Letters

Probability, Logic and Medical Diagnosis

Ledley and Lusted [*Science* **130**, 9 (1 July 1959)] have suggested the use of mixed strategies in the treatment of patients. While it may sometimes be useful to know the strategy that would be optimum against an intelligent opponent, a doctor would have to be extremely pessimistic to use such strategy regularly. For example, if treatment T_1 has values 3 for disease D_1 and 10 for disease D_2, and if treatment T_2 has values 4 for D_1 and 3 for D_2, then Ledley and Lusted would suggest settling for the value 3⅞. If, instead, one assumes that in the absence of other information both diseases are equally likely to occur, then T_1 has an expected value 6½ and would certainly be chosen. As a patient, I would far prefer that the doctor follow the latter procedure. The use of mixed strategies in games against nature has frequently been suggested in other fields also and usually seems unsatisfactory.

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As a practicing physician who has been interested in the application of Boolean techniques to medicine, I read Ledley and Lusted's article with great interest. The authors' approach to the problem of differential diagnosis is naively simple. Their basic premise appears to be that most difficulties in diagnosis arise because the physician is either not aware of all the possibilities or is insufficiently acquainted with the symptom complexes. While this may be occasionally true, unfortunately most difficulties in diagnosis arise because the patient does not present the *classical* picture. A computer crammed chock full of textbook descriptions of disease, with minute listings of differences in syndromes, will rarely come up with the answer to a difficult problem in differential diagnosis. This stumbling block is fundamental and is inherent in the technical exposition of the authors.

I submit that the authors have handled the data sometimes in the manner of the propositional calculus and sometimes as class algebra, but always as if each variable were universally either true or false. The moment we go from the textbook to the patient, we must quantify. We must say, "some patients having certain symptoms have certain diseases," or even, "sometimes, some of the patients, presenting some of the symptoms, have some of these diseases." Thus, if the statements are properly quantified, the machine will hem and haw like a physician at the bedside.

This is not the time or the place to examine in detail the manner of arriving at a differential diagnosis. Sometimes we deal with diseases which affect many systems; in this case some of the techniques presented by the authors might prove valuable. In other cases a disease affects a particular system, in which case the physician first tries to determine which system is affected (for example, circulatory, respiratory, gastrointestinal) and then tries to pin down the particular entity involved. In many cases it is only by having intimate knowledge of the natural history of the disease, and by following the manifestations as they unfold, that we can arrive at a diagnosis. Many times the symptoms we have learned by rote (and unfortunately there is much of this) completely fail us. The astute physician must fall back upon his knowledge of physiology and disturbed physiology in order to arrive at a logical conclusion.

All this is not to say that a computer approach cannot help us. If a computer were properly programmed, as I am sure it can be, to rearrange medical knowledge into a more useful form, which could then be published, physicians would certainly benefit. A likely approach would be to employ the method of dichotomy. For example, there are probably 30 or more causes for shoulder pain. If we apply a single criterion—that the pain is elicited or aggravated by motion of the shoulder—we can divide these causes into two groups. In the group in which pain is elicited by motion, we apply a second criterion, limitation of shoulder motion and lack of such limitation. In two strokes the 30 possibilities have been reduced to nine. Further grouping on the basis of one or two symptoms would quickly narrow down the range of possibilities. To go through a list of possibilities sometimes enormously larger than this by the method proposed by Ledley and Lusted would require a much greater amount of time and work than the method of dichotomy. I should like to quote from a recent textbook (*1*): "If the set U were to contain 2^{20} (approximately 1 million) logical possibilities and we were able to ask yes-no questions in such a way that the knowledge of the truth value of each question would cut the number of possibilities in half each time, then we could determine with twenty questions any possibilities in the set U." Ashby (*2*) gives an even more striking description of the value of dichotomy. Another likely application for Boolean algebra in medicine would be to simplify criteria for diag-

nosis. The prototypes of this approach are the well-known Venn "club rules" problem (*3*) and the so-called simplification of insurance rules (*4*). Much more could be said about this approach.

Finally, the suggestion that game theory concepts be applied to medicine is an excellent one. It is a pity, however, that the authors, who quote Williams in another connection, do not mention the fact that his remarkable little book published in 1954 put forth this very same suggestion (*5*).

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References

1. J. G. Kemeny, J. L. Snell, G. L. Thompson, *Introduction to Finite Mathematics* (Prentice-Hall, Princeton, N.J., 1958), p. 81.
2. R. Ashby, *An Introduction to Cybernetics* (Wiley, New York, 1957).
3. Quoted in J. T. Culbertson, *Mathematics and Logic* (Van Nostrand, Princeton, N.J., 1958).
4. E. C. Berkeley, "Boolean algebra (the technique for manipulating 'and,' 'or,' 'not,' and conditions) and applications to insurance," *Record Am. Inst. Actuaries* **26**, pt. 2, No. 54, 373 (1957).
5. J. D. Williams, *The Compleat Strategyst* (McGraw-Hill, New York, 1954), p. 122.

The concept of mixed strategies is one of the fundamental concepts embodied in Von Neumann's so-called "game theory." When the strategy of the opponent is *unknown,* a mixed strategy on the part of the proponent will *minimize his maximum loss.* The concept does not require that the opponent be intelligent, as P. L. Bender seems to believe, but rather that the proponent has *no* information about what the opponent will do. If a patient has either disease D_1 or D_2, and if we have no further information, probabilistic or otherwise, then why assume that the chances of his having one disease or the other are equal? Why not assume that the chances are nine out of ten that he has D_1? With no information, the assumptions are equally valid—or, more precisely, equally invalid. As a matter of fact, the article observes that, "in actual practice, some further information bearing on the choice of treatment would be sought—that is to say, the formulation of the problem of which treatment to give the patient is far more complicated than that posed by the single problem discussed above." We then go on to quote J. D. Williams: "Perhaps its [the mixed strategy and game theory's] greatest contribution is . . . the general orientation given to people who are faced with overcomplex problems."

In replying to Milton Kunin, we first want to thank him for his interest in our work. The exposition given in our article was intended for readers who are not primarily mathematicians, but this should not lead Kunin to believe that our treatment of the subject is "naively simple." This is far from true, and judging from Kunin's letter many of the nonsimple aspects of our article evidently escaped his observation. In no way did we imply that the computer should be crammed "chock full" of textbook descriptions of diseases. In fact we devoted a whole section to the "Conditional probability or learning device," suggesting that the computer "learn" from current statistical experience (which of course it will compile from *nonclassical* as well as classical diagnostic "pictures"). It is this statistical experience that comprises the "medical knowledge" often referred to in the article. We even considered in some detail the effects of time and location on such statistical records and noted in the "Conclusions" that such a technique "emphasizes the greater significance and value of current statistics; it depreciates the significance of past statistics." Hence, Kunin's implication that "a computer crammed chock full of textbook descriptions of diseases" is a "stumbling block . . . inherent in the technical exposition of the authors," besides being irrelevant, is simply incorrect.

Another not-so-simple point evidently missed by Kunin is the relationship between logic and conditional probabilities. He seems to imply that we have not taken into account that only "some of the patients having certain symptoms have certain diseases." However, a large portion of the article is devoted to such conditional probabilities of patients with a certain symptom complex having a certain disease complex. In fact we open the section on "Probabilistic concepts" with the following remarks: *"Need for probabilities.* In the previous section we considered statements such as, 'If a patient has disease 2, he must have symptom 2.' While such positive statements have a place . . . , it is also evident that in many cases, the statement would read, 'If a patient has disease 2, then there is only a certain *chance* that he will have symptom 2—that is, say, approximately 75 out of 100 patients will have symptom 2.' Since 'chance' or 'probabilities' enter into 'medical knowledge,' then chance, or probabilities, enter into the diagnosis itself." The use of probabilities and the use of logic are not mutually contradictory, as Kunin seems to imply. In fact the propositional calculus of symbolic logic is one of the cornerstones of the theory of probability.

Finally, Kunin suggests that we use the "method of dichotomy," to use his words. Kunin is correct: The application of symbolic logic to the reasoning foundations of medical diagnosis as described in our article is *precisely* the

(Continued on page 930)

Letters

(Continued from page 892)

method of "dichotomy," as more thorough consideration of the article would reveal. However, as described in the article, the logical computations involved are of necessity far more complicated than the simple example Kunin gives in his letter. The references to Kemeny, Ashby, and Culbertson noted by Kunin are exceedingly superficial remarks which, in essence, claim that logic is good and useful. In our article we attempted to go somewhat further, to present an introduction to the means by which logic can be utilized and integrated with other mathematical disciplines into a multistage decision process. Kunin's remark is analogous to telling a physicist that mechanics is based on Newton's laws. This we know; the problem is how to apply them. Algorithms for the more complicated logical computations are given in references 5, 6, and 7 of our article. [See, for example, R. S. Ledley, *Digital Computer and Control Engineering*, McGraw-Hill, New York, in press.] Note however that in its simplest form the "conditional probability or learning device" described in the article is in a sense a "logic machine" as well as a probability machine.

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Struggle and Stimulus

The recent editorial by Warren Weaver, "Dither" [*Science* **130**, 301 (7 Aug. 1959)] is highly interesting and perhaps reflective of something deeply significant.

It is common to look at situations like the complete absence of friction, or the complete absence of invasion of the human body by afflictions of any sort, as the optimum toward which to work. The heaven of which one dreams is one devoid of all adversity—a place where wants are fully and constantly satisfied.

But can it be so? Weaver points out a function of irritation. Some evidence persists that optimum "health" is a state of successful struggle against organisms; that from such struggle the body gains a quality it would not otherwise attain. Economic endeavor, a persistent battle against want which can never be completely won, may be useful therapy against a sense of futility. A life totally devoid of need and struggle and choice, in other words, describes a hell rather than a heaven.

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Warren Weaver's editorial pleases me because it seems to go along with my own ideas on overspecialization in this world of ours. It is useful to see the woods sometimes as well as the trees.

I should like to go even farther than he does and say that some town ought to invest more money in training and hiring its teachers for the first four grades of elementary schools than it does for its high schools. The young mind, stimulated by the exciting new ideas of our present world, ought to be trained to work and think efficiently during the enthusiastic days of its first discoveries. Years of wasted time could be saved for many of our coming scientists.

Our fabulously rich foundations give millions to colleges. This is to be commended, but they could be missing their great chance. Whatever our children accomplish in their lives, their accomplishments will be greater if they learn to think at 6 instead of 16.

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