Why do we need clinical epidemiology? - A practice-oriented clinical science

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The care of each patient is analogous to an experiment in which a baseline state, exposed to an intervention, emerges in an outcome. The clinician's challenge is to evaluate past experience and knowledge as the «control» background for choosing a best intervention for each patient. The events that follow the intervention are then appraised and suitably added to the available background. In an era of extraordinary complexity, power, benefits, harm, and costs in the technology of modern medicine, clinical decisions and evaluations can no longer be satisfactory if they depend only on the anecdotes and undocumented «judgment» of past clinical practice. A suitable scientific approach is needed to provide appropriate documentary evidence in data, comparisons, decisions, and analyses. This humanistic science cannot be developed or transposed from laboratory work, which uses different methods, and which does not focus on intact human beings as the «material». Clinical Epidemiology *is the name of the new intellectual domain that provides the «basic scientific» methods needed for decisions and evaluations in modern medical care.*

The basic scientific challenges of nature can be divided into two kinds. There are challenges of *explication* and challenges of *intervention*. In explication, the challenges that we ask are: What has nature done and how does it work? What are the mechanisms? In intervention, we ask: How can we change what has happened, and how can we prevent what might occur? Those are two different kinds of fundamental questions.

For example, in explication for the physical world, we have *physics*, but for intervention we have *engineering*. For explication of words in language, we have *linguistics*, but for interventions with words to create new things, we have *poetry*. In the craft of patient care, we have *molecular biology* for explication, and the activities of *clinical practice* for intervention.

If we consider the activities of clinical practice, they follow the exact same scientific sequence of an experiment. There is a preparation that is followed by a manoenvre that is followed by a response. The scientific orientation is quite different, however, for laboratory activities and for clinical therapy. The general orientation of laboratory activities is the explanation of mechanisms, but the

general orientation of clinical therapy is the management of events. The motivation of laboratory activities is inquiring. In clinical therapy the motivation is either remedial, to fix what has happened, or prophylactic, to prevent adverse things that might occur.

The hypothesis in laboratory activities is innovative. The person who designs a laboratory experiment wants to learn something new. The hypothesis in clinical therapy is repetitive. The doctor wants to repeat or exceed, if possible, the best successes obtained in the past. To assess the value of laboratory activities, the main question is what has been learned for the sake of science. For the value of clinical therapy, the main question is what has been accomplished for the sake of this patient.

In scientific method, however, both activities have an absolutely parallel structure, but the structure also differs. In laboratory activities, the material is manipulated by the investigator. The investigator can take a rat, remove both ovaries, remove both adrenals, connect the ureters to the salivary duct, and then the experiment is ready to begin. The investigative manoenvre consists of the experimental procedure, where one group of rats might be injected with adreno-corticotrophic hormone, and the other group of rats might get saline. In laboratory activities, the response is examined by looking at isolated variables that are of greatest interest to the investigator. In clinical therapy, things are quite different. We do not usually create the diseases that we treat: they come to us already formed by nature, and the clinician's job of «preparation» is to classify patients. The clinician's manoenvre is the administration of therapy, and for evaluating response, the clinician's job is to select, from the huge panorama of things that can occur in a person's life, the particular indexes that are most appropriate for the therapy.

What happens in nature is that a healthy host is exposed to a cause of disease and becomes a diseased host. The disease undergoes a natural course and the person becomes an evolved host. If the person is lucky enough (or unlucky enough) to encounter a doctor, the doctor imposes her or his reasoning upon the situation. The doctor gives to the disease a name that we call **diagnosis**, then thinks backward to determine the etiology or what the cause may have been, and thinks forward to anticipate what that natural course is going to be.

The doctor can then impose two different kinds of experiments, in preventing disease or in treating disease. Meeting a healthy host who has been exposed to a cause or who might be exposed to a cause, the doctor engages in vaccination, or some other means of preventing disease, with the hope that the host will stay healthy instead of becoming diseased. Meeting a host who has already become diseased, the doctor anticipates what the natural course might be, contemplates what the evolved host might be, and then, if the doctor thinks that treatment has

something better to offer than no treatment, the therapeutic procedures are imposed. The host then goes through a post-therapeutic course, emerging as a treated host. The way we contemplate what has been accomplished is to compare the patient's state as a treated host with what we think it might have been if the patient had continued to evolve without treatment.

If you contemplate the experiments that are carried on every day in clinical care, the average practicing doctor conducts more experiments in a single day than the average laboratician does in a year, or sometimes in a lifetime. If you contemplate those experiments, you can ask what are the methodological requirements in judgment for the human interchange with the patient. The requirements are concern and understanding and compassion; and I am willing to label that activity as *art*, because it is very difficult to give specifications for the methods. On the other hand, when we talk about the choice of agents among the powerful therapeutic weapons that exist today - weapons that can produce miraculous cures and that can also produce brutal mutilations or death - when we choose among those agents, one would expect the choice to be an act of science, with documented data and logical analysis and valid proof. We can therefore ask what kind of science is available to deal with these clinical activities? The science that is taught in laboratory work is absolutely inadequate, because the material is different and the methods are different. A human being is the only experimental preparation that can talk. That attribute makes all our laboratory methods unsatisfactory. It makes us need a totally different approach for treating patients, because we cannot use laboratory methods. Where do we get the new methods?

We might consider the contents of classical, public-health epidemiology, which has a magnificent and honourable history. Epidemiology began by studying the cause and transmission of infectious diseases; it looked at the distribution of disease in time and space, in calender and geography; it applied statistics to the causes and distribution of chronic disease; and it was concerned with trials of agents for the primary prevention of disease, which might be called *«contrapathic»* therapy - things such as polio vaccination and tests of other vaccines. What is omitted from the contents of classical epidemiology, however, are all the things with which clinicians are mainly concerned, things such as prognosis of chronic disease, surveys of clinical therapy, experimental trials of agents for remedial therapy, experimental trials of agents for what might be called *«contratrophic»* therapy or secondary prevention.

The average doctor in clinical practice constantly engages in acts of prevention, but it is secondary prevention. We treat *diabetes mellitus* to prevent vascular complications; we give *beta blockers* or *calcium channel blockers* to prevent various

kinds of complications or death after myocardial infarction. We lower the blood pressure of people with hypertension, not merely to lower the blood pressure, but to prevent strokes, or death. Those are all acts of secondary prevention. Clinicians are also interested in the outcome of chronic disease, particularly the functional status of patients and their quality of life. Clinicians are also interested in the purveyance or delivery of health services. What are the best methods to arrange appropriate delivery of health care? And clinicians are certainly interested in a clinical taxonomy for classifying the ailments of sick people.

All of those things are available as the contents of what might be called *clinical epidemiology*. In that sense, *classical* or *public health epidemiology* gets its etymology from the word *epidemics*, used in the 19th century to indicate transmission of contagious outbreaks of disease in human beings. The heroes in classical epidemiology are people like WILLIAM FARR, who introduced the strategies now used for *vital statistics*, and the very famous JOHN SNOW, who took the handle off the *Broad Street* pump to end an epidemic of cholera. The topics of classical epidemiology are things such as sanitation and public health, the etiology of infectious disease, statistics for the etiology of chronic disease; and the focus is on strategies for preventing disease *in the community*. In *clinical epidemiology*, the etymology comes from the Greek *«epi-demos»* – upon people. Its heroes are people like PIERRE CHARLES ALEXANDRE LOUIS, who in 1835, about a century and a half ago, introduced the *méthode numérique* in France, and did the very first clinical studies in which the results were reported with *means*. He used his new method to study the value of *blood-letting* and to show that 2,000 years of blood-letting had not been particularly efficacious. Another hero was IGNAZ SEMMELWEIS, working not too far from here in Vienna, who demonstrated that puerperal sepsis was being transmitted by the unclean hands of the physicians who were delivering the mothers. Both of these two clinicians worked in hospitals, and studied clinical problems that were most apparent in the hospitals.

The main topics of *clinical epidemiology* are the estimation of prognosis, the evaluation of therapy, and the appraisal of diagnostic procedures. The main focus is on strategy for the management of individual patients.

We can then ask what is the science and scientific method for this work? One of the first activities in any domain of science is classification. Modern chemistry could not have developed successfully if MENDELEYEV had not created a *periodic table* that would classify and structure the elements in such a way as to have them make sense.

As shown in *Fig. 1*, clinical activities consist of a mixture formed by a **host** shown in the circle on the right and by a **disease** shown in the circle on the left that intersect to produce an **illness** in the middle. To achieve scientific

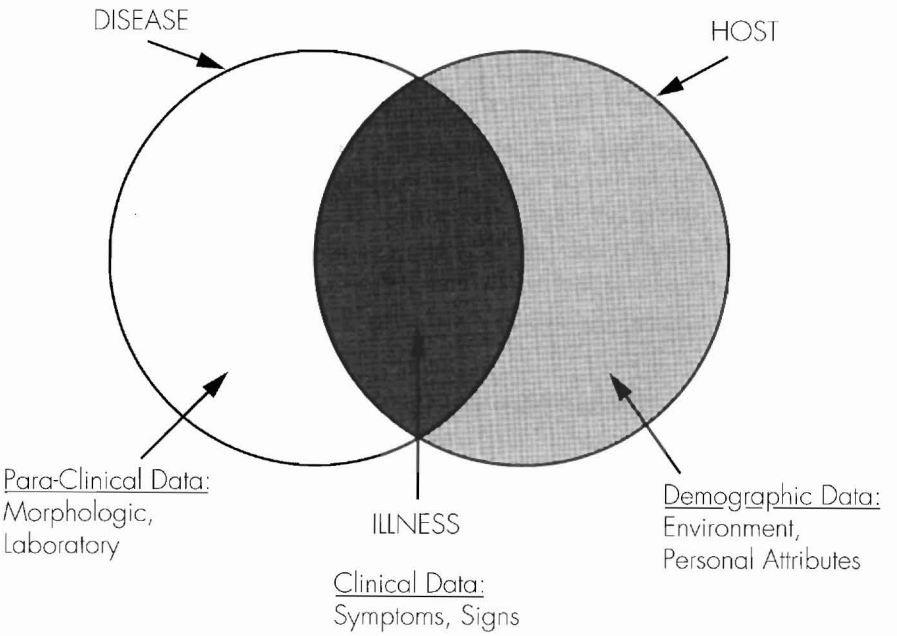

Fig. 1: Disease, host, and illness

reproducibility, we must classify all three parts of this group: the host **and** the illness **and** the disease. For this classification, we have an excellent system of taxonomy to categorize the demographic data of hosts, their environment and such personal attributes as age, race, sex, and socio-economic status. We also, thanks to modern technology, have a magnificent taxonomy for classifying disease. We use the paraclinical data obtained with various morphologic examinations and laboratory tests. What is generally lacking, however, is an effective *taxonomy of illness* for such clinical data as patients' symptoms, functional capacity, quality of life, satisfaction, and anguish of family. Lacking an adequate *clinical taxonomy*, we become poor scientists, because two people may have the same demographic state and the same disease, but a different illness; two people may also have the same disease and illness, but different demographic features; and so on. To achieve the scientific goal of reproducible identification of the material under study, we must be able to classify all three elements of the patient: the host, the disease, and the illness. In the current state of medicine, however, a taxonomy for the clinical data of illness is underdeveloped. Our failure to suitably identify what is being treated has the scientific and humanistic consequences discussed in my earlier contribution in this book.

Suppose we decide to deal with these issues in taxonomy and in measurement. They are prime issues in any type of science, but we first must realize that clinical activities involve two different kinds of measurement. One kind of measurement can be called *mensuration*, and the other can be called *quantification*.

Mensuration is what we do in converting observed phenomena into raw data. To express individual *height*, we set up a mensurational scale in *centimetres* or *inches*. To express *gender* (or *sex*, if you prefer), we set up mensurational scales such as *male* and *female*. To classify severity of illness, we might set up scales such as *mild*, *moderate*, *severe*, or *one plus*, *two plus*, *three plus*. The various scales and criteria used to describe types of therapy all emerge as acts of mensuration, where we convert the observed phenomena into established categories that can be analysed.

Quantification is what happens when we take the basic raw data, put them into groups, and perform comparisons. In grouping, we might form some kind of summary expression for the raw data in each group. Thus, we might talk about mean height as a summary expression in very sick men receiving treatment A. This activity would be an act of grouping. An act of comparing occurs when we contrast the rates of success for treatment A in very sick people versus treatment B in mildly sick people. You should realise immediately that such a comparison is improper. To contrast treatment A in very sick people against treatment B in mildly sick people is not a fair comparision of the two treatments. Doctors have been doing those biased comparisons for a long time, and one of the goals of randomized trials was to avoid those biases.

Let me elaborate now on some of the challenges in measurement, for mensuration and for quantification. In quantification, for groups and comparisons, clinicians, not mathematicians - clinicians! - must create models that will fit the observed phenomena, rather than forcing clinical events in a Procrustian manner to fit mathematical models that may not be appropriate. Clinicians need to demarcate the pathways, events, and data for evaluating clinical decisions. Clinicians who are in the front lines of «combat», taking care of patients, and who see what is going on, should demarcate the pertinent phenomena. This demarcation cannot be done by a statistician (or by someone sitting in an armchair) formulating models that do not fit the data and the decisions.

We also need to develop observational substitutes for randomized trials in cause-effect reasoning. Let me say immediately that I will yield to no-one in my support and admiration for randomized trials when they can be done and when the answer to the question in the trials provides information that is suitable for the question that clinicians want answered in treating patients. Unfortunately, randomized trials are aimed at answering a question about average efficacy. They do not necessarily give the information that a clinician needs for dealing with

individual patients. For the many clinical decisions that cannot be tested with randomized trials, we need to develop better observational substitutes. Those substitutes will be used to give valid, creditable data in cause-effect reasoning for all of the technologic agents that will have to be evaluated in the 21st century. We also need to use the computer for imaginative new activities, not just automation of the status quo! What I mean by computerized automation of the status quo is such things as storing inventories of financial data for the hospital or doing the number-crunching statistical calculations of multiple logistic regression. An imaginative new activity is *computerized tomography*, and there are various other imaginative new ways in which clinicians can use computers to get, examine, and process data.

We have a major set of challenges in mensuration for basic data. We need to get clinical evidence of relief and comfort, not just cure. Our statistical colleagues have diverted us into a *hard data creed*, which we have willingly accepted. We have therefore sought evidence of cure, while ignoring evidence of relief and comfort. We have thus forsaken the clinician's ancient obligation: *to cure occasionally, to relieve often*, and *to comfort always*. You should recognize that statement as an English translation of the wonderful old *French* aphorism describing a clinician's obligation: *Guérir quelquefois, soulager souvent, consoler toujours*. We need to get evidence of benefit, not just risks and costs. The current calculations of risk-benefit ratios and cost-benefit analyses are being done by economists; and I am sure you have heard the definition of an economist as *someone who knows the cost of everything and the value of nothing*.

A critical challenge for clinicians is to get evidence of the benefits we accomplish. Because medicine has become a large fiscal enterprise, the economists are out there, and the costs are being calculated, but we are not producing adequate evidence of benefits. Suppose we take an 80-year old man, crippled by bilateral osteo-arthritis, unable to walk for about ten years. We now give him two new hips and he becomes able, not merely to walk, but also to go fishing, and to play with his grandchildren. According to the economists, we have not done anything. We have not extended that man's life-span. We have not increased his earnings, because he was retired and on pension before the operation, and he is still retired and on pension afterwards. All we have done is to redeem his life, but we have no way of expressing that benefit for the economists who are calculating only the costs of the operation.

Suppose a man and woman have been trying for fifteen years unsuccessfully to conceive and bring a baby to term. After *in-vitro fertilization*, they succeed. How do we calculate that benefit? Do we measure the anticipated life-time earnings of the child?

To develop appropriate ways of describing relief, comfort, and benefit is another major part of our scientific as well as humanistic challenge. To master these challenges of mensuration for basic data, we need to improve the methods of clinical observation, particularly when symptoms and patients' experiences become research data. We need not take five hours for each patient's history, but if dyspnea is an important element of the chief complaint for the treatment being given, we need to get more careful detail about dyspnea, not just «shortness of breath with exertion». If angina pectoris is the chief symptom being treated, we need to get better details of its provocation and severity, so we can evaluate what improvement has occurred.

We need to review the value of each type of clinical data for each type of clinical decision. We can then begin to eliminate redundant or useless information. For example, as someone who teaches medical students the introductory clinical examination course, which you might call *«physical diagnosis»*, I and many other such teachers have given the students an enormous amount of nonsense and redundant data. For example, there is little value in teaching that rales (or rhonchi) in the lungs are *moist*, *dry*, *sibilant*, *sonorous*, or any of the other musical adjectives that are essentially useless in the mǫdern era. What is important is to recognize and teach the things we can do with a stethoscope that are just as good or better, in diagnosing pulmonary anatomy and pulmonary function, than what can be done with an X-ray or röntgenogramme. For example, if I am going to order a chest X-ray, one main reason for listening to the chest is to know which side is the candidate for the lesion, to decide which lateral view to order. In listening to rales or rhonchi in someone with congestive failure the important thing is their height on the chest. Is the entire chest filled with rales? If so, we can use their declining level as an index of improvement, allowing us to discern changes, with a stethoscope, that a chest X-ray cannot always detect. For someone with an asthma attack, the pattern of wheezes and distress are far more effective guides to what is going on than the X-ray may be.

These are examples of the kind of work modern clinicians should do in dissecting out the large accretion of information, and determining what to teach. Let me give you another example. With regard to a patient's family history, I always take that history myself if I am working as a general internist. My purpose is **not** to find out whether the patient's father, grandmother etc., have had tuberculosis or cancer. That old «diagnostic» information is usually too unreliable to be worth much attention. The thing about the family history for a general doctor is to learn something about the patient's life. The fact that the patient's mother died when the patient was six years old can be an important thing to know in your ongoing interchange with that patient. Certain elements of the family history might be important to a geneticist, establishing a pedigree for a special study,

but if so, the geneticist will try to determine and verify all of the diagnostic details. The point is that there are different reasons for different information. As clinicians, we need to begin specifying those reasons, so that their importance can be recognised by our students and colleagues.

We need to establish scales, rating systems, and criteria to identify and harden the important soft data that constitute the domain of *clinimetrics*. It is our domain and our responsibility. It cannot be successfully delegated to anyone else, although we can be greatly helped by sympathetic statisticians, sympathetic sociologists, and other consultants who will actually pay attention to the problem instead of dumping their pre-conceived models upon us. We can effectively collaborate with those consultants, but we have too long refused to use our own brains, a superb computer that we all have «upstairs».

As we prepare to enter the 21st century, in an era of majestic technology and computation, it's our job now to begin making much better use of our own computer for improving the primary, but currently primitive, data of patient care.

One of the main things that keeps doctors from doing this job is the intellectual snobbery of our colleagues who say: «Clinical medicine is not *scientific* and it's not *basic*; but I, a biochemist or molecular biologist, do basic science, whereas you are a mere clinician!» My answer to that type of remark is to ask: «What is *basic*? Does *basic* depend on the size of the particle?» If so, there is only one basic science: physics. The physicists have the smallest particles that anyone has ever seen or not seen. If molecular biologists want to claim they are *basic*, I just say: «You are wrong! You are not at all *basic*. You are just a mere applier of what is learned in the basic activities of physics!»

If basic science is the absence of pragmatic usage for what is learned, the idea does not apply to most good basic science. When my friends who are biochemists or molecular biologists are asked what they have in mind when they do an experiment, they usually give a very careful description of what the experiment can lead to and what they would do next. They do not say: «I shoot an arrow in the air and hope it lands somewhere». So the absence of any kind of pragmatic usage is not *basic science*. In fact, if *basic biomedical scientists* said, «We are really interested only in basic molecular science; we are not interested in any medical applications», they would not get any funds to do research. They are well supported in their «basic research» because they say: «What I do can unlock the secrets of the medical universe.» And they will always suggest a possible pragmatic usage for the results.

Does *basic* refer to something that is fundamental to everything else? No, because

human life is much too complex, much too rich, much too varied for any single thing to be basic to everything. Is human molecular biology more important than human speech? Is human speech more important than human spirituality, whether it be expressed with organised religion or in other approaches? There is no single thing that can be so *basic* that everything else depends on it.

On the other hand, if we acknowledge that there are *basic* questions in explaining nature, and *basic* questions in altering nature, then everyone can be a winner. Clinicians can do basic scientific work attacking the problems that challenge clinicians in patient care, and biochemists and molecular biologists can do basic work in attacking their explicatory challenges. The two sets of activities are complementary, and each group needs the other. Without the work of the biochemists and molecular biologists, clinicians would not have magnificent new things to test, and without the clinical work, the explicatory scientists would not know where to look.

The seminal act that introduced modern molecular biology occurred in 1952 when LINUS PAULING did the electrophoresis of hemoglobin. If *PAULING* had simply taken his electrophoresis equipment and put blood into it, he would have found non-specific variations. If he had put blood from a collection of patients with anemia into his electrophoresis machine, he would also have found non-specific variations. It so happens that clinicians had demarcated, from the collection of anemias, a particular entity called *sickle-cell anemia*. That was where PAULING looked and that was where he struck molecular gold. In many other conditions today, our colleagues working in the laboratory will produce utterly sterile results, unless we, as clinicians, give them better information with which to correlate what they find, and to allow their otherwise isolated and meaningless discoveries to become able to achieve biologic and clinical meaning.

Even if we restrict ourselves to the world of explication for the phenomena of **clinical medicine**, we can see the inter-relationships shown in *Fig. 2*. **Physiology** explains a great many clinical phenomena, but physiology is not basic, because **biochemistry** explains a lot of what goes on in physiology. This explanation doesn't make biochemistry basic, however, because biochemistry is merely an application of what goes on in **chemistry**. Chemistry is not basic, because chemistry is an application of **physics**. And physics, as my old mathematics professor used to say, is a set of experiments conducted by extroverts who are unable to handle pure **mathematics**. Mathematics, of course, is merely an application of **philosophy**.

Philosophy could not exist without **semantics**, semantics requires **linguistics**, and linguistics requires **human speech**. What is basic to human speech is **human development**; what is basic to human development is **human health**;

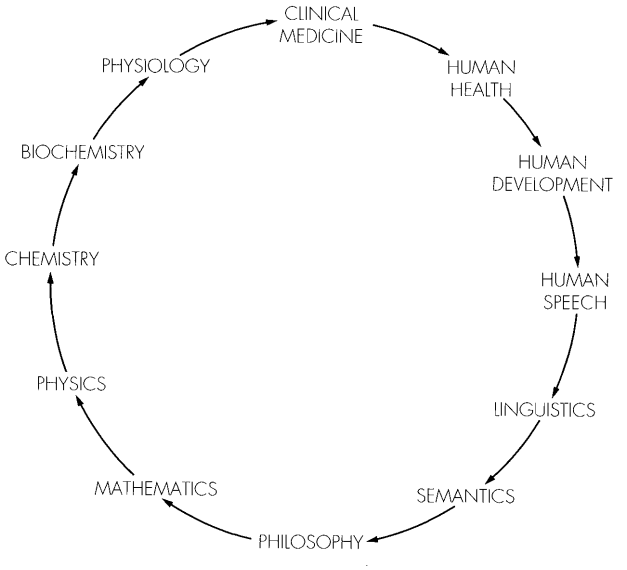

Fig. 2: Circle of disciplines

and what is basic to human health, let us hope, is **clinical medicine**. So when you encounter some arrogant basic snob who says he or she is more basic than you are, just find out what they do, remember what you do, and arrange yourselve accordingly.

Further reading

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