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Evidence-based medicine: the clinician's perspective

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Clinical medicine: from art to science

During the past 50 years or so, the scientific approach to medical problems has transformed several dreams of early century doctors into reality: the antibiotic revolution and the polio vaccines represent the first fundamental results of science applied to medicine. Modern medicine has conjugated clinical observation and pathophysiological research, and few would dispute the value of such an inspired approach. Molecular genetics has now deciphered the genetic code, and it is expected that, within the next decade, the application of techniques of molecular biology to clinical medicine will eventually bring into the realm of treatable conditions several diseases which are now considered untreatable. Nonetheless, there is a mounting feeling of unease about the relationship between science and medicine, both within the medical community and in the general population, because many perceive a sort of 'voltage drop' between science and patient care [1]. The fact that many clinicians still continue to consider their profession an art rather than a science and encourage scepticism on the 'new medicine based on numbers' certainly widens this 'voltage drop', but other factors are important as well. This unease is also a result of the expectations produced by the achievements of modern medicine. In other words, these achievements have generated a kind of scientific faith, holding that the understanding of a pathophysiological process and the prescription of a treatment that has been shown to interrupt or modify the process is a guarantee of therapeutic success. The relatively recent case of the cardiac arrhythmia trial is a disconcerting example of the fallacy of such a tenet [2]. This and other examples are often quoted as clear signs that clinical medicine has lagged behind epidemiology and basic sciences in regenerating its foundations. The lesson to be learned is that there are no experimental shortcuts in animal or *in vitro* models to extrapolate the eventual benefit of a given treatment in human beings, the required approach to which is the randomized clinical trial.

The adoption of clinical epidemiology as a basic science for clinical medicine [3] is the response to this unease. Doctors are increasingly aware that every decision in diagnosis, prognosis and therapy involves an assessment of probabilities and is thus a type of statistical exercise. Powerful methods have been developed to determine the validity of clinical history and physical examination and the usefulness of diagnostic tests, while the value of randomized clinical trials to establish the validity of a given treatment is now universally considered an inescapable standard.

Evidence-based medicine

Clinical epidemiology is thus the new intellectual territory where doctors find firm ground for practising a novel type of medicine integrating traditional clinical expertise with the best external evidence, i.e. with clinically relevant research (i.e. patient–centred) concerning the reliability of diagnostic tests, the value of prognostic markers and the efficacy of treatments [4]. The recipe for this new medicine requires both elements, clinical expertise and the information derived from solid clinical studies, to generate good clinical practice (Figure 1). There is no substitute for the clinician's judgement in making sound diagnoses and in properly identifying the physical and social difficulties of individual patients. By the same token, consulting accurate, updated and valid sources of

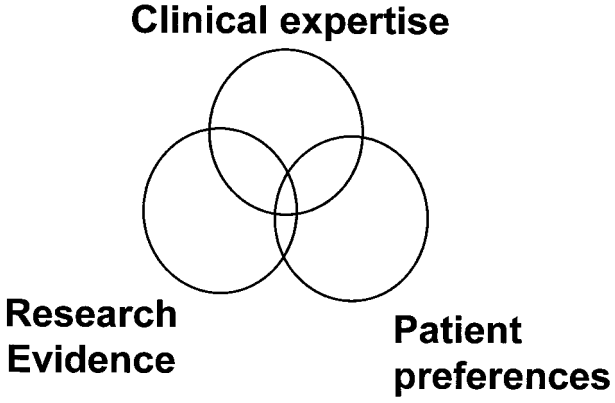

Fig. 1. Evidence-based medicine.

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knowledge, be they diagnostic, prognostic or therapeutic, for approaching a given clinical problem is a prerequisite for guaranteeing safe and efficient care for our patients. However intellectually appealing, this new approach to clinical problem solving is far from being accepted conceptually and practised effectively on a large scale. Evidence-based medicine still encounters much philosophical [5] and social resistance [6]. Here, I will try broadly to expose the main characteristics of this approach, alluding wherever possible to the particular field of nephrology. Some of the difficulties and weaknesses of this approach will also be discussed.

How we become outdated

The past generation of clinicians practised medicine mainly on the basis of their own experience and on that of a few authoritative colleagues. Asking a professionally respected colleague for advice was the most efficient way for a doctor facing an unusual or complicated problem to ensure the best care for his patient. These counsels were incorporated into the personal experience of the doctors, thus establishing a sort of continuous medical education 'by osmosis'. The new science of clinical medicine now demands that every clinical decision be based on evidence. Everyday experience shows that often we fail to obtain such evidence. When such failure endures for a long time, it results in deteriorating clinical performance. Such a situation, which has been defined as 'clinical entropy', is bound to produce inaccurate or even wrong diagnoses and inappropriate treatments. The risk is real because it has been found that doctors devote little time specifically to address problems presented by their patients, the more so as they get older [7].

The new approach

The main constraints to clinical practice: time and knowledge. The importance of obtaining pertinent information during clinical activity has been investigated specifically [8], thus exposing several problems that doctors face for accessing appropriate, timely knowledge. Basically, evidence-based medicine is a different approach to clinical learning. The knowledge required is that needed to answer specific questions encountered in the real world of clinical practice: how reliable a test is in confirming/excluding a diagnosis, how confidently a prognosis can be made and how the best therapy can be chosen. Thus evidence-based medicine aims at formulating answerable clinical questions and at answering these questions on the basis of studies which are pertinent to a particular, well-defined problem. This approach to clinical problem solving is fascinating, and it now has an increasing number of proselytes. However, once entered in the field, one immediately perceives the tyranny of time. Shaughnessy has condensed the usefulness of medical information in a formula: relevance $\times$ validity/work to access [9]. The relevance of given information is based on the frequency of the problem being addressed and on the strength of the evidence retrieved. Validity is the likelihood of the information being true and the work to access is the time spent in obtaining that information. Saving time is probably an important reason why doctors often ask colleagues for advice in the first place (a chat with an experienced doctor gives quick and clear answers and it is often reassuring). Consultation is a cornerstone of medical work but, for it to be an enriching experience, it should not be the main approach to problem solving because it would preclude independent intellectual growth and constructive criticism. On the other hand, the inadequacy of traditional sources of medical knowledge, textbooks and journals, cannot be overemphasized. Textbooks are often outdated, while medical journals are unfocused and rarely give immediate help to the doctor in everyday clinical activity. In such a situation, practising evidence-based medicine may appear a tantalizing and pretentious effort, but the scene is changing rapidly: a new type of scientific publication, computers, compact disks and the Internet now make possible gathering relevant and valid information in a reasonable amount of time, thereby generating a more optimistic attitude towards evidence-based medicine.

The remedies: formulating answerable questions and finding the best evidence. The solution requires a full restructuring of the way doctors keep themselves updated: from the traditional continuous medical education to evidence-based medicine. The first step is learning how to formulate answerable clinical questions. This may not be an easy task because clinical practice is a wide and an inherently uncertain territory. Each patient poses particular problems which reflect his personality, his goals and expectations and, ideally, should receive personalized medical responses. The lack of time for direct exchange of information between doctors and patients certainly does not help the definition of problems. We naturally tend to adhere blindly to the traditional rituals of clinical practice, ordering investigations and failing to check the effects of previous actions. What distinguishes good doctors is their ability to formulate the most appropriate questions and clearly and quickly to separate problems which may easily be solved routinely from the main, critical problems that characterize the clinical picture of a given patient. Often the key questions are obvious and easily answerable (what is the standard dose of this drug?) but, in some cases, they may be difficult to identify, especially for those who are not trained to apply 360° probabilistic reasoning or when the required information is in the form of external evidence, i.e. information that should be searched for specifically, from the various sources of medical knowledge. Nonetheless, specific skills can be developed with diligent application of some rules [7]. The group of clinical epidemiologists who established the theory and the practice of evidence-based medicine at the McMaster University in Canada and at Oxford University in the UK have created an Internet site devoted to teaching

Table 1. New and old sources of medical knowledge

	Validity	Work to access	Usefulness
Standard textbooks (updated every 3–4 years)	Low	Low	Moderate
Standard journal review	Moderate	Low	Moderate
Evidence-based textbooks (*Scientific American Medicine*, W. N. Kelley's *Internal Medicine*)	*High*	*Low*	*High*
Uptodate (CD)	High	Low	High
Secondary publications (*ACP Journal*, *Evidence-Based Medicine*)	High	Low	High to Moderate
Internet (online searching)	High	High	Moderate
Medline	Low–high	Low	High

this new discipline [10]. This site is an invaluable source of information for those who are eager to learn evidence-based medicine because it gives full details about courses and teaching sessions of evidence-based medicine world-wide and is linked with other important sources of information, such as the Cochrane Collaboration.

Once the key questions are formulated information should be retrieved. The wide array of new and old sources of medical knowledge is shown in Table 1. Each source is rated for its relevance, validity, work to access and usefulness. The ideal information source should be directly relevant to the clinical problem being addressed, should give valid information and allow a quick access. Presently, the evidence-based electronic book *Uptodate* is the most useful source for nephrologists. The *ACP Journal Club* and *Evidence-based Medicine* are secondary publications of structured abstracts and commentaries which solve many of the problems created by the volume of medical literature. These journals select and synthetically present relevant information from clinical studies which can be applied directly to patient care. The interest in this type of secondary publications is on the increase and, in the near future, the collections of these structured abstracts and systematic reviews, such as the Cochrane Library, will probably be the most used databases. The number of systematic reviews in nephrology is limited, but it is relatively high in comparison with that of other medical specialities. There is fresh interest in this issue [11] and, in the next few years, we will certainly have a flurry of critically appraised and well organized information about renal diseases.

Weaknesses of evidence-based medicine

It should be clearly recognized that evidence-based medicine gives very little help in the many grey zones of clinical practice where the evidence about risk–benefit ratios of competing options is incomplete or contradictory. Only $\sim$20% of clinical policies are supported by rock solid scientific evidence (i.e. randomized studies) [12]. The Canadian Task Force on the Periodic Health Examination has identified as many as 76 preventive manoeuvres characterized by inconclusive evidence where 'decision making must be guided by factors other than medical scientific evidence' [13]. A minimalist view is that 'clinical medicine seems to consist of a few things we know, a few things we think we know (but probably don't), and lots of things we don't know at all' [14]. Evidence-based medicine can gain the widespread diffusion dreamed of by its supporters only if it is used properly. Proper use means that it should be used to identify the best evidence in a given clinical problem in ways which fairly acknowledge the areas of ignorance (i.e. the lack of valid clinical research) within that problem. Clinicians cannot in any way substitute uncertainty and ignorance by fictitious algorithms or highly speculative risk calculations. Rationalism should not be confused with reason. Factual knowledge is the basis of clinical reasoning and there is no easy surrogate for this hard matter. Systematic reviews or meta-analyses, probably the most powerful instrument of evidence-based medicine, are very much criticized on the grounds that different meta-analyses on the same topic may produce conflicting results. Methodological errors occur in meta-analyses just as they may occur in traditional reviews. In no way can such an instrument be considered a perfect solution for collating diverse sources of information. Nonetheless, there is no question that meta-analyses represent a breakthrough with respect to traditional reviews and that they give much strength to the process of clinical decision-making [15].

Evidence-based medicine in the real world

Evidence-based medicine encompasses all aspects of the clinical decision-making process, from diagnosis to treatment. Here I present a practical application of evidence-based information in the diagnostic process.

A 53-year-old lady is admitted to the ward with a pulmonary–renal syndrome. She had a recent episode of haemoptysis and has a serum creatinine of 2.8 mg/dl. The chest roentgenogram reveals a poorly defined pulmonary infiltrate and a mild pleuritic fluid collection in the right lung. Wegener granulomatosis is a possible diagnosis and we know that cANCA testing may be helpful.

To know more about cANCA and Wegener granulomatosis, we consult the two nephrology manuals we have in the library: *Brenner*'s (1996 edition) and *Oxford Textbook of Nephrology* (unfortunately the 1992 edi-

Table 2. Practical application of evidence-based medicine in the diagnostic process (see text)

	Definitions and formulae	Data	Results
Sensitivity	% of patients with a given disease and with a positive test	66%	
Specificity	% of patients without the disease and with a negative test	98%	
Pre-test probability	Disease prevalence in a given setting	5%	
Pre-test odds	% of patients with the disease/ % of patients without the disease	5/95	0.053
Likelihood ratio	Sensitivity/(100 specificity)	66/(100–98)	33
Post-test odds	Likelihood ratio × pre-test odds	33 × 0.053	1.749
Positive predictive values	Post-test odds/(post-test odds + 1)	1.749/(1.749 + 1)	0.64 (64%)
False-positive rate	1 − positive predictive value	1–0.64	0.36 (36%)

tion, but that is what we have!). Both books give very superficial information about the reliability of the test. *Brenner*'s reports that '… Reliable serologic markers for Wegener granulomatosis have been elusive … until the identification of ANCA which is a sensitive …' and the *Oxford* says that '… a close association between ANCA and Wegener granulomatosis has been found … which appears sensitive …'. This vague information does not allow a probabilistic estimation of the usefulness of the test in the diagnostic process in our particular clinical setting. We then consult the Cochrane Library and, in <1 min, are able to retrieve the abstract review of a meta-analysis of studies about ANCA and Wegener granulomatosis. In this review, it is estimated that the pooled sensitivity of the test (from 15 studies) is 66% and the specificity is 98%. We know that in our clinical setting, the pre-test probability of Wegener granulomatosis in patients referred for pulmonary–renal syndrome is $\sim 5\%$. On the basis of these data, we can easily calculate the likelihood ratio for a positive cANCA test, the pre-test odds and, by multiplying the two, the post-test likelihood ratio (Table 2). We finally obtain the positive predictive value and the false-positive rate. We become aware that the final result of a putatively positive test in our patient (positive predictive value 64%, false-positive rate 36%) would be of relatively little help for concluding that the patient has the disease. We therefore decide to pursue a renal biopsy. Once having made the clinical decision (biopsy), out of sheer curiosity we resume calculations and discover that for the test to have a satisfactory positive prediction power ($>80\%$), the pre-test probability of Wegener granulomatosis has to be 12%. This example gives an idea of how useful it may be tracking specific information and integrating it with clinical expertise (the pre-test odds express the clinical expertise of the hospital units dealing with this problem). The key question about evidence-based medicine is not whether this approach is useful or whether it should have a role in clinical decision-making but to establish this role effectively and efficiently [16].

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