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Predicting outcome: a fourfold delusion!

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Essay

Definitions

Diagnosis: a judgment about what a particular illness or problem is, made after making an examination. [*Cambridge Dictionaries Online*. Diagnosis. Cambridge University Press 2011. Accessed February 17, 2012. *http://dictionary.cambridge.org*.]

Diagnose (to): to recognize and name the exact character of a disease or a problem, by making an examination. [*Cambridge Dictionaries Online*. Diagnose. Cambridge University Press 2011. Accessed February 17, 2012. *http://dictionary.cambridge.org*.]

Prognosis: (1) a doctor's judgment of the likely or expected development of a disease or of the chances of getting better; (2) a statement of what is judged likely to happen in the future, especially in connection with a particular situation.

Prognose (to): to make a prognosis. [*Cambridge Dictionaries Online*. Prognosis. Cambridge University Press 2011. Accessed February 17, 2012. *http://dictionary.cambridge.org*.]

According to the definitions above, a diagnosis is an affirmation based on an examination, recognition and naming of the **exact** character of a **present** disease. For example the identification of *Mycobacterium tuberculosis* in sputum implies a certainty: the patient has tuberculosis.

All to the contrary, prognosis is a statistical computation of **what might occur in the future**. By its very nature, statistical evaluation is uncertain. Statistics is nothing but a precise quantification of uncertainty. Diagnosis is certain; prognosis is uncertain. A patient with tuberculosis may die from his disease or he may not. Nobody will try to "adjust therapy to prognosis" for a tuberculous patient; antituberculous drugs will be prescribed.

During the last few decades, and for reasons not entirely clear (some even suspect such as the redefinition of diseases according to the medications available in the market), in cases of cancer pathologists have been asked more frequently to evaluate the prognosis of (to "grade") neoplasms on the basis of the histological characteristics of tumors. The "grading systems" are more and more elaborate, proliferate everywhere, occupying an ever-growing part of textbooks. This even goes to the point where diseases tend to be defined by their prognosis. It is not rare to find in the literature statements such as:

> "The evolution of dermatopathology, along with the development and introduction of new molecular biology techniques with the identification of new biomarkers, has opened a new field that may *[emphasis ours]* allow the classification of lesions in function of their prognoses in a completely objective and reproducible manner, putting an end to the eternal debates regarding the subjectivity of the currently utilized grading criteria." [Arumi-Uria M. Dysplastic nevus: the eye of the hurricane. J Cutan Pathol. 2008;35 Suppl 2:16-9.]

and even:

> "A diagnosis is a clinical tool that assists in the process of codifying patients into disease groups that share a common outcome and a common set of

response to therapy." [Elder D, Elenitsas R, Johnson Jr BL, Murphy GF, Xu X (eds.) Lever's Histopathology of the Skin. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2009.]

How far we are with this definition from the classic definition quoted earlier that has been the cornerstone of the practice of medicine for centuries! At least such a redefinition should be the subject of a debate among pathologists but no objection, no reaction is raised in the community of pathologists against those assertions and against new entities defined on the basis of them. They are even received with enthusiasm! Such profession of faith meets consensus if not unanimity. According to this textbook definition, penicillin sensitive pneumonia, pyelonephritis and meningitis would be one single diagnosis: each entity being able to cause death if untreated ("common outcome") and all of them responding favourably to penicillin ("common set of response to therapy")!

In fact even if the promise of "objective" classification of lesions according to their prognoses were met (and this is far from certain even in the mind of the author of the article quoted, as implied by his use of the word "may"), prognosis would still remain what it is: an approximation of the likely outcome; never a certainty. With time this leads to a devaluation of diagnosis and to confusion in the understanding of diseases, to a degradation of pathology itself.

Examples are numerous of the noxious consequences that result from confounding diagnosis and prognosis: It is the favorable prognosis of melanoma in situ that for years has impaired the recognition of its being melanoma; it is the "indolent clinical behavior" of small plaque parapsoriasis that continues to impair the recognition of its being mycosis fungoides; it is "outcome" of spitzoid melanoma metastatic to lymph node that purportedly justifies the flawed concept of "metastatic Spitz nevus"; it is purported indolent biologic behavior that constitutes the raison d'être of "small and medium cell cutaneous T-cell lymphoma" as an entity different from mycosis fungoides, etc.

In short, defining disease according to prognosis is a delusion. No clinician is satisfied by a "likely diagnosis" and no pathologist should accept entities defined by prognosis, a "judgment of the likely or expected development of a disease."

This is the first of four delusions hidden behind "prediction of outcome." It concerns the very understanding of diseases and affects the students of them.

The second delusion concerns the clinician and can be stated thus: informing a patient of his "individual prognosis" reveals a total misunderstanding of the nature of a prognosis—it being a statistical value and therefore applicable only to a population of patients.

It is perfectly true that various tumors have various prognoses and that any diagnosis comes with its associated prognosis. For instance, it is worse to suffer from small-cell carcinoma of the lung than from basal-cell carcinoma of the skin. One is therefore justified in communicating to a patient the prognosis associated with his disease. It is even correct to specify the prognosis by specifying the diagnosis in terms cogent, for instance, by typing and sub-typing tumors according to solid morphological basis, but prognosis nevertheless remains a (more or less) likely statement concerning the future of a **population of patients**, whereas diagnosis must remain a sure fact concerning the present of an individual patient. The patient dying from metastatic basal-cell carcinoma does not care for a minute that he had a 99.99% chance of survival when the rare patient surviving 10 years with small-cell carcinoma of the lung has had these years spoiled by the constant threat implied that he had a 90% chance of dying as a result of his disease. And to all other patients, that information is useless.

The only conceivable usefulness of prognosis is to calibre the aggressiveness of therapy: "bad" cancers are worth being treated more aggressively than "good" cancers. To this end the prognosis implied by a precise diagnosis should suffice.

Other aspects of the misunderstanding of prognosis by clinicians are illustrated well by the two following examples:

(1) We have seen a patient surviving 30 years with metastatic melanoma or small-cell carcinoma of the lung, who refuses to believe the diagnosis even after the slides had been reviewed and the diagnosis confirmed. Outcome was inconsistent with the diagnosis according to them and therefore the diagnosis must have been wrong. This is nonsense. Delusion. No individual outcome is inconsistent. The chance of winning a lottery may be very low, but can you imagine a winner being told that the fact that he won meant that it was not a lottery to which he participated?

(2) We have seen patients who thought they were cured and told by their doctor that "one never is cured from cancer" with devastating consequences. Delusion once again! Some patients **are** cured from even the worst cancers. In every case, moreover, the fundamental diktat of medicine, *primum non nocere,* must be respected; "information" such as "one never is cured from cancer" simply violates it.

The third delusion afflicts the pathologist, and it is enough to make one paranoid. It is not sufficient anymore for him to make a correct diagnosis. He must now also report thickness in hundredths of millimetre, grades histological and/or cytological on scales of 3, 5 and even 10, distances of margins in fractions of a millimetre, mitotic activity, percentages of tissue affected by cancer in a biopsy, presence of ulceration, necrosis, apoptotic rates, etc. And with all these "prognostic factors" added to it, his "diagnosis" soon fills two pages! Afraid of missing some "important prognostic factor" he

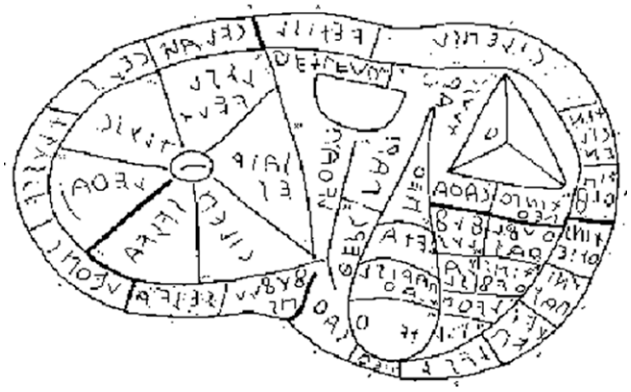

Figure 1. The bronze sheep's liver of Piacenza, with Etruscan inscriptions, intended as a guide to the haruspex of Roman antiquity for "predicting outcome" of battles. [Wikipedia. Haruspex. 18 February 2012. Accessed February 18, 2012. http://en.wikipedia.org/wiki/Haruspex.]

forgets to concentrate on diagnosis. After a while it becomes necessary for him to take refuge in the no man's land of "dysplasia" and other "entities of unknown or indeterminate significance" and, compiling data for "predicting outcome," he becomes something like a haruspex, this diviner of antiquity whose function was to predict, for the benefit of the Emperor (the clinician), the issue of a battle by reading in the viscerae of a sacrificed animal (the patient) (Figure 1).

Poor pathologist caught in such a cruel trap of being mocked!

The fourth delusion is induced in patients when, as a result of the first three delusions already described, they are informed of "their" prognosis. It may take various forms. For instance, a "good" prognosis may induce reassurance, perhaps even euphoria, only to be deceived later by facts whereas a "bad" prognosis if not inducing depression or despair, may spoil the duration of survival. More importantly perhaps, a subtle form of delusion is created in the mind of patients through a drift from "prediction of outcome" for diseased individuals to "evaluation of risks" for healthy persons.

After all, if it is legitimate for a suffering person to ask "what will happen to me?" it is just as legitimate for a healthy person to ask, "What are my chances of getting sick?" And when experts pretend to have answered the first question, it is only a matter of time before they become tempted to answer the second, acquiring the power to cure diseases even **before they occur!** Ultimately this transforms risks into diseases and makes **everybody** sick! After all, isn't life the ultimate risk in itself, the ultimate "disease" from which everybody shall die?

Without entirely discrediting "evaluation and treatment of risks," we wish to stress here the dark sides of it that can take delusional proportions. First, the apparent benefits of such an approach may appear as positive as to hinder any critic of it. Second, these same benefits apparently may induce, in a very delusional manner, denial of the side effects of "treating risks." Third, economical interests generated by treating a huge number of healthy persons may create massive incentive in favour of possibly useless or even harmful "risk therapy." Fourth, patients refusing to have their risks evaluated may be refused insurability or, worse, be brought to feel guilty for their insouciance [1].

In short, a diagnosis certain must remain the cornerstone of therapy; prognosis in individual case is of little, if any, utility to a clinician and may, in many ways, be harmful to patients. Pathologists therefore should concentrate exclusively on the diagnosis and forget about the prognosis if they want to avoid, as modern haruspices, being the laughing stock of future generations.

Reference

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