Principles of evidence based medicine

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Health care professionals are increasingly required to base clinical decisions on the best available evidence. Evidence based medicine (EBM) is a systematic approach to clinical problem solving which allows the integration of the best available research evidence with clinical expertise and patient values. This paper explains the concept of EBM and introduces the five step EBM model: formulation of answerable clinical questions; searching for evidence; critical appraisal; applicability of evidence; evaluation of performance. Subsequent articles will focus on the principles and critical appraisal of randomised controlled trials, systematic reviews, and meta-analyses, and provide a practical demonstration of the five step EBM model using a real life clinical scenario.

WHAT IS EVIDENCE BASED MEDICINE?

The concept of evidence based medicine (EBM), defined as the "integration of best research evidence with clinical expertise and patient values",[1] has been gaining popularity in the past decade. The practice of EBM involves a process of lifelong self directed learning in which caring for patients creates the need for important information about clinical and other health care issues. EBM recognises that the research literature is constantly changing.[2] What the evidence points to as the best method of practice today may change next month or next year. The task of staying current, although never easy, is made much simpler by incorporating the tools of EBM such as the ability to track down and critically appraise evidence, and incorporate it into everyday clinical practice.

The work of people in the field of paediatrics and child health centres on the problems of children and their families and carers. Questions about diagnosis, prognosis, and treatment often arise and sometimes the answers to these questions need to be sought. EBM allows the integration of good quality published evidence with clinical expertise and the opinions and values of the patients and their families or carers. Deciding on how to treat patients should not be based solely on the available evidence. Other factors such as personal experience, judgement, skills, and more importantly patient values and preferences must be considered.

The practice of EBM should therefore aim to deliver optimal patient care through the integration of current best evidence and patient preferences, and should also incorporate expertise in performing clinical history and physical examination. Figure 1 illustrates a typical flow chart of EBM, depicting how knowledge and experience may be integrated with patients' preferences and available evidence in the making of clinical decisions.

WHY EVIDENCE BASED MEDICINE?

The most important reason for practising EBM is to improve quality of care through the identification and promotion of practices that work, and the elimination of those that are ineffective or harmful.[4] EBM promotes critical thinking. It demands that the effectiveness of clinical interventions, the accuracy and precision of diagnostic tests, and the power of prognostic markers should be scrutinised and their usefulness proven. It requires clinicians to be open minded and look for and try new methods that are scientifically proven to be effective and to discard methods shown to be ineffective or harmful.

It is important that health care professionals develop key EBM skills including the ability to find, critically appraise, and incorporate sound scientific evidence into their own practice.

THE FIVE STEP EBM MODEL

The practice of EBM involves five essential steps[3 5]: first, converting information needs into answerable questions; second, finding the best evidence with which to answer the questions; third, critically appraising the evidence for its validity and usefulness; fourth, applying the results of the appraisal into clinical practice; and fifth, evaluating performance.

Step 1: Formulating answerable clinical questions

One of the difficult steps in practising EBM may be the translation of a clinical problem into an answerable question.[6] When we come across a patient with a particular problem, various questions may arise for which we would like answers. These questions are frequently unstructured and complex, and may not be clear in our minds. The practice of EBM should begin with a well formulated clinical question. This means that we should develop the skill to convert our information needs into answerable questions. Good clinical questions should be clear, directly focused on the problem at hand, and answerable by searching the medical literature.[7]

A useful framework for making clinical questions more focused and relevant has been suggested by Sackett *et al*.[1] They proposed that

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Abbreviations: EBM, evidence based medicine; CASP, critical appraisal skills programme

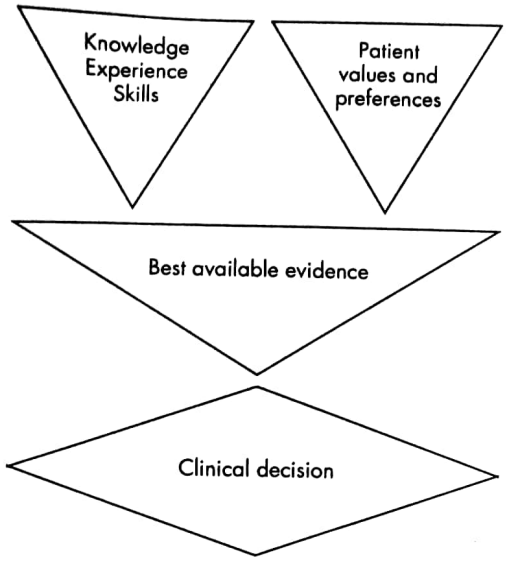

Figure 1 Flow chart of evidence based medicine.[3]

a good clinical question should have four (or sometimes three) essential components:

- the patient or problem in question;
- the intervention, test, or exposure of interest;
- comparison interventions (if relevant);
- the outcome, or outcomes, of interest.

Thus an answerable clinical question should be structured in the **PICO** (**P**atient or **P**roblem, **I**ntervention, **C**omparison, **O**utcome/s) or **PIO** (**P**atient or **P**roblem, **I**ntervention, **O**utcome/s) format.

To illustrate the concept of PICO/PIO, imagine that you have a four month old baby admitted to your ward with viral bronchiolitis. The child's symptoms get progressively worse and you wonder whether giving corticosteroids might help the child improve and reduce the length of stay in hospital. You decide to use "clinical score" as a measure of improvement. The key components of your clinical question would be:

Patient or problem: 4 month old baby with viral bronchiolitis.
Intervention: corticosteroids.
Comparison: no corticosteroids.
Outcomes: clinical score, length of hospital stay.

A four part clinical question may be formulated as follows: *In a 4 month old baby with viral bronchiolitis, does the administration of corticosteroids compared with not giving corticosteroids improve clinical score and reduce length of hospital stay?*

Step 2: Finding the evidence

Once you have formulated your clinical question, the next step is to seek relevant evidence that will help you answer the question. There are several sources of information that may be of help. Traditional sources of information such as textbooks and journals are often too disorganised or out of date.[8] You may resort to asking colleagues or "experts" but the quality of information obtained from this source is variable. Secondary sources of reliable summarised evidence which may help provide quick evidence based answers to specific clinical questions include *Archimedes* (http://adc.bmjjournals.com/cgi/collection/archimedes), *Clinical Evidence* (http://www.clinicalevidence.com/ceweb/conditions/index.jsp), and *BestBets* (http://www.bestbets.org/index.html).

Other important sources of evidence include the online electronic bibliographic databases, which allow thousands of articles to be searched in a relatively short period of time in an increasing number of journals. The ability to search these databases effectively is an important aspect of EBM. Effective searches aim to maximise the potential of retrieving relevant articles within the shortest possible time. Studies have shown that, even in countries where hospitals have facilities for internet access allowing health care personnel access to a number of electronic databases, many people are not familiar with the process of carrying out efficient searches and often conduct searches which result in too few or too many articles.[9,10] It is therefore important for health care professionals to undergo basic training in search skills, either through their local library services or through the attendance at formal courses.

BASIC SEARCH PRINCIPLES

Convert the clinical problem into an answerable question

The key to successful searching is to convert your clinical problem into a clear answerable question, which should ideally be framed in the PICO/PIO format as discussed above.

Generate appropriate keywords

A word list can be generated, based on keywords from the clinical question. For example, from the clinical question above, the following keywords could be used for the search: viral bronchiolitis (*patient or problem*); corticosteroids and synonyms: glucocorticoids, steroids, prednisolone, dexamethasone (*intervention*); clinical score, hospital stay (*outcomes*)

Choose a bibliographic database

Numerous online databases are available. These include the Cochrane Library databases, MEDLINE, EMBASE, and CINAHL. In day to day clinical practice, I will suggest that becoming familiar with one or two databases will suffice in most cases. I recommend the Cochrane Library databases and MEDLINE. The Cochrane Library databases—which include the Cochrane database of systematic reviews, the Database of abstracts of reviews of effectiveness, and the Cochrane controlled trials register—is maintained by the Cochrane collaboration, an international initiative which began in the early 1990s and was designed to prepare, maintain, and disseminate systematic reviews of health care interventions.[3] The Cochrane Library is updated quarterly and is available through the internet or CD-rom. There is usually a charge for

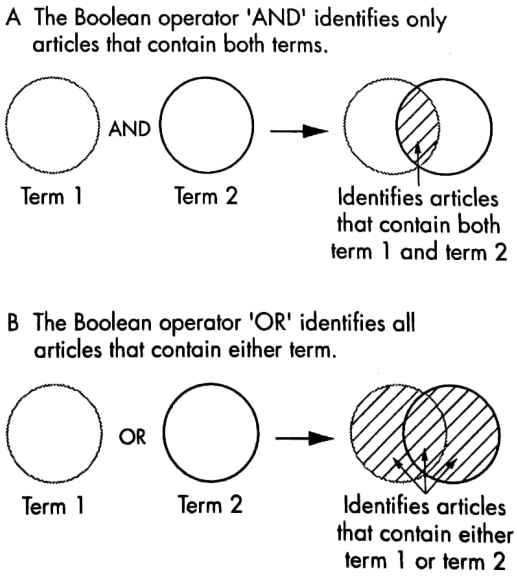

Figure 2 Venn diagram illustrating the use of Boolean operators AND and OR.

using the library, although NHS staff in the United Kingdom have free access to the service through the National Electronic Library for Health.

MEDLINE is probably the most widely used database for searching the biomedical literature.[3] It is maintained by the National Library of Medicine, USA. A version of MEDLINE (PUBMED) is freely available on the internet, is updated regularly, and is relatively user friendly.

When looking for articles on effectiveness of interventions or treatments, the first point of call should probably be the Cochrane database of systematic reviews or the other secondary sources mentioned above such as Archimedes, Clinical Evidence, and BestBets. The Cochrane controlled trials register provides an index of published randomised controlled trials. Randomised controlled trials and systematic reviews may also be searched for using MEDLINE. SUMsearch (http://sumsearch.uthscsa.edu) is a useful search engine that allows direct searches of external databases with a focus on clinical topics.

Conduct the search

Once the key words and databases have been identified, the next thing is to run the search. At the basic level, an efficient method is to combine individual words or terms using the Boolean operators "AND" and "OR".[11] If you are combining two terms, AND allows only articles containing both terms to be retrieved, while OR allows articles containing either term to be retrieved. A simple Venn diagram consisting of two overlapping circles may be used to illustrate this principle. In fig 2A, the two terms have been combined using AND, and in fig 2B, they are combined using OR.

When too many articles come up after the initial search (which is often the case), PUBMED has a feature that allows you to limit the results of your search. You can limit your search by publication type (for example, randomised controlled trials or review articles); by date of publication; by language, by study population, and so on. PubMed also has a feature called "Clinical queries" which provides an easy to use approach to evidence based searching within the Medline database. "Clinical queries" is a preprogrammed research methodology filter that helps busy practitioners access the best available evidence by providing a quick access to reliable clinical studies related to therapy, diagnosis, aetiology, or prognosis.

Example of a basic search strategy

To try to find evidence to answer the clinical question I formulated earlier, we can use the keywords generated to search the Cochrane database of systematic reviews and PUBMED, using the following search strategy:

- (1): Viral bronchiolitis
- (2): Corticosteroids OR steroids OR glucocorticoids OR prednisolone OR dexamethasone
- (3): Clinical score OR hospital stay
- (4): (1) AND (2) AND (3).

When this search strategy was used to search the Cochrane database of systematic reviews on 10 December 2004, four articles were retrieved, but only one of these was relevant.[12]

Other strategies that may be used to improve the sensitivity and specificity of literature searches have been described by Sackett *et al*.[1]

Step 3: Appraising the evidence

After you have obtained relevant articles on a subject, the next step is to appraise the evidence for its validity and clinical usefulness. Although there is a wealth of research articles available, the quality of these is variable. Putting unreliable evidence into practice could lead to harm being caused or limited resources being wasted.

Research evidence may be appraised with regard to three main areas: validity, importance, and applicability to the patient or patients of interest. Critical appraisal provides a structured but simple method for assessing research evidence in all three areas.[13] Developing critical appraisal skills involves learning how to ask a few key questions about the validity of the evidence and its relevance to a particular patient or group of patients. Such skills may be learnt within small tutorials, workshops, interactive lectures, and at the bedside.[13]

Several tools for appraising research articles are available. I like the tools developed by the Critical Appraisal Skills Programme (CASP), Oxford, UK. These include tools for appraising randomised controlled trials, systematic reviews, case–control studies, and cohort studies. The CASP tools are simple, easy to use, and freely available on the internet.[14]

A detailed discussion of the critical appraisal of randomised controlled trials and systematic reviews will be provided in the next two articles of the series.

Step 4: Applying the evidence

When we decide after critical appraisal that a piece of evidence is valid and important, we then have to decide whether that evidence can be applied to our individual patient or population. In deciding this we have to take into account the patient's own personal values and circumstances. The evidence regarding both efficacy and risks should be fully discussed with the patient or parents, or both, in order to allow them to make an informed decision. This approach allows a "therapeutic alliance" to be formed with the patient and the parents and is consistent with the fundamental principle of EBM: the integration of good evidence with clinical expertise and patient values.[15] The decision to apply evidence should also take account of costs and the availability of that particular treatment in your hospital or practice. A practical illustration of issues to consider before applying research evidence will be provided in the fourth article of the series.

Step 5. Evaluating performance

As we incorporate EBM into routine clinical practice, we need to evaluate our approach at frequent intervals and to decide whether we need to improve on any of the four steps discussed above. As Strauss and Sackett have suggested, we need to ask whether we are formulating answerable questions, finding good evidence quickly, effectively appraising the evidence, and integrating clinical expertise and patient's values with the evidence in a way that leads to a rational, acceptable management strategy.[15] Formal auditing of performance may be needed to show whether the EBM approach is improving patient care.

CONCLUSIONS

EBM aims to improve quality of care through the integration of best research evidence with clinical expertise and patient's and parents' preferences. In this article, I have explained the five essential steps for practising EBM, which are: formulating answerable clinical questions; searching for evidence; making a critical appraisal; assessing the applicability of the evidence; and evaluating performance. The principles and critical appraisal of randomised controlled trials, systematic reviews, and meta-analyses, and a practical demonstration of the five step EBM model will be explored further in later articles in this series.

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EVIDENCE BASED MEDICINE AND ITS IMPACT ON MEDICAL EDUCATION

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SUMMARY

The knowledge and skills obtained during the training in a medical college, during undergraduate and post graduate courses are insufficient to carry on lifelong successful clinical practice. To make clinical decisions, the practicing physician, even today is largely dependent on his obsolete knowledge and expertise derived from unsystematic observations made during his training, which can be as old as his medical course itself. It needs to be updated periodically with the findings of scientific/medical research. The scientific research has to be translated in to clinical practice for improving the patient care provided to the community. Patient's values are rarely acknowledged and current practices are often outdated, with the result that the patient rarely gets the 'Best' currently available medical care. The application of evidence based medicine (EBM) principles can help us with this daunting task that challenges us daily.

Evidence Based Medicine (EBM) is the optimal integration of best research evidence with clinical expertise and patient values. The essential feature of EBM is that the practitioners, when faced with any problem/dilemma in the clinical context of a patient, should be able to: perform a literature search; identify the evidence available pertaining to the clinical condition; critically evaluate it; and determine the "Best Evidence" to diagnose/treat/manage the patient. The key element in this cycle is the ability of the clinician to search and retrieve the literature in the shortest possible time in an efficient manner. The adoption of EBM is all the more imperative since the 'Internet Revolution' has provided access to medical literature, not only to the medical world but also to the common man as well. The time-honored undergraduate and postgraduate curricula need to be revamped to train the graduate as a lifelong, self-directed learner by imparting the skills required for practice of EBM.

Clinical Practice – Historical Perspectives

With years of robust biomedical research, since the end of World War II, and worldwide investment of over 50 billion $ in new research each year, it is hardly astonishing that health care practitioners and patients are having a tough time keeping in touch with new knowledge.[1] What then has been the basis of clinical practice historically? The answer to that appears rather simplistic. By and large the physician has tended to rely on the knowledge and expertise gained through the years in making clinical decisions. He adopted into his regimen the strategies that worked in a patient and discarded those that were found to be not so successful. The decision to adopt or discard was based mostly on individual observations. Very seldom was it a result of systematic and scientific analysis or for that matter of consensus arrived by a body of 'experts'.

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The success story of the first public demonstration of the modern practice of general anaesthesia for a planned surgery on 16th October 1846 by WTG Morton is a famous example that illustrates such practice. Morton's demonstration was based entirely on unsystematic observations made by him as a student (possibly of Horace Wells) and his intuition (which was the strong basis of his confidence), and there was no scientific study available to validate his success. The rest, as they say, is history. He became a legend. This, news of ether anaesthesia spread all over the world over night and it became the accepted practice in almost all the countries where in surgical anaesthesia was practiced[2].

The story of Archie Cochrane has a special place in the history of clinical practice.[3] This physician was captured by Germans and placed in charge of 20,000 prisoners of war during the II World War. Almost all of them were suffering from various communicable diseases like dysentery, malaria, typhoid etc. He had Aspirin and some other primitive methods of management at his command. He therefore expected that a majority would

die before the war ended. He was however astonished that only four among them died, and that too due to gunshot wounds. Hence, he argued that they all survived, either because of their inherent immunity to fight the diseases or, that Aspirin, had a 'Placebo effect'. He summarized the clinical practice prevailing at that time in these words:

"...(there was a) very widespread belief (among laymen) that for every symptom or group of symptoms there was a bottle of medicine, a pill, an operation, or some other therapy which would at least help. With this background, it is not surprising that the advent of the NHS (National Health Service, which provides care for all British citizens) led to an original sharp increase in prescription particularly for appliances. Between 1951 and 1968, requests for pathology tests increased three times, x-ray units of work nearly doubled. The patient expected the doctor to do something to help him : the more the better. The doctor wanted to help, and he could usually think of some new drug he had not tried (ably abetted by the pharmaceutical companies) or of some new diagnostic test (ably assisted by medical research) he had not tried out."

He proposed that a research study employing the 'Randomized Controlled Trial' design was the correct way of establishing the efficacy of any new intervention and/or testing the efficiency of health services. This and the contributions of other clinicians paved the way for standardizing the four types of epidemiological research designs by the international community.

Despite these developments clinical practice appears to be continuing in unscientific and unsystematic manner. The 'Institute of Medicine' at Washington, DC, has found, that only four percent of our clinical practice is based on evidence from scientific research. In another forty five percent of cases, there was no evidence but a strong consensus among colleagues. And astonishingly in the remaining fifty percent of cases there was neither evidence nor consensus[4]. Similarly the usefulness of administering corticosteroids to the mother in 'preterm' deliveries for improving lung maturity and preventing mortality of babies from Respiratory Distress Syndrome was established by research in the early eighties.[5, 6] Seven RCTs in 1981 and twelve more in 1990 proved that steroids improved neonatal outcome. Yet by 1994 it was found that only fifteen percent of doctors practiced it, and with disastrous consequences. Tens of thousands of infants succumbed and millions of dollars were spent on interventions. The wide gap between availability of scientific evidence and its application in practice persists till today.

What is Evidence Based Medicine?

EBM is an approach to caring for patients that involves the explicit and judicious use of the clinical research literature combined with an understanding of pathophysiology, clinical experience, and patient preferences to aid in clinical decision-making. EBM de-emphasizes (but not eliminate) intuition, unsystematic clinical experience and physiologic reasoning as sufficient grounds for clinical decision-making and emphasizes the systematic evaluation of evidence from clinical research.

The conception of EBM, despite its brief history has undergone a subtle but important change .An initial goal of EBM was to minimize the use of non-documentary knowledge and reasoning in clinical practice. More recently focus has shifted to integrating clinical expertise, patho-physiologic knowledge and patient preferences in making decisions regarding the care of individual patients.This shift marks a critical but necessary of the value of alternative forms of medical knowledge and reasoning.

EBM is a process of life long, problem based learning. The process involves:

i) Converting medical information in to competent, searchable, focused questions.
ii) Efficiently tracking down the best evidence with which to answer the question.
iii) Critically appraising the evidence for validity and clinical usefulness.
iv) Applying the results in clinical practice.
v) Evaluating the performance of the evidence in clinical application.

Evidence Based Medicine has thus been defined as the optimal integration of the best research evidence with clinical expertise and patient values[7,8,9]. Best research evidence is generally derived from patient-centered clinically relevant research from the basic sciences of medicine regarding the accuracy and precision of diagnostic tests, the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative, and preventive regimens. Clinical expertise would include the ability to use clinical skills and past experience to evaluate the unique health state of the patient, assess the risks and benefits of potential interventions, and incorporate the personal values and expectations into clinical decision making. The unique preferences, concerns and expectations brought to the clinical encounter by an individual patient represent the third component to be integrated into the clinical decision making process. Triangulation of these

three elements results in the forging of an alliance between clinicians and patients for optimizing clinical outcomes and quality of life.

Is EBM a new concept?

Even though the group led by Gordon Guyatt in 1992 consolidated the concept of Evidence Based Medicine, mention about the practice of evidential research - Kaozeng - can be found in ancient Chinese medicine during the reign of Emperor Qianlong. In more recent times physicians like Pierre Louis in the post-French-Revolution era rejected the pronouncements of authorities and sought truth through systematic observations.[7,9] The most dramatic of these being the rejection of the authoritarian pronouncement that venesection was good for cholera.

Why the sudden interest in EBM?

There are several reasons for the sudden interest in EBM. There is increasing realization among clinicians that years of experience that has enabled them to sharpen the clinical skills and improve clinical judgment, if unaccompanied by updating of knowledge can result in decline of clinical performance. The need for valid information about diagnosis, therapy, prognosis, and prevention on a daily basis has assumed added significance in this era of consumer activism. The awareness level in the general public about health related has increased tremendously especially due to the Internet revolution sweeping the world. The common man has access to the very same medical literature as the clinicians through numerous sources, from the traditional print and electronic media to the mushrooming portals on the World Wide Web. The patients are increasingly accessing medical information and are looking to their physicians for interpretation and opinion. It is in this context that the physician of today pursues clinical practice. The traditional sources of information for the clinician are generally found to be inadequate because they are out of date (textbooks), frequently wrong (experts!!), ineffective (didactic continuing medical education), too voluminous and highly variable in their validity for practical clinical use. Additionally the limited time available to the clinician for acquiring information is a major impediment for updating the knowledge from traditional sources. Information revolution in the new millennium equips the clinician with newer and more efficient tools of information gathering and helps him arrest the decline in his clinical performance.

What are the factors facilitating the practice of EBM?

At least four major factors are facilitating the adoption of EBM by clinicians. The type of literature being made available to the medical fraternity has undergone substantive qualitative change. The unstructured review articles based on personal opinions of experts in the field have been replaced by peer-reviewed reports of research studies designed and executed with scientific rigor. Systematic reviews of multiple research studies and the publication of a number of evidence-based journals provide validated information to the reader. The second major advance has been in the area of evolution of electronic information systems. Information dissemination systems have come a long way from the days of storing information in large mainframe computers at few privileged academic centers to making the information available on the desktop of users all across the globe through the World Wide Web. Simultaneously the librarians (Information Science specialists in modern day parlance) have evolved faster and far more efficient strategies for sifting through tons of literature and locating the evidence of interest to address the issues raised during a clinical encounter.

How does one practice EBM?

A clinician who wants to practice EBM must able to understand the patient's circumstances or predicament (including issues such as social supports and financial resources) to identify knowledge gaps and frame questions to fill those gaps, to conduct an efficient literature search, to critically appraise the research evidence and to apply that evidence to patient's care. This whole process has been divided into five simple steps, which if followed systematically can bring out a very successful outcome and a desired benefit to the patient care.[10]

The Five-Step Approach to Practicing EBM

Step 1- Framing a Proper, Pertinent, Focused, and Answerable Question : The first and foremost step in the practice of EBM is to convert the need for information into a patient focused, pertinent, relevant and answerable question. This need for information may be related to find out the cause (etiology) of a disease process, or to encounter the difficulty faced in diagnosing a syndrome or to optimize the treatment of a disease or to answer a query put forth by a patient's or a patients relative to know the course (prognosis) of a clinical condition. We will illustrate the practice of EBM using an example of a real clinical problem that was encountered recently at the KLES Hospital, Belgaum.

Clinical Scenario : *A 12 years old only male child of a schoolteacher was admitted to RICU with a history of accidental ingestion of O. P compound 4 hours back. On admission the patient was comatose but haemodynamically stable. The anaesthesiologist used his past experience, knowledge, skill & expertise and treated the patient with*

an infusion of atropine, but inspite of that patient developed respiratory paralysis in the next 2 hours. Again the clinician used his expertise, anticipated the respiratory paralysis & puts him on mechanical ventilation. Now, the consultant understands the gap in his knowledge & he identifies the same. The consultant wanted to administer Inj Pralidoxime. But he was not sure of the dosage and the mode of administration (a single bolus dose or an infusion).

In this clinical scenario, there is a need for information regarding the appropriate therapy for Organophosphorous poisoning. This need has to be converted into an answerable question. A very useful tool that could be adopted in the process of formulating a proper/pertinent/focused question has been described.

PICO Model - 4 Criteria

'P' — **Patient Problem:** *How would I describe a group of patients similar to mine?* In this clinical situation it is a male pediatric patient (12 years) who has developed organophosphorous poisoning following its ingestion.

'I' — **Intervention strategy:** *Which main intervention, prognostic factor or exposure am I considering?* Here the intervention is the therapy with Pralidoxime in optimum dosage.

'C' — **Comparison:** *What is the main alternative to compare with the intervention?* In his patient the clinical dilemma pertains to the dosage and mode of administration of Pralidoxime (low dose infusion vs. single large bolus dose).

'O' — **(Outcome):** - *What can I hope to accomplish?* Recovery from OP poisoning and decrease in morbidity & mortality would be the primary concern of the clinician.

The physician would be interested in reducing the chances of the patient going into intermediate syndrome. He would be looking for evidence for minimizing mortality, duration of ICU stay, the need and duration of ventilation, time to recover consciousness, the odds of developing intermediate syndrome and infections.

Additional criteria to be considered while framing the question : In addition to the four PICO criteria, there are two additional considerations in formulating the question.

Type of Question : How would I categories this question? Is it related to etiology, diagnosis, therapy or prognosis? In this example the question is about the therapy of OP poisoning.

Type of Study: The other consideration is the type of study that will answer a therapy question. Various study designs provide specific answers. The accompanying table provides the guideline for choosing the type of study design for each category of questions.

Using the PICO model the question that the clinician is encountering in this clinical scenario can thus be stated as: "In the drug therapy of Organophosphorous poisoning in a 12 year old patient, whether Pralidoxime should be administered as a single bolus dose or as an infusion and in what dosage to prevent the chances of development of intermediary syndrome?"

Table1: Type of study design to be chosen for answering the question

Type of Quetion	Type of Study/ Methodology	MEDLINE Filter
Therapy	Double-Blind Randomized Controlled Trial	Randomized Controlled Trial [pt], double [tw] and blind [tw], EXP Clinical Trials
Diagnosis	Controlled Trial	Sensitivity and Specificity [MH], EXP Diagnosis
Prognosis	Cohort Studies, Case Control, Case Series	EXP Cohort Studies [MH], Prognosis [MH], Survival Analysis
Etiology	Cohort Studies	EXP Cohort Studies [MH], Risk [tw]
Prevention	Randomized Controlled Trial, Cohort Studies	Randomized Controlled Trial [pt], Cohort Studies [MH], Prevention and Control [sh]

This being a therapy question, it can best answered by a systematic review of randomized controlled trials or in the absence of that evidence, by a single RCT.

Step 2 - Searching the Literature: The second step in the process is to locate the 'best' evidence to answer the question. The clinician has two basic choices for finding the evidence. He may search through the 'traditional' print resources like textbooks or journals or 'browse' online electronic databases. What is of paramount importance is of answering the question in the shortest possible time and in the most efficient manner. Manually searching through voluminous literature is an unenviable task requiring immense periods of time, a commodity that is in limited supply given the potentially life threatening situation that the patient is in. Browsing the

online electronic medical databases seems the most logical option to pursue.

There are a number of online information resources that the clinician may tap to find the evidence. These include : textbooks, journals, patient profiles, practice guidelines issued by specialty boards, EBM reviews, and databases of indexed publications. 'Medline' published by the National Library of Medicine USA is the most popular and most exhaustive database. There are several search engines that enable the clinician to browse this database. 'Pubmed'* service hosted by the same agency has several additional features and is probably the most versatile search engine for exploring Medline. This search offers a number of 'browsers' (Clinical Queries, MesH etc) for searching the information. Additionally it also permits narrowing down the search by application of limits (type of publication, language, age group, period of publication etc) Using the MeSH browser and restricting the search to publications in English and with abstracts available of Randomized Controlled Trials it was possible to locate what appears to be the 'best' evidence to answer the question.

* (Pubmed can be accessed at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed)

Johnson S, Peter JV, Thomas K, Jeyaseelan L, Cherian AM.: Evaluation of two treatment regimens of pralidoxime (1 gm single bolus dose vs 12 gm infusion) in the management of organophosphorus poisoning. J Assoc Physicians India 1996 Aug; 44(8): 529-31

Step 3 - Critical Appraisal of the Literature[11]: To know whether this is the best available evidence or not is the next step. The critical appraisal of the article is an important step in the whole process. It is essential that clinicians must master the skills of critical appraisal of the literature, if they are to apply evidence-based medicine to the daily clinical problems they encounter. Most busy clinicians do not have hours to spend critiquing an article. However, they do need a brief and efficient screening method of determining whether the information is valid and applicable to their practice. By applying this 'Fast Track' appraisal it is possible to approach the literature confidently and base clinical decisions on evidence rather than hope! The critical appraisal of literature involves 3 stages: 1. Screening for initial validity and relevance; 2. Determining the intent of the article; and 3.Evaluating the validity based on its intent. Validity of the literature pertains to determining the closeness to the 'Truth'. Different kinds of errors can creep in during the conduct of a study. There are many ways/methods of eliminating these errors in the study like: Blinding, Randomization, using placebo-controlled groups, minimizing loss to follow-up of patients, and treating the data by appropriate statistical analysis etc.

The clinician should ascertain whether the authors have used these methods to minimize the errors in the study or not. The article that was tracked down is a prospective randomized placebo controlled clinical trial of Pralidoxime in two similar groups of patients. (Control group-low dose and study group-high dose) Block randomization is used to give equal chance to all the patients to participate in the study in either arm of the trial. The investigators were not blinded to the two groups which if done would have made the results even more valid. The 72 patients who entered the trial were properly accounted for at the time of analysis and are attributed to at its conclusion indicating proper follow up in all the patients. The article is quite relevant to the clinical problem as it addresses the clinical scenario that is confronting the clinician. The intent of the article is to evaluate two treatment regimes of PAM in the management of OP poisoning. The next thing to determine is the strength of the outcome. How large was the treatment effect? The incidence of intermediate syndrome and the ventilator requirement was significantly higher in the high dose group. This was an equivalence study designed to show that the low dose was as effective as high dose. The results attain higher significance as the low dose group fared better than high dose group, even though the research hypothesis was in the reverse direction.

Lastly, the study is quite beneficial to our patient; because the treatment effect is quite precise in bringing down the risk of prolonged ventilation, intermediate syndrome, time required to regain consciousness, the cost of therapy, and the duration of ICU stay. PAM is a very expensive imported drug requiring considerable amount of foreign exchange and there are difficulties in procuring it. It is imperative for the clinician to find a cost-effective and yet effective treatment. Patient's father, being a primary school teacher, cannot afford the exuberant cost of the drug. Hence, the out come of this research study is very much relevant and beneficial in solving the clinical dilemma.

Step 4 –Integrating the Evidence with Clinical Expertise and Patient Values: EBM, by definition, is the optimal integration of best research evidence with clinical expertise, and patient's biology and values. The best-documented critically appraised research evidence is already with the clinician. The physician has already exercised his expertise arising from prior knowledge and past experience in treating his patient by starting an infusion of Atropine, and putting the patient on mechanical ventilation. He now

has to take into consideration the patient values for example: The patient is a precious, lone male child of the parents. The economical/financial status of the parents does not permit expensive therapies. He also has to consider the patient's biology. Fortunately though there are no contraindications for the drug to be administrated. He has found the evidence that low dose regime requiring 1/16 of the high dose has better effect.

Step 5 – Evaluating the Process: Once the therapy is administered the clinician needs to evaluate the previous four steps. Was he able to formulate a focused question? Was he able to devise a precise search strategy for locating the evidence? Did he use the most appropriate resource? Were more pertinent resources like practice guidelines available to him? Did the 'evidence' work in his patient? The final step is to reassess the strategy and take it onwards from there. The clinician should document the outcomes of the application of the evidence and based on his experiences and those of his colleagues should be able to develop management protocols. Beyond this he must also collaborate with professional bodies in developing practice guidelines. This last step completes the feedback loop of EBM.

What are the benefits of adopting EBM?

The greatest advantage of EBM is that it will minimize the errors in patient care, reduces the cost of treatment to the patient, and most importantly it optimizes the quality of patient care. Further, the skills learnt in practicing EBM are the very same ones needed for being a lifelong, self-directed learner. The habit of accessing literature on a daily basis is the best guarantor of ensuring advancement of knowledge and keeping abreast of scientific progress[1, 7,8].

What are the challenges in adopting EBM?

There are three major challenges in adopting EBM.[7] First and foremost, technology and online information resources must be available to the clinician. This issue seems to be resolving due to the rapid pace at which information technology revolution is occurring. Personal Computers are becoming cheaper, Internet rentals are declining and a number of health portals and databases are offering free access to electronic journals and periodicals. This will enable a practitioner to collect evidence on a daily basis sitting at home and or at his clinic.

The second challenge for the clinician lies in learning the skills required for accessing the medical literature and finding the best evidence from that. Once the evidence has been located, he must be able to determine the validity of the evidence found. This will require an understanding of the epidemiological study designs and concepts of biostatistics. It is here that the training in the medical college both at undergraduate and postgraduate levels needs to be strengthened. The medical colleges could also offer refresher courses to the practicing clinicians. Acquiring the basic skills is not difficult and critical appraisal of available evidence could be mastered with some effort. With six million medical articles being published each year, the amount of information available is overwhelming. Despite this large volume of medical literature, less than 15% of all articles published on a particular topic are found to be useful. Most articles are not peer-reviewed, are sponsored by those with commercial interests or arrive free in the mail. Even the articles published in the most prestigious journals are far from perfect. Meta-analysis of a wide variety of clinical trials have described major deficiencies in the design, analysis and reporting of the research findings. Many diagnostic tests and therapies are not rigorously evaluated before becoming established as routine procedures. Readers must take personal responsibility for judging the validity and clinical importance of the medical literature.

The most important challenge in adopting EBM is an attitudinal one. The clinicians will have to realize that they have a moral, ethical, and professional obligation of providing the current best health care to their patients. Change in attitude will take place only when there is realization that clinical performance depends upon regular updating of knowledge and does not merely accrue by years of clinical experience. This last one is the most important challenge that the medical fraternity will have to address. Inculcating the principles of EBM during the formal training of a medical graduate can go a long way in ensuring that at least the future generations of clinicians will be better equipped to practice evidential research.

Another potentially negative impact of EBM is that evidence may be viewed as static rather than dynamic[12]. Guidelines are increasingly influencing medical practice, yet these guidelines require frequent review and revision to incorporate new literature. The use of out-of-date guidelines may be associated with decreased quality of care compared with the use of more recent evidence. As such, it is imperative that anaesthesiologists have the ability to critique guidelines and the medical literature to determine whether the guideline is valid and current.

What are the alternatives to EBM?

Since EBM asks us to incorporate valid scientific literature in to our practice without significant data and tells us that such approach improves patient outcomes and

the practice of EBM consumes time and may detract from other educational initiatives, it is wise to reflect some alternatives to the practice of EBM.[12, 13] A recent review by Isaacs D, (1999) of alternatives to EBM demonstrates the pitfalls of the practice of EBM without incorporation of valid scientific evidence. In the absence of scientific literature to guide clinical decision-making personality characteristics such as seniority (eminence based medicine) drive clinical decision-making. Indeed, traditional medicine uses the lack of scientific evidence of efficacy as a defense against alternative forms of medicine

What are the special considerations for EBM in Anaesthesia?

Evidence Based Anaesthesia:[12]

1. Professional societies in anaesthesiology (including the Anaesthesia Patient Safety Foundation) have attempted to apply the principles of EBM to improve patient care. As a result, anaesthesiologists are recognized as leaders in the development and widespread adoption of practice guidelines that may have contributed to major, sustained, widespread reductions in morbidity and mortality attributed to the administration of anaesthesia .

2. Because of the paucity of valid randomized clinical trials to help inform anaesthesia practice, many decisions in the operating room (OR) are based on evidence from pathophysiologic reasoning or evidence obtained from studies of animals, healthy volunteers, or observational studies focusing on biologic (arterial blood pressure, heart rate, pulmonary artery occlusion pressure) or patient (mortality, morbidity, functional status) outcomes. EBM sees evidence broadly. There is always evidence; however, it is often unsystematic or physiologic. Dispersed literature sources and insufficient clinical research data enhance the need for evidence-based anaesthesiology, whereas the need to make critical decisions under the pressure of time challenges the application of EBM in anesthesiology.

3. Literature Sources : The body of literature pertaining to anaesthesiology is dispersed across multiple journals, including journals in general medicine, medical subspecialties, critical care, anesthesiology, pediatrics, and surgery, as well as basic science journals such as cell, shock, and circulation journals. This diversity increases the need for efficient methods to access and search relevant literature. Techniques for improving efficiency when searching the medical literature have been published.

4. Both the breadth of knowledge required for anaesthesiology and the diverse sources of clinical literature demand efficient access and evaluation of relevant literature.

5. Need for Rapid Decisions: The need to make rapid clinical decisions may complicate the application of EBM in the OR or intensive care unit (ICU).

6. In the OR and ICU, decisions are routinely made faster than on a general medical ward, and there are few data regarding whether EBM can be applied practically where rapid decisions are required. There are some data suggesting that EBM treatment and diagnostic protocols may be used effectively even in the treatment of acute processes such as acute respiratory distress syndrome. Without such protocols, practical applications of EBM in the OR and ICU will be limited to problems we see repeatedly.

7. In procedure-oriented specialties such as anaesthesiology, the skill of the provider and hospital-level factors may affect risk and should be considered in the risk/benefit analysis .

Conclusions

Medicine is not an exact science, but a science of probability. The challenge to physicians is to provide up to-date medical care. The ultimate goal for clinicians should be to help patients live long, functional, satisfying, and pain and symptom free life. To do so requires us to balance compassion with competence. By adopting the principles of Evidence Based Medicine, it will be possible to maximize the benefits of scientific research for patient care. Medical educators and medical colleges have the singular responsibility of indoctrinating the principles of EBM as a concept, a philosophy, and a religion necessary for being efficient, compassionate, caring, and responsible clinician among the future physicians during their formative years of training.

References

1. *R. Brian Haynes*. Foreword in PDQ Evidence-Based Principles and Practice by McKibbon, A., Eady, A., Marks, S.: B. C. Decker Inc. Hamilton, Ontario, 1999.
2. *R S Atkinson, G B Rushman J. Alfred Lee;* A Synopsis of Anaesthesia 9th Edition John Wright & Sons. 1982.
3. *Cochrane AL.* Effectiveness and Efficiency : Random Reflections on Health Services London: Nuffield Provincial Hospitals Trust 1972.
4. *Field M J, Lohr K.N* Guidelines for clinical practice. Institute of Medicine Washington DC National Academy Press 1992;34
5. *David A* Grimes Introducing EBM into a Dept of Ob. & Gyn. Obst & Gyn Survey 1995; Vol 86; 451-57.