

Instrumental Tests in Medicine: Are they determinant tests or supplementary tests?

“Science explains experience but it does not for all that annul it”...
That explains why “*When a symptom or an isolated functional mechanism is considered pathological, there is a tendency to forget that what turns it into pathology is its relation in the indivisible totality of an individual behavior.*”

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The Normal and the Pathological

INTRODUCTION

The points that will be developed are designed as dialogues between two symbolic characters, which stand for two different medical concepts.

Even though struggle forces, interests, coercion, and advertisement play a greater role in knowledge and even in medical science growth than the role rational points commonly play, formal education relates “enunciations” to “apparent facts”, which are imprinted as ideological beliefs introduced in physicians’ everyday language terminology. After such training, they seem to belong to the natural interpretation of facts.

In order to change this situation, it is “also” necessary to be shaken up by a critical discussion of these convictions.

In a way, and keeping in mind the essential aspects, the idea is to paraphrase, as Feyerabend says, the “tag-team intrigues” used by Galileo in his *Discorsi e Dialogo* that is, like the *Discourses and Mathematical Demonstrations*, or the *Dialogue Concerning the Two Chief World Systems*, a friendly conversation among three symbolic characters -although Sagredo and Salvati were also real characters and friends whom Galileo wished to immortalize.

Salvati stands for him in the dialogue; his opponent is Simplicio, a defender of the university Aristotelic tradition, and there is also the clever Sagredo, open-minded and free from school prejudices. In these dialogues -first time written in ordinary Italian language-, Galileo unmasks the “natural interpretations” in Cosmology that were used in the everyday discourse of his time.

Two contradictory characters take part in the development of this work. One of them is the “**Physiocybernetic**” (“*fisiocibernético*”), a coinage made up of two words that, according to the

Diccionario de la Lengua de la Real Academia Española, would mean something like the following: “*a person who cultivates a science of the body nature and studies the comparison between the communicational and automatic regulation systems of living beings and the electronic and mechanical systems similar to them.*” And the other one is the “**therapist**”, a term derived from the Greek word *therapeia*: “*to serve, to care for, to assist*”, which, in its primitive acceptance, means the one who serves, the serf, the servant; that is, the one in charge of looking after the patient and being at his service.

Now, let’s listen to the dialogue:

BEGINNING THE DISCUSSION ABOUT DIAGNOSTIC TESTS

– **Physiocybernetic**: Up to the last decade, the clinical diagnosis of the coronary artery disease was rather old-fashioned in cardiology; the same criteria established by Heberdeen two hundred years ago regarding the diagnosis of acute myocardial infarction were still being applied.

Fortunately, the evolution in science and technology has given birth to dynamic tests and allowed for the massive use of graduated stress test, stress echocardiogram to evaluate non-stress and stress ventricular function, and thallium isotopes, which helped infer the perfusion during stress and its post redistribution in basal conditions.

At present, all these techniques have resulted in accurate and secure diagnosis, even for those patients with asymptomatic ischemia.

– **Therapist**: Even though it is true that on certain situations these diagnostic practices and many others under development are representative of sig-

nificant progress, its workings and routine usage poses questions that might sound paradoxical...

For instance, we should ask ourselves: What diagnostic value does a positive test have? Is it necessary to perform the new dynamic tests to all patients or just to some of them? At what stage of the coronary artery disease should tests be performed? In what order of priority? What do two discordant tests –a positive one and a negative one– mean? Which one is worth for this patient?

– **Physiocybernetic:** Let us take it step by step. I think your position is anachronic, and with your skeptic questions you fall back doubts on the new techniques, and on the techniques being developed to measure perfusion and metabolism, which, though not perfect since we all know there is nothing perfect in this world, are quite good and much better than the clinical criteria we had before.

– **Therapist:** This time I do agree with you.

– **Physiocybernetic:** Well, at last!

– **Therapist:** I agree on the fact that the idea of the “perfect tests” is an illusion for all those who are not experts in medicine and, to be honest, even for some physicians who even believe that a test with a positive result is “undoubtedly” an indicator of a disease, and when it is negative, it is “always” discarded.

Take into consideration that if *perfect tests* did not exist in medicine, we would just need **only one test** to diagnose each clinical condition. And this conversation would end up right now.

Moreover, there would be the additional fact that if a test for a given disease were very simple and cheap, we could even do away with the physician, because the test itself would be enough for diagnosis.

That would leave you satisfied! Wouldn't it?

– **Physiocybernetic:** Putting aside your truly ironic tone, I am sure the scientific advances will fortunately lead us to this, whether you like it or not.

– **Therapist:** But that never works out that way; all of us physicians know the *perfect tests* in medicine **never exist**. When we say a test is perfect, what we mean is that it would detect **all** the patients, or better said, that all the patients would have a “positive test”; this is what they call the “*sensibility*” of a test, the capacity –in percentage– to detect patients. It is obvious that a perfect test should have a 100% of sensibility. But also, at the same time, the test interests us and is used to rule out the condition; in the case of a perfect test, we should be able to identify 100% of non-ill or healthy individuals. That is called the “*specificity*” of a test.

Within the biological sciences, physicians know, because they have experienced it themselves, that tests are “*less than perfect*”; and they are valued among themselves, recognizing their greater or lesser degree of deviation.

TESTS DO NOT DETERMINE THE DISEASE, IT IS THE NOTION OF THE DISEASE THAT ASCRIBES THE VALUE OF ABNORMALITY TO A TEST

– **Physiocybernetic:** I believe what you say will become part of the past. Tests created in the near future will make it possible to tell a person if he is healthy or ill of “such disease”, and they may become perfect. It will only depend on the technological development, which grows faster and faster. I see **no** theoretical impracticability; it should be a plausible goal.

– **Therapist:** However, its impracticability lies in that the criteria of health or disease, more than a quantifiable fact, is a value judgment for the individual who suffers from it; consequently, according to the words of the philosopher and physician Georges Canguilhem (1): “*We argue that life of a living being, even if it were an amoeba, only recognizes the categories of health and disease at the experiential level, which is mainly a test in the true sense of the term, but not at the scientific level. “Science explains experience but it does not for all that annul it”.*”

That is why: “*When a symptom or an isolated functional mechanism is considered pathological, the tendency is to forget that what turns it into pathology is its relation in the indivisible totality of an individual behavior.*” Thus, if the physiological analysis of separate functions detects the presence of pathological facts, it is because this detection is due to previous clinical data, since clinics relates physicians to complete and concrete individuals and not to organs and their functions. Pathology, whether anatomic or physiological, analyses to learn more data, but it can only get to know what pathology is, that is to say, the study of the mechanisms of disease, because it gets that notion of disease from clinics, whose origin is to be found in the experience individuals have about their group relations with the environment.

The conclusion may be the following: “*To put it in a nutshell, when speaking about objective pathology, when believing that the anatomic and histological observation, the physiological test, the bacteriological test, are methods that allow for scientific diagnosis of the disease, which can be applied without any interview or clinical exploration, we become victims –we believe– of the most serious and at times, therapeutically speaking, the most dangerous philosophical confusion. A microscope, a thermometer, a culture medium is not acquainted with a medical science that even the physician would be unaware of. They provide a result. That result has no diagnostic value in itself. In order to make a diagnosis, it is necessary to observe the patient's behavior... With regard to pathology, the first word, historically speaking, and the last word, logically speaking, corresponds to clinics.*”

Medicine in itself is unable to recognize the “*judgment it means to be ill*”, if that “value” has not

emerged in the individual's conscience. *"Now, we believe **there is nothing in science which has not emerged before in the individual's conscience...** If nowadays the physician's knowledge of the disease prevents the patient's experience of that disease, this can be explained because, a long time ago, it was the latter that generated the former. Thus, it is certain that the medical science, always legal or even factual nowadays, exists because individuals do feel ill and not because they inform physicians of their diseases."*

The "gold standard" of physiological or lab tests, both in the past or in the future, is the individual's conscience which expressed itself in a different way from its normal state; that is why there are no perfect tests, since **tests do not determine a disease but it is the notion of disease which assigns the abnormal value to a test.**

– **Physiocybernetic:** It's ok! Enough of philosophy! I had already accepted that perfection does not exist in this world; but in everyday life, a small percentage of inaccuracy does not invalidate the results of these important physiopathological tests.

– **Therapist:** We should accept and discuss what we imply when we say that tests in medicine "are the least perfect".

This means 100% sensibility is not possible; consequently, apart from those ill patients diagnosed by the test –those would be the "true positives" (TP)– there are ill patients who cannot be diagnosed by the test –the so-called "false negatives" (FN); together with these two groups, a third group of non-ill patients coexist, wrongly labeled as ill patients because they have a positive test –"false positives" (FP)–, so the specificity is also lower than 100%.

Therefore, the physician has lost his/her virgin ingenuity forever, and when he/she has a positive test, he/she should bear in mind it is possible, at times, to make a false diagnosis (FP); or the other way round: when the test is negative, he/she should have a healthy distrust, because from time to time the test is false negative (FN) and he/she may mistakenly tell an ill patient for sure that he is healthy, with the expected consequences this could result in.

SOME SIMPLE MENTAL CALCULATIONS TO LEARN HOW DIAGNOSTIC TESTS WORK

– **Physiocybernetic:** Everything's fine! But the exception proves the rule, and the rule is the significant advance generated by the diagnostic tests.

– **Therapist:** I see you will not be persuaded by theoretical discussions, so my proposal is to put forward ordinary situations in the clinics of patients.

– **Physiocybernetic:** That's good! It seems to be a reasonable proposal. Do start!

– **Therapist:** Fine. Let's suppose a 55 year-old man, who is hypertensive and heavy smoker, visits your office. This patient tells you that when walking, especially in the morning, he feels an oppressive

retrosternal pain that radiates to the left arm and recedes in a few minutes, when he stops walking.

– **Physiocybernetic:** You are putting forward a common case of angina pectoris.

– **Therapist:** But what is **not** so common is that, upon asking him for a cardiac stress test, he reaches the expected maximum heart rate, with no angina or alterations of the ST segment of the ECG. What would you think about it?

– **Physiocybernetic:** Well, I think I would consider the possibility that I was wrong and would admit the patient does not have angina pectoris. But if it was you who put forward the case, it is almost sure you will now say he is a "false negative"; I would like to know how you would manage to convince me with something else than talkative dialectics.

– **Therapist:** Instead of words, I propose you to use numbers and the elementary algebra, to learn the different possibilities. Will you agree on this?

– **Physiocybernetic:** Absolutely! Numbers are more definite and accurate than words.

– **Therapist:** Ok, as an approach to reality, let's use numbers that are mentally easy to handle. Would you agree on a 90% sensibility to the ergometric test? In that case, we would detect 90 "true positives" out of 100 patients, and we would have 10% "false negatives"; if you also agree on a similar specificity of 90%, we would classify 9 "non-ill patients" out of 10 healthy ones, and we would have 10% "false positives".

– **Physiocybernetic:** I guess a test with those characteristics would prove effective. However, I would like to know what the true sensibility and specificity percentages are.

– **Therapist:** With this approximation, I am giving you an advantage, since it is known that the ergometric test has an approximate sensibility of 75% and a specificity of about 85%.

– **Physiocybernetic:** Ok, these being the case, please go on.

– **Therapist:** Will you agree that, for a 55 year-old man with two coronary risk factors, and an interview of typical effort angina pectoris, his chances of having coronary artery disease are higher than 90%?

– **Physiocybernetic:** Agree; what is technically known as "prevalence" of coronary artery disease is more than 9 out of 10 patients with those characteristics.

– **Therapist:** That said, now we could calculate what possibility a patient with a negative test would have to have coronary artery disease, of course with these clinics.

– **Physiocybernetic:** That is precisely what I want you to prove me!

– **Therapist:** What we have to do is get to know what the percentage of "false negatives" is –ill patients, in spite of a negative ergometric test– out of all the negative tests (false negatives + true negatives).

– **Physiocybernetic:** That's right, but how would you calculate it?

– **Therapist:** In a group of 100 individuals with these clinical characteristics, we said there would be a “prevalence” of 90 patients with coronary artery disease, and therefore 10 “non-ill” patients, out of which we would detect 9 as “true negatives” due to 90% specificity of the test. Of the 90 ill patients, as we have a 90% sensibility, we detect 81 “true positive” patients and 9 would be “false negatives” for the test. In this situation, there would be an equal number of “true negatives” and “false negatives”; hence, despite the negative ergometric test, there would still be 50% likelihood of developing coronary artery disease.

– **Physiocybernetic:** Can’t it be you arrived at these conclusions because you used sensibility and specificity values that are not real?

– **Therapist:** This isn’t so. If I used 75% sensibility with 85% specificity to calculate post-test probabilities of the so called Bayes’ Theorem, developed by Reverend Thomas Bayes in 1736, the likelihood of developing coronary artery disease after a negative ergometric test would be around 80%.

– **Physiocybernetic:** So that would mean that if your patient’s individual clinical characteristics show a high likelihood for coronary artery disease, a negative test **does not** discard that disease.

– **Therapist:** No doubt you are right; you have come to a reasonably right conclusion.

– **Physiocybernetic:** So please let me bring into your attention an example opposed to the previous one, because I want to know about your reasoning. If your patient was a 38 year-old woman, with no risk factors, very short-timed shooting pains, no spread, and no effort-related, but bringing an ergometric test prescribed by another physician, and its report reads the test has been positive for the ST segment depression of 1 mm with no pain at this work load. What would you think about it?

– **Therapist:** In a 38 year-old woman with a **non**-coronary pain, the prevalence of the coronary artery disease may be around 1%, and in fact we would detect fewer than 1 out of 100 patients with those characteristics, because we do not have 100% sensibility but rather a conventional percentage we set at 90%; however, to make it even simpler, let’s accept we detected only that female patient as a “true positive”. There remain 99 women who would not be ill, but with the 90% specificity; 89 out of 99 would be “true negatives” and 10 out of 99, “false positives”.

So we would have 1 “true positive” and 10 “false positives”, that is, only 9% of the individuals who had positive tests would be ill. Making exact calculations using the Bayes’ Theorem, the likelihood of developing coronary artery disease would not reach 5%.

– **Physiocybernetic:** I imagined so; this means that, if we are seeing a patient whose likelihood of developing coronary artery disease is low due to his/her characteristics, a positive test **cannot** confirm the disease.

– **Therapist:** In conclusion, through the analysis of these polar examples, we can state clearly that if the likelihood of developing coronary artery disease is low enough, as in the case of this 38 year-old patient with non-angina pain, whose likelihood is around 1%, when the test is negative, it will lower to 0.2%, and when it is positive, it will reach 5%. So, the result of a test –whether negative or positive– does not tell us anything new and does not add useful data in a patient with low disease prevalence. If it is negative, it confirms what we already knew, its low likelihood of developing the disease, and if it is positive, the disease **cannot** be confirmed.

In the other example, with the 90% of pretest likelihood, it lowers to less than 80% if it is negative and reaches 99% if it is positive; similarly, the test result does not tell us much either, since in both situations –a positive or a negative test– the likelihood of developing coronary artery disease is still high.

– **Physiocybernetic:** In the given examples, no matter what the results of the test are, they do not provide us with any data to be able to confirm or discard the diagnosis. But since the tests and lab data are still in use, it may be of help in certain situations. Which ones?

– **Therapist:** As you may already be suspecting, it will be useful for those patients with an intermediate likelihood of disease. For instance, for those patients with 35 to 65% likelihood of coronary artery disease.

– **Physiocybernetic:** Which groups of patients are those?

– **Therapist:** Let’s lay out some of them; there are women younger than 45 years old with typical angina pectoris, or the atypical angina in a woman older than 55 years old; the atypical angina in men of any age; or also in situations in which pain does not meet the defining characteristics due, for instance, to its location –in the epigastrium, the jaws, the elbow, or the arms–, but looks suspicious of being caused by a coronary disease, due to its repetitiveness. The suspicion itself gets the likelihood for coronary artery disease being in an intermediate level. In these cases, an ergometric test is indeed of value, since the discomfort associated to ST segment depression would confirm the diagnosis of coronary artery disease.

Therefore, in all that group of patients for whom doubts are justified, the likelihood of coronary artery disease will be high enough to allow for indications of dynamic functional tests to get to an approximate diagnosis.

– **Physiocybernetic:** If I have understood correctly, we could say the important thing is to reach high diagnostic likelihood. If this is achieved during clinical consultation, a positive test does not add information, and a negative test does not discard the diagnosis, because if you gave ear to it, you would be overmuch mistaken.

Conversely, to those individuals with a very low likelihood of disease, such as those who attend check-ups, the positive test adds very little likelihood and most of the times it would not indicate disease. If this is so, wouldn't the physician move little by little, either with clinical or lab steps, to increase the certainty of his/her diagnosis?

– **Therapist:** When the patient sits down at the doctor's office and the doctor gets to know the patient's sex and age, the doctor gets a first idea of the prevalence of the coronary artery disease; after interviewing his patient, he moves from that first likelihood towards a second likelihood; the signs he finds may help form a new likelihood, and finally –if these findings are not enough– the tests, in the same way as the signs and symptoms do, will complete the diagnosis, increasing the patient's degree of likelihood of developing coronary artery disease.

So the physician works gradually with the symptoms, the signs, and the tests, approaching or separating the likelihood of the disease, which, in this particular situation, means the likelihood of developing coronary artery disease.

THE CRITERIUM OF TRUTH OF THE DIAGNOSIS IS PROVIDED BY THE "PRACTICE" IN THE FOLLOW-UP EXPERIENCE

– **Physiocybernetic:** It's okay; here comes the time when there is high "statistic" likelihood, I mean, mathematic likelihood of developing a disease. In spite of my unlimited support to the technique and procedures, a high likelihood is not enough for me to feel unalarmed for a patient.

– **Therapist:** You have reasons to be alarmed. If we tell a given patient that his/her likelihood for a given disease is 90%, this is true only for a limited number of individuals who had those characteristics; but in this patient's particular case, the one we are talking about, I will be right if he/she is indeed ill, and I will still be right if he is not, because he would belong to the 10% of healthy patients we had anticipated.

– **Physiocybernetic:** But to be always right, whatever the result and in spite of the use of very precise numbers, means the same as not knowing or not being able to say anything about that particular situation.

– **Therapist:** That is precisely what I am trying to tell you; because of their formal learning, physicians tend to consider that statistics allow for assigning numbers to the chance; however, empiric generalizations for large numbers of people are statistic-probabilistic and inferential affirmations, only applicable retrospectively to the population from which the sample comes from. Logically speaking, they will be "*retrodictions*", and not "*predictions*" to be used to anticipate the progress in individuals undergoing the disease *a posteriori* of the statistical study, since in that case we should admit the persistence and immo-

bility of the universe facts: just think of mutations of bacteria and viruses. Thus, the statistic and inferential method loses a major incentive for medical studies, which consists of being able to take action on future ill patients.

To be considered scientific, any affirmation should be submitted to practice, and practice will determine if such affirmation is verifiable or false, depending on the different epistemological schools.

If anything occurring in practice always acknowledged you to be right, an affirmation would be irrefutable and therefore not scientific; moreover, it would be useless to practical application.

Since physicians work with concrete and individual persons, who are obviously not populations, statistical affirmations of empiric generalizations are irrefutable but not scientific when applied to a single person.

– **Physiocybernetic:** So how shall we get out of this awkward situation?

– **Therapist:** To solve the problem, let's see how those physicians who take major and minor decisions everyday without arriving hundred percent at the diagnostic possibility behave.

It means the diagnostic problem is not solved through the "theory" of the tests; rather, it is useful for analyzing at what stage in the diagnostic chain – interviews, clinical exam, test– the likelihood of a disease is "acceptable enough" and, consequently, the risk of a treatment is "reasonable" for that patient in particular.

But that's not the end of the problem. We are still mid-ride. As for any other diagnosis, the criterion of truth in diagnosing coronary artery disease is provided by the "clinician" by experiencing his/her patient's longitudinal follow-up.

Diagnosis is a process in which the physician gets into first contact with the nature of his/her patient and, through various methods –interview, observation, exams, tests–, goes from a sensation to an abstract concept of the patient's problem. This interaction pivots on the generalization of theoretical patterns that anchor the social experience and summarize the medical knowledge of humanity.

But if we stay here we will not generate any concrete knowledge for our patient; this abstraction turns into "guides for action" and thus becomes a starting point for a spiral movement in the process of knowledge, which is now subordinated to the practical activity of transforming the patient's situation.

This link to the practice, in our case the medical practice, will allow us to "move away" from the number to return to the quality; we have moved away from the abstract generalization to go back to the concrete reality of the patient, who is related to particulars and multiple determinations; that way it is possible to verify the truth, especially about diagnostic reality, in this dialectic movement.

– **Physiocybernetic:** So I understand that when I begin a course of treatment I may be formulating a

“hypothesis” about the diagnosis, which has a high degree of reliability, but is never absolutely certain. If with the later practice I notice the patient’s discomfort has disappeared with the treatment and does not reoccur, and that in certain circumstances the tests improve or even get normal, I might be satisfied because my diagnosis has been plausible and my treatment has met my patient’s needs. But if the patient does not respond to treatment, what should I believe?

– **Therapist:** We tend to think the treatment is not right for the patient; but we should also consider that it is a “wrong” diagnosis.

VALUE OF THE VARIOUS TESTS FOR THE SAME DIAGNOSIS

– **Physiocybernetic:** So we should leave open the diagnostic hypothesis when we follow up patients, and this hypothesis is gradually confirmed if they adequately respond to treatment; but if they do not improve as expected, we have to consider the two alternatives: is this the right treatment?, or have I made a wrong diagnosis? Now, we have discussed the tests in general, but isn’t there a very significant difference in quality among the diagnostic tests developed in recent years?

– **Therapist:** What do you mean?

– **Physiocybernetic:** My exact question would be the following: Aren’t the newest diagnostic tests, such as the ones with isotopic markers, better than the previous ordinary tests? And shouldn’t they replace the older or the already conventional tests?

– **Therapist:** There is a particular idea among physicians that the latest tests are the best ones. But, as we have already discussed, the role a test plays is to increase or reduce the likelihood of disease after being performed, which is called post-test probability.

Hence, the efficacy of a test depends on its sensibility, specificity, and on the target population it is performed on; that is to say, when tests have similar sensibility and specificity, their efficacy is similar.

Although at the beginning a new test seems to have better sensibility or specificity than the definitive one because it is used in patients with advanced stage of disease, as years go by, it has been demonstrated that even though the radio-isotope tests may have a bit higher sensibility and better specificity, they are not definitively more efficient than the ordinary ergometric test.

– **Physiocybernetic:** Does that mean it is not necessary to begin with sophisticated or costly diagnostic tests?

– **Therapist:** Exactly. We “should” begin with simple tests, which are also cheap, and if they do not give us a convenient diagnostic certainty, they may be supplemented by a more complex test.

– **Physiocybernetic:** Isn’t it possible to begin searching for calcifications in the coronary arteries in a radioscopy with the image intensifier, as it is performed in other places?

– **Therapist:** Yes, it is. This method is not used in our country, but since its sensibility and specificity are similar to the ergometric test, it may be used as initial test instead of the ergometric test. Look! We cannot tell one test is better than the other one; the possibility of using one or the other at the beginning depends on the criteria associated to the medical practice in each country, such as provision of machines, costs, prevailing medical culture, etc.

This is so when the test is used to diagnose; but if the intentional goal was the prognosis of coronary artery disease, a functional variable such as the exercise duration would probably have more prognostic than diagnostic value, whereas an anatomic variable, such as the presence or absence of calcifications in the coronary fluoroscopy would probably have more diagnostic than prognostic value.

– **Physiocybernetic:** In addition to these conditions, there should be special clinical conditions for which it is preferable to use one test and not another.

– **Therapist:** Undoubtedly, there are situations in which we use a test instead of another, not because of its general characteristics, but because that test provides trustworthy information under certain special conditions of that patient that another test would not provide.

As an example, we may say we used to have patients who were difficult to treat, with suspicious clinics of angina pectoris and left bundle branch block or left ventricular hypertrophy, for which the analysis of the cardiac stress test was very equivocal due to basal repolarization alterations. In these patients, the problem is resolved by performing a stress echocardiogram, in which the ischemia marker will be determined by the transitory segment alteration of the parietal motility, and not by the electrophysiological alteration of the electrocardiogram.

At the same time, it is possible that a new test provides confusing data. In the case of a patient with cardiomyopathy and angina pectoris, if the stress echocardiogram shows a fall in the stress ejection fraction, it may be due not to ischemia but to alterations of the “load” in the patient with chronic myocardial damage, and an ordinary test with angor and manifest ST segment depression may constitute a clear diagnosis for coronary artery disease.

Sometimes, due to the prognostic and therapeutic implication, it is possible to begin with one test instead of with the other. Let’s imagine we have a patient with angor pectoris and signs of coronary artery disease. To start with a stress echocardiogram allows us for measuring the global basal left ventricular ejection fraction –chronic damage rate–, and recognizing the amount of ischemia by the magnitude of the fall in the stress ejection fraction. Of course these patients have a guarded prognosis, and if ischemia predominates in the pump failure, the resolution for the coronary artery disease would probably imply a better distant prognosis.

– **Physiocybernetic:** At this moment, I should re-ask one of your first questions. In the case of those patients undergoing more than one test, which test is valuable in discordant situations? In other words, what conclusion would you arrive at?

– **Therapist:** At times, it becomes a clinical problem, difficult to solve. In general, we may say that if the likelihood of coronary artery disease is very high and, out of two performed tests, one is negative, the likelihood will still be high, and no matter which test is negative, the test will not discard the diagnosis. Conversely, when the likelihood is very low, as in checkups, and only one test is positive out of two, it is impossible, by no means, to sustain the diagnosis of coronary artery disease.

The concrete problem comes up when the tests are used for those patients with intermediate likelihood. In that case, with two tests, one positive and one negative, whatever it is, the diagnosis cannot be confirmed or discarded. Unfortunately, the tests do not provide any useful information and leave us in the same position we were before the tests; in this situation, the physician must use all the resources acquired throughout his clinical experience to solve the problem.

VALUE OF DIAGNOSTIC TESTS AS SCREENING

– **Physiocybernetic:** Despite I agree with what has been discussed so far, and even being aware of the low likelihood for the disease and the deficient predictive value, wouldn't it be reasonable to perform the test all the same, to detect some patients and treat them, since there is no other way to find them?

– **Therapist:** This would mean that, even though the positive test has a low predictive value in asymptomatic or oligosymptomatic patients, those few "true positive" patients would benefit from an effective treatment. Since at the same time "false positives", that is, "non-ill" patients, will frankly predominate, whom we should also treat due to the test result, these healthy patients will be under the risk of performing the test they should not even run, whether minimum or not, and they will also receive a course of treatment, which may be prolonged, with its side effects and underlying risk. And although we cannot quantify it, these healthy patients would be "recognized" as ill, in a much higher proportion than the true ill patients, with the social and personal load of undergoing a daily treatment of an undoubtedly lower life quality.

When dealing with groups and not with individuals, we can consider a disease likelihood "threshold" to decide –below its level– "not to treat" anyone, or –above its level– "to perform" the test and treat those individuals with positive test. This threshold will vary according to the balance between the benefit of treating "ill patients" versus the risk of treating "non-ill patients"; at the same time, it will depend on how safe the test that determines the "false positives" is,

which is inversely related to its specificity, the test risk and the treatment benefit/risk balance.

While we physicians do not like to make the mistake of leaving a real patient untreated, the problem of these patients we do not diagnose is not solved with the tests; in fact, there is no solution at that stage of the diagnostic chain. If any of these alleged patients has a real disease, such as coronary artery disease, at some point in the clinical follow-up made by his primary care doctor, or during the patient's consultation for some discomfort he feels, due to his self-care, the patient clearly refers the onset of the symptoms, which is generally defining with respect to the diagnosis.

This problem is not solved in the static cross-section of a consultation or a lab test, but in the course of a temporal process of a person's care; this is a phenomenon clinicians were aware of some years ago and which makes current healthcare system much more difficult.

– **Physiocybernetic:** And what about the reverse situation?

– **Therapist:** You mean when the prevalence of the disease is not high enough for the test to provide relevant data.

– **Physiocybernetic:** Shouldn't we prescribe the test all the same, to avoid the risk of treating some "non ill" patients?

– **Therapist:** It is reasonable to think that, even if there are not many patients –in the example we analyzed before there were 10 out of 100 patients–, it would be appropriate and correct not to treat the healthy patients detected by the test.

The problem we have is that, with a test sensibility under 100% –imperfect tests–, not only will we not provide treatment to those non-ill patients –the "true negatives"– but also we will not treat a certain number of patients the test did not detect –the "false negatives"–, who are inversely related to sensibility but **are indeed ill**.

Again we must balance the risk of treating "non-ill" individuals we should not treat versus the loss of the benefit –with its due risk– of leaving untreated true ill patients because the test wrongly classifies them as healthy ones.

By being acquainted with the test efficacy –especially sensibility–, the test risk and the treatment relation risk/benefit, it is possible to set the "threshold" above which treatment can be done without performing the test, and below which the course of treatment will be determined according to the test reply.

TEST VALUE TO DETERMINE THE COURSE OF TREATMENT

– **Physiocybernetic:** Specifically, when is a test performed to determine the course of treatment if the test is positive, or not to determine it if the test is negative?

– **Therapist:** You are again dealing with the "intermediate prevalence group", this time not to diag-

nose, but to determine the course of treatment. This group may be increased or reduced, depending, as I said many times, on the test efficacy –specificity and sensibility–, its risk, and the risk or benefit the treatment implies.

I may say that if the test was very efficient and the risk was very low, that group would increase in number and more ill patients with high or low likelihood should undergo the test. If tests implied a risk to be considered, as in the case of punctures such as the endomyocardial biopsy, or if tests were not safe enough, or if treatment implied a certain risk, as in the case of immunosuppressants, the need to perform a test lowers significantly.

TEST VALUE FOR PROGNOSIS

– **Physiocybernetic:** I would like to discuss a prevalent issue in diagnostic tests: the long-term prognostic value of the ergometric test in asymptomatic individuals, that is, in groups with a very low prevalence of disease, as shown by the follow-up prevalence study carried out by the Lipids Research Clinics. (2)

– **Therapist:** This is one of the latest works on the prognostic value of the ergometric test. This was a multicenter trial; a heterogeneous group of researchers admitted patients including a high proportion of hyperlipidemics, since its aim was to investigate their treatment. A close reading of the work tells us that 3% of the patients had angina pectoris, and about 13% had dyspnea on exertion, with ages ranging from 30 to 79; this means it was not a population selected by lack of symptoms.

It should be strongly emphasized that, even if it is true that patients had an increased mortality risk for cardiovascular disease, they also had an increased mortality risk –close to the first one– for non-cardiovascular diseases; so it seems that a positive ergometric test not only predicts an increased likelihood of dying of cardiovascular disease, but also indicates an increased possibility of dying of non-cardiovascular diseases.

The work methods prevent from learning the initial symptom of the cardiovascular disease, because patients were contacted annually, and when they died, the death certificates were obtained and some of the physicians from the events committee were able to interview a close relative; with these elements, patients were classified as having died of a “cardiovascular” or “non cardiovascular” disease.

The problem of learning if the “cardiac events” in asymptomatic patients are “a bag of tricks” of equal significance still remains. By “cardiac events” we refer to angina pectoris, non-fatal myocardial infarction, and sudden death. Most works deal with these different final points, as if they were homogenic to the term “coronary event”; however, I’m strongly doubtful regarding the prediction of the alteration in the cardiac stress test in asymptomatic patients.

– **Physiocybernetic:** Do you mean the ergometric test in asymptomatic patients selectively predicts some “coronary event”?

– **Therapist:** A thorough work carried out by Paul Mc Henry et al, published in 1984, (3) answers that disturbing question.

They did the following: they monitored about 1,000 patients for 12 years on average, performing serial ergometric tests to learn when they became abnormal and, through close individual follow-up care, learn when the first symptoms appeared.

This way they found out an interesting fact: for those individuals with alterations of the ST segment in the cardiac stress test, the first symptom that appeared 80% of the times was the angina pectoris; the non-fatal myocardial infarction appeared 10% of the times, and the remaining 10% of patients had sudden death. However, the initial symptom on those individuals with no alteration of the ST segment in the test was only 27% for angina pectoris –versus 80% of the ones who had alteration of the ST segment–, 57% for myocardial infarction, and 16% for sudden death. Apparently, the incidence on the first coronary event is different between patients with or without alteration of the ST segment in the test.

– **Physiocybernetic:** What you pose would be the “proportional” percentage of those patients who have a first event; in fact, it would be necessary to know the “absolute rate” by hundred or by thousand of each group, differentiated by the ergometric test.

– **Therapist:** The angina pectoris as “first coronary event” was present in almost 22%, in an average follow-up of 12 years in individuals with ST segment depression, versus 1.4% in those who did not have it; The “relative risk” of angina increased significantly more than 15 times. However, the occurrence of non-fatal myocardial infarction was not higher –1.2% in those who had ST segment alteration, and 3% in those who did not have it–, and sudden deaths did not occur either –1.2% versus 0.8%, respectively. As the first coronary event, those patients with alteration of the ST segment showed a tendency to a lower rate of myocardial infarction and sudden death, although it was not statistically significant.

The title of the work is very explicit. It says, literally: *The abnormal exercise electrocardiogram in apparently healthy men: a predictor of angina pectoris as an initial coronary event during long-term follow-up.* (3)

In his work, Mc Henry concludes that the only prediction an abnormal stress cardiac test can make on asymptomatic individuals is the possibility to develop “angina pectoris”; out of those patients who developed angina pectoris, about 30% had “myocardial infarction”, but the minimum period between the occurrence of angina pectoris and the infarct was of three months.

That is to say that the abnormal stress cardiac test selectively predicts the angina pectoris as the first

coronary event –though later almost one out of three from this group had myocardial infarction–; but it does not seem to predict a population having non-fatal myocardial infarction or sudden death as initial coronary symptom.

– **Physiocybernetic:** Anyway, it is known that all studies in asymptomatic patients show low sensitive and predictive values, the latter varying between 14% and 27%, that is to say, around 3 out of 4 individuals, in spite of their positive tests, will not develop a coronary event during follow-up.

– **Therapist:** The “positive predictive value” of the tests in asymptomatic individuals could be improved.

– **Physiocybernetic:** How can this be done without reducing the test sensibility?

– **Therapist:** The methodology used during the latest years has been carried out with a submaximum or maximum work load –the work we have been commenting on uses a maximum test; however, as you said, they show a relatively low predictive value, even though the sensibility to detect patients with maximum tests is about 30% to 35%, that is to say a third of the individuals who will develop a “coronary event” in the future may be detected with a test, even at maximum stress.

The problem when using these high load tests in asymptomatic patients is that the alterations of ST segment at high cardiac frequency is not specific enough, and with many “false positives”, ending up in low positive predictive values.

Why a maximum test in asymptomatic individuals would be performed to predict exclusively the occurrence of angina pectoris, if we can only predict 1 out of 3 future coronary events, but also 3 out of 4 considered abnormal will not even develop a “coronary event” in 12 years?

However, we should deduce that if the alterations occurred at lower cardiac frequencies and work loads, the specificity would be higher. It also used to occur in the past in the works about the first Master’s two-step test, and also in a detailed work carried out with low work load test by Joseph Doyle’s group, published in 1970. The test lasted 10 minutes and it was performed on a sliding platform with 5% inclination at 3 miles per hour –outdated methodology for the present

criteria–, and it proved a 25% sensibility (as high as the present maximum tests), but significantly improved the “positive predictive value” of developing a coronary event at 85% in 5 years.

So, the methodology of the tests that have currently been discarded to diagnose coronary artery disease, the low work load tests, seem to be the right ones for asymptomatic patients, because they do not reduce significantly the sensibility to detect future patients, but increase a lot the predictive value; and they also allow those physicians who wish to continue performing them on presumably healthy individuals to keep the iatrogenic potential of medicine.

CONCLUSIONS

– **Physiocybernetic:** Well, well... This dialogue, as interesting as extended –at least for me– is coming to its end.

It is clear for me that the tests themselves cannot determine the disease; and even more, their results may induce gross misdiagnosis, since it is the notion of disease clinics provides what gives abnormal value to any test data.

– **Therapist:** We may add that, regarding analysis and tests, it is possible –in fact, it is mandatory– to analyze their concrete value for each patient in a critical and scientific way.

– **Physiocybernetic:** That is why tests have always been called “complementary tests”.

– **Therapist:** “Complementary test” means: a test used to complement or improve a diagnosis, prognosis, or therapeutic answer... See you next time.

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