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Special Article

Evidence-Based Medicine : Past, Present and Future

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The term evidence-based medicine (EBM) has attracted wide interest over the last ten years or so. The interest in the topic has led to important reflections on the way we teach and practise medicine. However, the use of evidence is not a new development for doctors. Since earliest times doctors have observed the natural history of disease in their patients and applied this knowledge to subsequent patients. The observation was subject to anecdote and to bias. The application of an increased scientific discipline to this area resulted in the production of better evidence around natural history, diagnosis or treatment. This was more likely to be reliable when applied to future patients provided they matched the population in the study that gave rise to the evidence.

BERIBERI AND KANEHIRO TAKAKI

The prospective, randomised, double-blind, placebo controlled trial has become the gold standard of evidence based medicine. Two of the early studies moving towards this standard have striking connections, both being concerned with vitamins and involving naval medicine. The first is James Lind's demonstration that scurvy could be prevented by the consumption of fresh fruit. British sailors in the 18th century frequently suffered from scurvy during long voyages. Lind's study in 1747 was small, involving just 12 sailors and six treatments, not results to which conventional statistical tests could be applied. In his study 2 sailors given apple cider improved after 20 days, while 2 given 2 oranges and a lemon daily improved after 6 days. Lind's results were not immediately accepted by the establishment. However, subsequently this led to the addition of fresh fruit, particularly limes, to the diet on board ship with the prevention of scurvy. Through this British sailors acquired the name "limeys".

Over one hundred years earlier beriberi had been described by two Dutch physicians, Bontius and Nicolaas Tulp. Tulp is perhaps more famous for his appearance in the Rembrandt painting of the Anatomy Lesson of Dr. Tulp. The cause of beriberi was still unknown in the late 19th century and was causing a very high mortality on long voyages of the Japanese navy. This was around the time of Pasteur and Koch and an infectious agent was a popular suggestion for the cause of beriberi, with many publications on the beriberi bacterium.

The real cause was established by a famous experiment and great insight from Kanehiro Takaki. In 1873 William Anderson had come from St. Thomas's Hospital in London to the Naval Medical School in Japan. Two years later Takaki went to St. Thomas's Hospital in London on a journey that, at the time, took 4 months. He studied there for 5 years and was a prize winning student. He returned to Japan and was appointed chief of the Naval Hospital. In 1882 the vessel Ryujo with 376 sailors went on a 272-day voyage to New Zealand and South America and Hawaii. On reaching Honolulu 169 sailors had become ill with beriberi and there were 25 deaths. Takaki was in charge of the investigation. He arranged that a similar ship, the Tsukuba, the next year, sail the same route but with a diet rich in carbohydrates. Out of 287 sailors there were just 14 cases of beriberi and no deaths. A crucial study, albeit with historical controls. Another important element

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of clinical trials emerged from the experiment as all the 14 sailors who developed beriberi on the Tsukuba were found to have been non-compliant with the diet, preferring polished rice as before.

Although cases of beriberi in the Navy fell dramatically with the introduction of Takaki's dietary regime his findings were not widely accepted despite the evidence. Mori Ogai who had a similar post in the Army had experience in mainland Europe closer to the germ theories of Pasteur and Koch. He did not introduce Takaki's diet to the Army until the effectiveness of the Japanese Army was being seriously compromised by beriberi in wars against China in 1894-5 and then Russia in 1904-5. Subsequent changes in diet based on Takaki's evidence produced the same great benefits that came to the Navy in the 1880's.

Takaki had therefore produced one of the first great pieces of scientific evidence in a crucial area, demonstrated also the importance of compliance in such trials and had his findings disputed on the basis of opinion without evidence. Of course, he went on to form a medical research body, the Sei-I-Kai Medical Education Institute and the Tokyo Hospital, both forerunners of the Jikei University School of Medicine.

EBM in Clinical Practice

The present position is that the term EBM or evidence-based healthcare (EBH) has entered widespread use. It has acquired its devotees but also, as with most movements, its detractors. One of the major enthusiasts has been David Sackett in Oxford, UK[1]. He produced a definition of EBM in common use: "Conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients." There are some important terms in this statement. The process should be explicit, that is, clear, for others to see. It should be judicious, applied with good clinical sense. It should be current, based on the best, up to date information. There is no reason why it should not extend beyond the care of individual patients to be applied to the organisation of health care, to management and to education. Another definition that has been widely used is: "integrating clinical expertise with best available external clinical evidence from systematic research." Again this description places clinical expertise and judgement at the forefront, backed up by the best information available. This is an approach to medical care that is difficult to dispute. This importamt aspect of clinical expertise has been lost in some subsequent publications on EBM.

A number of factors led to the rise of EBM at that time. They include the increase in available information making it impossible for individuals to ensure a full knowledge of the literature, the acceptance of the placebo-controlled, double-blind, randomised controlled trial as the gold standard, the availability of techniques to organise and access the information, the need from organisers of healthcare and from patients to ensure best practice and value for money. It is essential that the information component of EBM does not lead to a loss of the centrality of the patient as the most important element of the process, remembering William Osler's statement that "it is more important to know what sort of a person this disease has than to know what sort of disease this person has."

Conventionally, there are five steps to EBM:

1. Obtain information and formulate an answerable question
2. Search for the relevant information
3. Assess the information obtained for validity and relevance
4. Apply the results to clinical practice
5. Evaluate your performance.

The first of these is itself composed of a number of important steps. It can include the whole of the clinical history and examination together with information from other sources and the results of investigations and responses to treatment. The next process of formulating the question might occur at the end of this process e.g. when the diagnosis A has been made and the question is whether treatment B will work for this patient at this time; or it might be at an earlier stage: how reliable is the physical sign C elicited in predicting a certain underlying diagnosis D. The other vital part of the first step is formulation of the question. To some extent this is the essence of

EBM, deciding on the appropriate question for the clinical situation. In the education of medical students about EBM, this is often the most difficult part and they may need considerable help to make sure that their questions match the clinical situation and are answerable, appropriate questions.

Studies of questions that arise in doctor-patient consultations show that they can be divided in to generic types'. The three most common types identified by doctors in real clinical situations were very practical questions :

What is the drug of choice for this condition ?

What is the cause of this symptom ?

What test is indicated in this situation ?

The second step is the search for the relevant information. Technology has eased the access to the primary information through the organisation of databases as Medline. However, studies indicate that doctors in busy clinical practice spend little time exploring original scientific articles. They are far more likely to seek their information from colleagues, simpler, processed sources or even pharmaceutical representatives. The danger is that these may not be based on objective, reliable evidence. The situation has been helped by the organisation of the original material in to reliable meta-analyses and systematic reviews which impose a quality control on the material included. Unsubstantiated expert opinion is no longer considered sufficient. The Cochrane Collaboration provides an excellent example of systematic reviews with a set process involving a steering group, an explicit search process, a defined quality assessment and widespread dissemination.

The third step is to asess the information obtained. Students need to acquire the skills of critical appraisal of the literature. A classification of categories of evidence sources has been produced, related to the strength of the evidence :

I well-designed, randomised, controlled trials, meta-analysis or systematic review

II well-designed case-control or cohort studies or inferior trials

III peer opinion, consensus or uncontrolled

Where guidelines and protocols are developed there is an increasing tendency to back up statements with the evidence base and to rank the quality of this evidence in a series of grades :

A directly based on category I evidence

B directly based on category II evidence or extrapolated from category I

C directly based on category II evidence or extrapolated from category I or II

In this way evidence is found and incorporated so that the extent of the evidence base of clinical guidelines can be indicated clearly. Many guidelines are unable to provide category I evidence for most of their management and the process generates useflil, practical research questions. Peer or consensus opinion may still be very valuable in guidelines. Where evidence is lacking the views and experience of experts may be very helpful as long as the provenance of the information and recommendations is stated clearly.

Common reactions to EBM are to protest that evidence has always been the basis for medical practice. This is an unlikely defence judged by analysis of clinical practice. One study estimated that relevant questions arose with 2 out of every 3 patients with an average of 8 clinical decisions each day. Estimates suggest that a general physician would need to read, and remember, 19 original articles each day to keep up. In practice, when asked about their reading habits, consultants in the UK say they read 30-60 min each week, medical students 60-120 mm and house officers (interns) 20 min. There is an incompatibility and a need to use other methods of processing the information, easing the burden and providing the evidence at an appropriate site and time. However, also this study indicates that medical students can be reached more through written sources than any other group.

Attempts have been made to assess how much of every day practice has a strong evidence base[3]. Early estimation suggested that this was only 15 -20%[4]. However, later studies suggest levels of 60 -80%[5]. Higher percentages emerge when assessments are limited to the main intervention in real contacts rather than exploring other possibilities. In each consultation there are, in reality, a wide level of possible questions at each stage of the history, examination, investigation and management.

The concentration on the scientific evidence and the mechanics of the process must not be allowed to obscure the involvement of the individual patient. Ultimately the aim is to apply diagnostic tests, treatments to the benefit of individual patients. Attempts have been made to include the patient view systematically through weighted preferences in decision trees but they have proved difficult. The elements of patient choice and clinical judgement are essential in the introduction of medical students to EBM.

Medical Students and EBM6

Medical students need to be given the freedom, skills and wisdom to practise EBM. Each of these has implications for the medical programme and for teachers. Students need **freedom** to allow them to challenge and explore. They need to be allowed to test accepted wisdom ; the word of the professor is no longer enough. Teachers will to back up their information with evidence that students can assess and be prepared to justify their views and even their methods of teaching if EBM is to extend in to evidence based education. If students are to be free to explore their learning in this way they will need time to do it and the overload offactual information in many cases will need to be reduced.

The consequences of this freedom may be teachers who feel challenged or upset and a reduction in factual information offset by deeper learning skills.

The **skills** that need to be acquired are those to ask the questions, to find the answers and to assess the quality of the answers. The skills to ask the questions can be helped by encouraging problem solving in the course and finding ways to explore clinical reasoning. The answers come with IT skills, availability of the material and the technology and time to pursue these. The consequences may be the introduction of problem based learning in to the course with its training requirements for tutors, the costs of giving sufficient IT access and regular, small group meetings with tutors to explore the process. Students also need to acquire the skills to assess critically the quality of the information in clinical trials and other publications. This will need to be taught and practised.

The **wisdom** has to be acquired by observation of the process amongst teachers and by clinical involvement with real responsibility. The price of this is that students need to become involved with the clinical team with consequences for the students, the patients and for their supervising medical staff. Role models amongst teachers are likely to have an important influence on this development and need to be encouraged.

At the Guy's, King's and St Thomas' School of Medicine we have begun to address some of these factors but we have some way to go. The concepts of information skills, problem setting, asking the right questions, critically evaluating the material are all introduced early on in the course in the "Professional Skills" and "Practice of Medicine" courses which begin in Year I. Problem solving exercises are being introdused at various stages with the biggest component in Year 3 the first mainly clinical year. Integral to the process has been a Special Study Module in public health medicine undertaken as a group project in Year 3 or 4. Here the group decide on a question they need to explore and set about finding the information, from the literature and by their own original work. In the new final year (Year 5) we have introduced an increased responsibility for students who take on the care of a small group of patients each under close supervision and working with the pre -registration house officers (interns). They learn the practical skills of a junior doctor and the small work load gives them the opportunity to start a lifelong trend of taking time to use the appropriate information sources and pursue the right questions. Since so much of students' motivation and direction comes from assessment they are required to produce a series of extended case studies during the course which explore the evidence base of the management of their patients.

What would Dr Takaki have thought of the present situation with EBM ? I like to think he would have taken it up enthusiastically. The desire to find the right scientific answers, to use this information to prevent illness and, with clinical judgement, to treat individual patients were illustrated in his work. The

dissemination of information and the training of new doctors were also important features for him. It is anhonour to visit and speak at the institution founded by Dr Takaki, who can be seen as one of the pioneers of evidence based medicine.

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