adults and children*, quoted from 2nd ed. London, Newbery, 1793, pp. 3-4.
55. *Ibid*, pp. 4, 18.
56. Rowley W., (1804), *A treatise on putrid, malignant, infectious fevers and how they ought to be treated* ..., London, Barfield, pp. 29, 36.
57. *Ibid*, p. 21.
58. Quoted by Forrester J.M. (2000), 'The origins and fate of James Currie's cold water treatment for fever', *Medical History*, **44**; 57-74, p. 74.
59. *Edinburgh Med. Surg. J.*, (1821), **17**; p. 634.
60. Hamilton A. (1816), '*Dissertaeio medica inauguralis de synocho castrensi*' Edinburgh, J. Ballantyne, et al.
61. Currie J. (1797), *Medical reports on the effects of water, cold and warm as a remedy in fever and febrile diseases*, Vol. 1, Liverpool and London, M'Creery and Cadell, p. 199.
62. *Ibid*, pp. 4, 6-7.
63. *Ibid* (1804), Vol. 2, p. 408.
64. *Ibid* (1797), pp. 43, 199-200.
65. Quoted by Maehle A.H. (1999), *Drugs on trial: experimental pharmacology and therapeutic innovation in the eighteenth century*, Amsterdam-Atlanta, Rodopi, p. 270.

66. Fowler T. (1785) *Medical reports on the effects of tobacco in the cure of dropsies and dysenteries*..., quoted from the 2nd ed., London, for the author, 1788, preface (no pagination).
67. *Ibid*, London, for the author, 1788, pp. xi, xiii.
68. Millar J. (1774), *Observations on antimony*, London, Johnson et al., p. 83.
69. Lind J. (1768), note 27 above, pp. 275-80.
70. McLean C. (1817-1818), *Results of an investigation respecting epidemic and pestilential diseases*..., London, Underwood, Vol. 2, p. 501.
71. McLean C. (1818), *Practical illustrations of the progress of medical improvement for the last thirty years*, London, for the author, p. xxiii.
72. *Ibid* (1817-1818) as note 70 above, pp. 500-4; see also note 71 above, pp. xxiii-xxiv.
73. *Ibid* (1817-1818), Vol. 2, pp. 432-54; *Ibid* (1818), p. xxvi.
74. Quoted by Bell J. (1815), *The principles of surgery*, London, Longman, Vol. 2, p. 104.
75. Cheselden W. (1732), *The anatomy of the human body*, 4th ed., London, Bettesworth and Hitch, pp. 342, 344.
76. *Ibid* (1740), 5th ed., London, Bowyer, p. 332.
77. *Ibid*, (1740), as note 75 above, p. 346 and Morand, S.F. (1731), 'Recherches sur l'opération de la taille par l'appareil latéral', *Hist. Acad. Roy. Sci.* (Paris), pp. 144-59; 144-6, 158-9.
78. Morand S.F., as note 77 above, pp. 148, 158-9.
79. Baseilhac J. (1779), *Nouvelle méthode d'extraire la pierre par dessus le pubis*, Paris, D'Houry, pp. 77-8.
80. Deschamps J.F. (1796), *Traité historique et dogmatique de la taille*, Paris, for the author, Vol. 2, p. 68.
81. Marcet A. (1819), *An essay on the chemical history and medical treatment of calculous disorders*, 2nd ed., London, Longman et al, p. 24.
82. Dobson M. (1779), *A medical commentary on fixed air*, Chester, Monk, pp. 148-9.
83. *Ibid*, pp. 178-179. *Ibid*, p. vii.
84 Marcet A. (1819), as note 81 above, p. vii.
85. *Ibid*, pp. 24-47.
86. Martineau P. (1821), 'On lithotomy', *Med.-chir. Trans.*, **11**; pp. 402-13; 403, 405, 409.
87. Quoted by Batty Shaw A. (1968), 'The oldest medical societies in Great Britain', *Med. Hist.* 12; pp. 232-44; 248.
88. Smith R. (1820), 'A statistical inquiry into the frequency of stone in the bladder in Great Britain and Ireland, *Med.-chir. Trans.*, **11**; pp. 1-53.
89. Lind J. (1757), as note 4. above, pp. vii-viii, 159.
90. Locke J. (1894), *An essay concerning human understanding*, collated and annotated by A.C. Fraser, Oxford, Clarendon, Vol. 1, p. 14.
91. Lind J. (1757), as note 4 above, pp. xii, 147.
92. *Ibid*, pp. 60-1, 145, 154.
93. *Ibid*, pp. 50, 149.
94. *Ibid*, pp. 50-1, 152.
95. *Ibid*, pp. 248-50, 253-4.
96. Macbride D. (1764), *Experimental essays*, London, Millar, pp. 184-5, 187-8, 192-9.
97. *Ibid*, pp. 174-175.
98. Macbride D. (1767), *An historical account of a new method of treating the scurvy at sea*..., London, Millar and Cadell, p. 30.
99. *Ibid*, pp. 38, 40, 45, 49-50.
100. Clark J. (1773), *Observations on the diseases in long voyages to hot countries*..., London, Wilson, pp. 181-2.
101. Macbride D. (1772), *A methodical introduction to the theory and practice of physic*, London, Straham et al, pp. 653-4; Lloyd C. and Coulter J.L.S., as note 23 above, Vol. 3, p. 308.
102. Quoted from Beaglehole J.D. (ed.) (1967-1969), *The journals of Captain James Cook on his voyages of discovery*, Cambridge, Cambridge Univ. Press, Vol. 1, p. 632; also in Macbride, as above, pp. 659-60.

103. Clark J. (1773), as note 100 above, London, Wilson, pp. 283-300.
104. Lind J. (1772), *A treatise on the scurvy*, 3rd ed., London, Crowder, et al, pp. iv-v.
105. *Ibid*, pp. 504, 506, 531-2, 536.
106. *Ibid*, p. 180.
107. *Ibid*, pp. 537-40.
108. Hughes R.E. (1975), 'James Lind and the cure of scurvy: an experimental approach', *Medical History*, **19**; pp. 342-51.
109. Lind J. (1772), as note 104 above, pp. v-vi.
110. Robertson R. (1804), *Observations on the diseases incident to seamen*, 2nd ed., London, for the author, Vol. 1, pp. xxviii, 20.
111. Blane G. (1785), *Observations on the diseases incident to seamen*, London, Cooper, pp. 54-7, 285, 287, 295, 463-4.
112. Renwick W. (1792), *An inquiry into the nature and causes of sickness in ships of war*, London, Evans, pp. 14-5.
113. Trotter T. (1797), *Medicina nautica. An essay on the diseases of seamen*, London, Cadell, Vol. 1, 133-4.
114. Withering W. (1785), *An account of the foxglove, and some of its medical uses: With practical remarks on dropsy, and other diseases*, Birmingham, Robinson, pp. vi.
115. *Ibid*, pp. 189-90.
116. *Ibid*, pp. vii-viii.
117. *Ibid*, pp. ix.
118. *Ibid*, pp. xix.
119. Fowler T. (1785) *Medical reports on the effects of tobacco in the cure of dropsies and dysenteries*..., quoted from the 2nd ed., London, for the author, 1788, preface (no pagination).
120. Ferriar J. (1792), as note 14 above, pp. xxii-xxiii.
121. *Ibid*, p. 38.
122. Ferriar J. (1813), *Ibid*, Vol. 4, London, Cadell and Davies, pp. 40-1.
123. Charleton, R. (1770), *An inquiry into the efficacy of warm bathing in palsies*, Oxford, Clarendon, p. 3.
124. *Ibid*, pp. 10-12.
125. *Ibid*, p. 96.
126. Falconer W. (1790), *A practical dissertation on the medicinal effects of the Bath waters*, London and Bath, Robinson and Cruttwell, pp. vii, x, xiii, xv.
127. Fowler T. (1795), *Medical reports on the effects of blood-letting, sudorifics, and blistering in the cure of the acute and chronic rheumatism*, London, Johnson, pp. vii-ix.
128. *Ibid*, p. ix.
129. Haygarth J. (1805), *A clinical history of diseases* I. A clinical history of the acute rheumatism, or rheumatick fever, II. A clinical history of the nodosity of the joints, London, Cadell and Davies, p. 186.
130. *Ibid*, p. 33.
131. Haygarth J. (1800), *Of the imagination as a cause and as a cure of disorders of the body*..., Bath and London, Cruttwell and Cadell.
132. *Ibid*, p. 28.
133. Le Dran H.F. (1730), *Parallèle des différentes manières de tirer la pierre hors de la vessie*, Paris, Osmont, pp. 356-7.
134. *Prix Acad. Roy. Chir.*, (1769) **3**; p. 353.
135. Pott P. (1779), *Remarks on that kind of palsy ... to which are added observations on the necessity of amputation in certain cases and circumstances*, London, Johnson, p. 46.; Pott P. (1790), *The chirurgical works of Percival Pott*, London, Johnson, Vol. 3, p. 374.
136. Bell B. (1) (1778), *Treatise on the theory and management of ulcers*..., Edinburgh, Elliot, Vol. 6, 329-30.

137. O'Halloran S. (1765), *A complete treatise on gangrene and sphacelus with a new method of amputation*, London and Dublin, Vaillant and Wilson, pp. ix.
138. White C. (1770), *Cases in surgery*, London, Johnston, pp. vi-viii.
139. Bromfield (Sir) W. (1773) *Surgical observations and cases*, London, Cadell, Vol. 1, pp. 322-3.
140. Alanson E.A. (1782), *Practical observations on amputation and the after-treatment*, 2nd ed., London, Johnson, pp. vii-viii.
141. *Ibid*, pp. xv-xvi.
142. Blane (Sir) G. (1799), *Observations on the diseases incident to seamen*, 3rd ed., London, Murray and Highley, pp. 582-3.
143. Guthrie G.J. (1815), *On gun-shot wounds of the extremities*, London, Longman, pp. viii, 38.
144. *Ibid*, p. 39.
145. *Ibid*.
146. *Ibid*, pp. 39-47.
147. *Ibid*, p. 194.
148. Guthrie G.J. (1853), *Commentaries on the surgery of the war in Portugal, Spain, France, and the Netherlands...*, London, Renshaw, p. v.
149. *Ibid*, p. vi.
150. *Edinburgh Med. Surg. J.,* (1816), **12**; 221.
151. (1838), *Clinical lectures on compound fractures of the extremities...*, London, Churchill, p. 9.
152. Thomson J. (1816), *Report of observations made in the British military hospitals in Belgium after the battle of Waterloo, Edinburgh and London*, Blackwood and Cadell, p. 223.
153. Guthrie G.J. (1820), *Observations on gun-shot wounds and on injuries of the nerves*, London, Burgess and Hill, pp. 81-3.
154. Guthrie G.J. (1815), as note 143 above, p. 47.
155. Hutchison A.C. (1817), *Some further observations on the subject of the proper period for amputating in gun-shot wounds*, London, Callow, p. 16.
156. *Med. Obs. Inquiries* (1757), **1**; 365-412; (1762), **2**; 70-99.
157. Guthrie G.J. (1817), 'Observations on the treatment of the venereal disease without mercury', *Med.-chir. Trans.*, **8**; 550-81.
158. *Ibid*, pp. 180, 192-3.
159. Hennen J. (1818), 'Observations on the cure of syphilis without mercury...', *Edinb. Med. Surg. J.*, **14**; pp. 328, 333-5, 356.
160. Hennen J. (1829), *Principles of military surgery*, 3rd ed., London, Wilson, pp. 544-5.
161. *Ibid*, p. 551.
162. *Ibid*, (1818), as note 159, p. 203.
163. Millar J. (1777), as note 31, pp. 4, 7.
164. Black W. (1788), *A comparative view of the mortality of the human species at all ages...*, London, Dilly, pp. 36, 38.
165. Robertson R. (1783), as note 45 above p. 317.
166. *Med. Philos. Commentaries* (1785), **10**; pp. 123, 132 for Fowler; p. 10 for Withering.
167. *Ibid*, 2nd decade, (1795), **10**; 212, 170.
168. *Edinb. Med. Surg. J.* (1805), p. 1; pp. 67, 72.
169. *Ibid*, (1811), **7**; p. 220.
170. *Ibid*, (1808), **4**; pp. 80-1.
171. *Ibid*, (1809), **5**; p. 123.
172. *Ibid*, (1813), **9**; pp. 458-9.
173. *Ibid*.
174. Rosner L. (1999) *The most beautiful man in existence*, Philadelphia, Univ. of Pennsylania Press, p. 133.
175. Milne I. and Chalmers I. 'Tackling bias in assessing the effects of healthcare interventions: Early contribution from two Edinburgh men, Alexander Lessier Hamilton and Thomas Graham Balfour'. *Proc. R. Coll. Phys. Edinburgh* [in press].

176. Bostock J. (1833), 'History of Medicine', in Forbes J. et al. (eds.), *The Cyclopaedia of Practical Medicine*. London, Sherwood et al. Vol. 1, pp. i-lxxii, lxix.
177. Hawkins F.B. (1829), *Elements of Medical Statistics*, London, Longman, pp. 2-3.
178. As notes 129 and 45, p. viii.
179. As note 45.
180. As note 53.
181. As note 145.
182. Quoted from Maehle, as note 72.
183. As note 65, pp. 268-269.
184. As note 97.
185. As note 63.
186. Percival T. (1827), *Medical ethics*, 2nd ed., London, Jackson, pp. 32, 36.
187. Ansell M. (2000), "Is academic medicine for sale?', *N. Engl. J. Med.*, **342**; 1516-8; Weatherall D., (2000), 'Academia and industry: increasingly uneasy bedfellows', *Lancet,* **355**; 1574-5.

FURTHER READING

Introduction

For many general issues forming the historical background of this book, there are chapters in:

- Bynum, W.F., Porter, R. (eds.), (1993), *Companion Encyclopedia of the History of Medicine*, London-New York, Routledge.

A main theme of this book is the 18th century discussion about reliable knowledge in therapeutics. The basic question of certain knowledge versus probable results had already been debated, for medicine and other fields of natural sciences, in the context of the 17th century scientific revolution:

- Shapiro, B. (1983), *Probability and certainty in seventeenth-century England*, Princeton, Princeton University Press.
- French, R., Wear, A. (1989), *The medical revolution of the seventeenth century*, Cambridge, Cambridge Univ. Press.
- Shapin, S. (1996), The scientific revolution, Chicago-London, Univ. of Chicago Press.

It is interesting to see who defended which type of knowledge and what the argumentation was. Truth has indeed a social history:

- Shapin, S. (1994), *A social history of truth*, Chicago-London, Univ. of Chicago Press.

and changes of its basis have been important for the understanding and dominating of reality as well as for the social order in modern times.

Four contributions have followed the history of the clinical trial, one of the jewels of this book, up to the present:

- Lilienfeld, A.M. (1982), 'Ceteris paribus: The evolution of the clinical trial'; *Bulletin of the History of Medicine*, **56**; 1-18.
- Matthews, J.R. (1994), *Quantification and the quest for medical certainty*, Princeton, N.J., Princeton Univ. Press.
- Kaptchuk, T.J. (1998), 'Intentional ignorance: A history of blind assessment and placebo controls in medicine', *Bulletin of the History of Medicine*, **72**; 389-433.
- Tröhler, U. (1999), 'Die wissenschaftlichen Begründungen therapeutischer Entscheide - oder "Evidence-Based Medicines" - im Lauf der Geschichte', in:

Eich, W. et al (eds.), *Wissenschaftlichkeit in der Medizin*, Frankfurt a. M., VAS Verlag, 101-27.

While R. Matthews focuses on 19th century France and 20th century Britain, J. Cassedy looks at 19th century America:

- Cassedy, J. (1984), *American medicine and statistical thinking*, Cambridge, Mass., Harvard Univ. Press.

Medicine in 18th Century Britain

There is an enormous amount of literature on 18th century medicine, particularly in Britain. Edited volumes allow good insights from various standpoints, scientific, philosophical, clinical, public health, political, educational, etc.:

- Bynum, W.F., Porter, R. (eds.), (1985), *William Hunter and the eighteenth century medical world*, Cambridge, Cambridge Univ. Press.
- Cunningham, A., French, R. (eds.), (1990), *The medical enlightenment of the eighteenth century*, Cambridge, Cambridge Univ. Press.
- Porter, R. (ed.), (1995), *Medicine in the Enlightenment*, Amsterdam-Atlanta, Rodopi.

For a general view on early 19th century medicine see:

- Bynum, W.F. (1994), *Science and the practice of medicine in the nineteenth century*, Cambridge (Cambridge History of Science), Cambridge Univ. Press.

For surgery see:

- Tröhler, U. (1999). 'L'essor de la chirurgie', in: Grmek, M.D., (ed.), *Histoire de la pensée médicale en occident*, vol. 3, Paris, Seuil, 235-51.

Scottish medical societies have recently been dealt with by:

- Jenkinson, J. (1993), *Scottish medical societies 1731-1939: Their history and records*, Edinburgh, Edinburgh Univ. Press.

The 18th/early-19th century medical journals have been described and their function analysed by:

- Le Fanu, W.R. (1984), *British periodicals of medicine, 1640-1899*, Oxford, Wellcome Unit for the History of Medicine.
- Chalmers, I., Tröhler, U. (2000), 'Helping physicians to keep abreast of the medical literature: *Medical and Philosophical Commentaries*, 1773-1795', *Annals of Internal Medicine*; **133**; 238-43.

as well as in chapters by R. Porter, J., Loudon, I. in:

- Bynum, W.F., Lock, S., Porter, R. (eds.), (1992), *Medical journals and medical knowledge: Historical essays*, London, Routledge.

The hospital world in the 18th century has been described and analysed in a number of histories of single institutions. However, particularly relevant for this study is:

- Risse, G.B. (1986), *Hospital life in Enlightenment Scotland*, Cambrige, Cambridge Univ. Press.

because many of the clinical arithmetic observationists had come into contact with the Edinburgh Infirmary. 'Research' in the London hospitals (and also the London medical societies) have been explored in:

- Lawrence, Susan C. (1996), *Charitable Knowledge: Hospital Pupils and Practitioners in Eighteenth-Century* London, Cambridge, Cambridge Univ. Press.

I. Loudon and myself have written on dispensaries:

- Loudon, I.S.L. (1981), 'The origins and growth of the dispensary movement in England', *Bulletin of the History of Medicine*, **55**; 322-43.
- Tröhler, U. (1987/88), 'The doctor as naturalist: The idea and practice of clinical teaching and research in British policlinics 1770-1850', *Clio Medica*, **21**; 21-34.

and on midwifery charities (which are not dealt with explicitly in this book):

- Loudon, I.S.L. (2000), *The tragedy of childbed fever*, Oxford, Oxford Univ. Press.
- Tröhler, U. (1981), 'Klinisch-numerische Forschung in der britischen Geburtshilfe 1750-1820', *Gesnerus*, **38**; 69-80.

Evidence, quantification and therapy

The rise of statistical and probabilistic thinking in general is the background for its development in medicine as is revealed by reading:

- Stigler, S.M. (1986), *The history of statistics, The measurement of uncertainty before 1900*, Cambridge (Mass), The Belknap Press of Harvard Univ. Press.
- Daston, K.J. (1988), Classical probability in the Enlightenment, Princeton, Princeton Univ. Press.
- Gigerenzer, G. et al. (eds.), (1989), *The empire of chance: How probability changed science and everyday life*, Cambridge, Cambridge Univ. Press.
- Canguilhem, G. (1989), *Grenzen medizinischer Rationalität, Historisch-epistemologische Untersuchungen*, Tübingen.

There were many routes leading to quantitative outcome assessment in therapeutics. *Smallpox*, a public health issue, must be mentioned. Chapters by A. H. Maehle and A. Rusnock in Porter's (ed.), *Medicine in the Enlightenment* (see above) and:

- Rusnock, A. (ed.) (1996) *The correspondence of James Jurin (1684-1750), physician and secretary to the Royal Society*, Amsterdam, Rodopi.

illustrate this early 18th century use of numerical evidence.

Reasons of *professional politics*, i.e. doctors' delineation from fringe medicine, stood also behind the presentation of well attested numerical results (versus quack fantasy pretensions) - and quackery was well developed:

- Bynum, F.F., Porter, R. (eds.), (1987), *Medical fringe and medical orthodoxy 1750-1850*, London, Croom Helm.

Identification and *classification* of *disease entities* were another precondition for statistical comparisons. Both were very much 18th century ventures, also in Britain:

- Rosenberg, C.E., Golden, J. (eds.), (1992), *Framing disease. Studies in cultural history*, New Brunswick, N.Y.

The ever so practically relevant concepts of *fevers* are outlined in:

- Bynum, W.F., Nutton, V. (eds.), (1981), *Theories of fever from Antiquity to the Enlightenment*, London, Wellcome Institute.

They raise the question of retrospective diagnosis which, of course, holdss also for two further sections in the chapter, scurvy and syphilis. It is very aptly treated by:

- Leven, K.H. (1998), Krankheiten - historische Deutung vs. retrospektive Diagnose, in: Paul, N.,Schlich, Th. (eds.), *Medizingeschichte: Aufgaben - Probleme - Perspektiven*, Frankfurt/M., New York: Campus, 1998, 153-85.

The cold water treatment of continuous fevers by James Currie, and particularly the reasons for its limited success despite favourable statistical evidence have been elucidated by:

- Forrester, J.M. (2000), 'The origins and fate of James Currie's cold water treatment for fever', *Medical History*, **44**; 57-74.

The recrudescence of bloodletting against fevers has been analysed by:

- Niebyl, P.C. (1977), 'The English bloodletting revolution, or modern medicine before 1850', *Bull. Hist. Med.*, **51**; 464-83.

The mode of action and the efficacy of an alternative fever treatment, cinchona bark, deserved a chapter in:

- Maehle, A.H. (1999), *Drugs on trial: Experimental pharmacology and therapeutic innovation in the eighteenth century*, Amsterdam-Atlanta, Rodopi.

In another chapter of his perspicacious book, Maehle deals with the conservative treatment of *bladder stone* with so-called lithontriptics, such as Mrs Stephen's remedy awarded a huge sum of money from the British Parliament despite "weak" empirical evidence.

The concepts and treatment of *scurvy* have repeatedly found attention. A complete history up to the present is:

- Carpenter, K.J. (1986), *The history of scurvy and vitamin C*, Cambridge, Cambridge University Press.

W. McBride describes the experimental work and the ensuing theory of David Macbride consistent with the paradigms of established scientists of the time - whilst Lind remained marginal with this respect:

- McBride, W.W. (1991), 'Normal medical science and British treatment of the sea scurvy, 1753-75', *J. Hist. Med. Allied Sci.*, **46**; 158-77.

Withering's book on the *foxglove* has now been edited and commented: also from a present-day point of view:

- Aronson, J.K. (1985), *An Account of the foxglove and its medical uses 1785-1985*, London, Oxford University Press.

The correctness of the physicians' claim regarding the effectiveness of *taking the waters at Bath spa* has recently been scrutinized by comparison of the published with archival sources.

- Borsay, A. (2000). 'An example of political arithmetic: The evaluation of spa therapy at the Georgian Bath Infirmary, 1742-1830', *Medical History*, **45**; 149-72.

P. Wilson's chapter on surgical science is also contained in *Medicine in the Enlightenment* edited by R. Porter (see above).

W.F. Bynum has written on who treated whom with what for syphilis in the 18th century in his edited volume (with R. Porter) on *Medical fringe and medical orthodoxy* (see above).

Reflections

A majority of arithmetic observationist and experimentalist clinicians had been students in Scotland, particularly Edinburgh, for some time. C. Lawrence and L. Rosner describe the education they may have received there:

- Lawrence, C. (1988), 'The Edinburgh Medical School and the end of the 'old thing' 1790-1830', *History of Universities*, **7**; 259-86.
- Rosner, L. (1991), *Medical education in the age of improvement: Edinburgh students and apprentices, 1760-1826*, Edinburgh, Edinburgh Univ. Press.

while Th. Bonner looks also at the London situation:

- Bonner, Th.N. (1995), *Becoming a physician. Medical education in Britain, France, Germany and the United States*, 1750-1945, New York-Oxford, Oxford Univ. Press.

The processes of professionalisation and social upward moving of physicians and surgeons wherein quantification played a role is exemplified for Glasgow by:

- Geyer-Kordesch, J. (1999), *Physicians and Surgeons in Glasgow, The History of the Royal College of Physicians and Surgeons of Glasgow 1599-1858*, London, Hambledon Press (with Fiona Macdonald).

The British armed forces offered particular chances for dissenter and Scottish doctors on the meritocratic basis of empirical curative knowledge "good for everyone rather than tailored to unique individuals", as shown by:

- Cook, H. (1990), 'Practical medicine and the British armed forces after the "Glorious Revolution" ', *Medical History*, **34**; 1-26, p.26.

According to Th. Porter, marginal men have often used quantification as a new and own resource of power:

- Porter, Th.M. (1995), *Trust in numbers. The pursuit of objectivity in science and public life*, Princeton, N.J., Princeton Univ. Press.

Established doctors insisted instead on the vaguely defined notions of "medical art" or "medical judgement", specific qualities of the experienced physician only:

- Lawrence, C., (1985), 'Incommunicable knowledge: Science, technology and the clinical art in Britain 1850-1914', *Journal of Contemporary History*, **20**; 503-20.

Clinical trials were actually a form of human experimentation. L. McCullough shows that some related ethical problems were acknowledged in the context of the first elaboration of formal professional ethics:

- McCullough, L.B. (1997), *John Gregory and the invention of professional ethics and the profession of medicine*, Dordrecht, Kluwer Academic Publishers.

A brief history of human experimentation is:

- Bynum, W.F. (1988), 'Reflections on the history of human experimentation', in: Spicker S. et al. (eds.), *The Use of human beings in research*, Dordrecht, Kluwer, 29-46.

R. Faden et al deal with the (lack of) information of patients about planned trials:

- Faden, R., Beauchamp T.L., King, N.B. (1986), *A history and theory of informed consent*, New York, Oxford Univ. Press.

The discussions about Pierre-Charles-Alexandre Louis' *méthode numérique* in France and later in America are presented respectively by:

- Murphy, T.D. (1981), *Medical knowledge and statistical methods in early nineteenth century France, Medical History*, **25**; 301-319.
- Warner, J.H. (1986), *The therapeutic perspective: Medical practice, knowledge and identity in America, 1820-1885*, Cambridge, Mass., Harvard Univ. Press.

INDEX OF NAMES

ULRICH TRÖHLER was born in Bern, Switzerland, in 1943. He read medicine in Neuchâtel, Lausanne, Vienna, and Bern, qualifying as a physician in Bern in 1969. He received an MD at the University of Zurich in 1972 and embarked on a career in physiological research at the University of Bern, which he interrupted from 1976 to 1978 to complete a PhD in the history of medicine at the Wellcome Institute / University of London. From 1983 to 1984 he was Professor and Director of the Institute for the History of Medicine at the University of Göttingen, Germany. In this capacity he established the newly founded German *Akademie für Ethik in der Medizin* in his Institute. He is Professor and Chairman of the Department of the History of Medicine at the University of Freiburg, Germany, where he also co-ordinates a Centre of Medical Ethics and Law at the University Clinics. He also teaches at the University of Basle, Switzerland.

Professor Tröhler's major historical publications concern the origins and development of present-day issues, such as quantification of clinical experience, research in surgery and obstetrics, and (anti-)vivisection. Among these, he considers his monograph on *Richard Wagner, The Anti -Vivisectionist* as the most original. He has also written on 18th century medical students and is currently working on the origins and impact of ethics codes in 20th century medicine.

He is a member of the German Academy of Natural Scientists (Leopolina) and was the founding President (1991-1995) of the European Association of the History of Medicine and health. In 1997 he presided over the First World Conference on Ethics Codes in Medicine and Biotechnology. In 1998 he had the honour of giving the John Locke Lecture in London.