



# FUNDAMENTALS OF REGULATORY BIOLOGY AND REGULATIVE INTERVENTIONS

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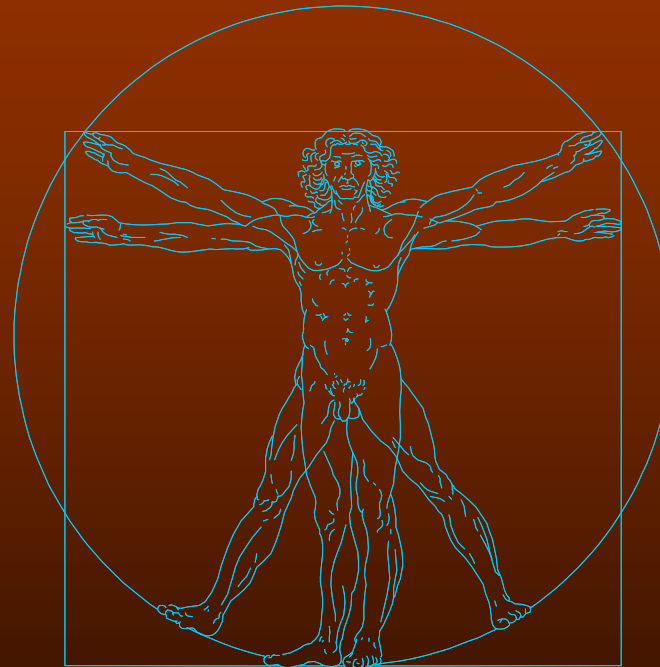
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## 2. PATHOLOGY



## DISEASE AS SYSTEMIC INFORMATION DISORDER





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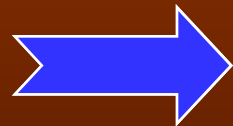
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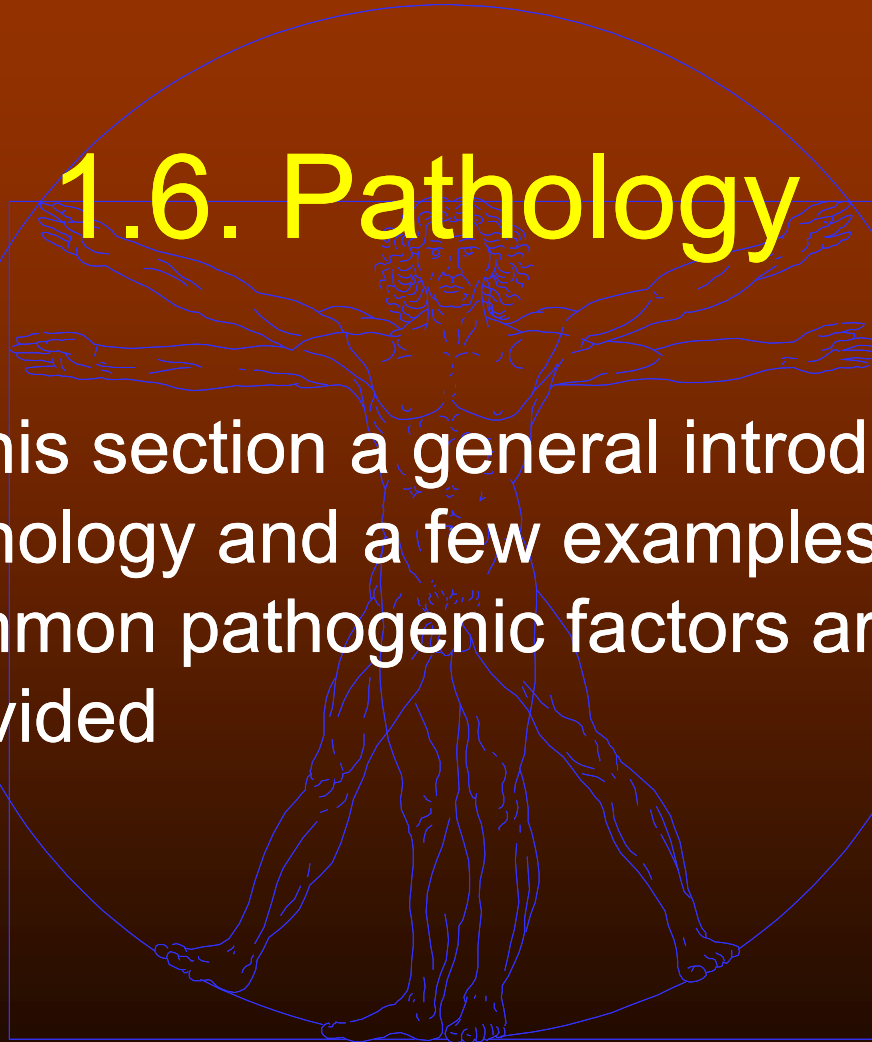
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## 1.6. Pathology



In this section a general introduction to pathology and a few examples of common pathogenic factors are provided





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❖ Unfortunately the positive restoration of normal homeostasis after a perturbation is not always the outcome.

❖ A number of external or internal pathogenic factors, such as biological, chemical or physical harmful agents, or errors of diet or life style, can modify permanently or semi-permanently the health state of a person, particularly when they interact with genetic predispositions.

❖ Moreover, there are internal factors (i.e. HLA molecules, blood coagulation, oxygen radicals formation, amyloid deposition, platelet aggregation and so on), linked to the very defense mechanisms, that may amplify instead to counteract the external harmful agents and can become self-damaging and aggressive factors.

❖ In these conditions, the “natural” healing power shows its limits, so that chronic or even progressive diseases may develop.





# THE "NATURAL" HEALING POWER SHOWS ITS LIMITS

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Caspar David Friedrich(1774-1840), Abbey in oaks field, 1809





# General concepts

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- At the opposite extreme to the organization of life is death, which therefore represents the maximum disorder, dissipation of information, and increase in entropy, tending towards thermodynamic equilibrium. Disease lies somewhere between the two, consisting in partial disorder of systems of information, energy, and matter, localized in space and time.
- Disease is thus essentially an information disorder. Genetic diseases are the most striking examples of this: the *order* of the genetic code sequence is changed, and the disorder lies in the very information store itself. Genetic disease can also be caused by a very minor transcription error in the basic cell library. Even acquired diseases, or diseases in which genetic and environmental factors are mixed (these are by far the majority) are disorders of information at a more complex level: what is altered is not just the molecular order of the DNA, but also the information order governing the supramolecular systems. In most diseases we can identify an imbalance of the homeostatic biological systems at various levels. The molecular, cellular, tissue, organic, and neuroimmunohematological systems, tend in themselves to function according to deterministically correct parameters.
- For example, in inflammation, thrombosis, atherosclerosis, hyperplasias, and endocrine disorders, it often proves possible to identify not a primary defect of the system itself, but a defect in its regulation. The platelet, when it causes a thrombus, is doing its job, as are thrombin and fibrin. The macrophage, when it engulfs oxidized lipoproteins, is doing its job (scavenging), even if this then causes an accumulation of foam cells in the tunica intima of the artery. It is true that a particular genetic defect may cause the pathological event (e.g. a lack of C/S proteins in thrombosis or a lack of LDL receptors in atherosclerosis), but more often than not, in practice, such genetic defects are neither marked nor decisive.
- Furthermore, every disease, even if primarily genetic, depends to a large extent in its clinical course on the occurrence of regulatory imbalances, inasmuch as the system would tend to counteract every defect with an adequate compensation mechanism.





# AT THE OPPOSITE EXTREME TO THE ORGANIZATION OF LIFE IS DEATH

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Gustav Klimt (Wien, 1862-1918) Life and death, 1912





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- A new vision of matter and life is emerging on the frontiers of science, particularly from the fields of quantum physics and mathematical theories and research which have yet to be systematized. Organisms are seen as highly regulated, complex, dynamic systems which display a characteristic meta-stability around certain homeostatic levels. This meta-stability is the net result of continual oscillations, rhythms, networks, amplifications and feedback cycles.
- Living systems are “suspended” between order and chaos; they partake of these two fundamental characteristics of matter and exploit them in a manner designed to promote survival. We cannot see how these new perspectives can fail to have an impact on the new orientations and trends in medicine. Medical theory, methodology and technology have always proceeded hand in hand with the general scientific theory and socio-economic situations of the times.





# LIVING SYSTEMS ARE "SUSPENDED" BETWEEN ORDER AND CHAOS

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Vincent Van Gogh (1853-1890) Wheat field with rooks (part)





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- When reflecting upon the question of disease, one problem which immediately springs to mind is understanding which of the various events observed are primary and which secondary: not everything in the disease process is pathological, in the sense that it is damaging.
- Disease is disorder, but it nevertheless obeys certain laws, and thus embodies some measure of order, though this is conditioned by chance events. The homeostatic biological systems which govern health are the same that cause most pathological phenomena, when activated inadequately, excessively or unsuitably in relation to the circumstances.
- On the other hand, it is also true to say that many phenomena that are called pathological are biologically useful (even if they cause pain), representing a stage of transition to a state of greater vitality, energy, and resistance to pathogens (= information gain).
- For instance, we need only mention inflammation and immunity, both of which are pathophysiological processes which, though carrying a certain price to be paid in terms of subjective symptoms and possible organ damage, in actual fact serve the purposes of repairing, defending, and inducing a state of enhanced resistance. This enhanced resistance derives from the biological memory of past experience.





# DISEASE IS DISORDER, BUT IT NEVERTHELESS OBEYS CERTAIN LAWS

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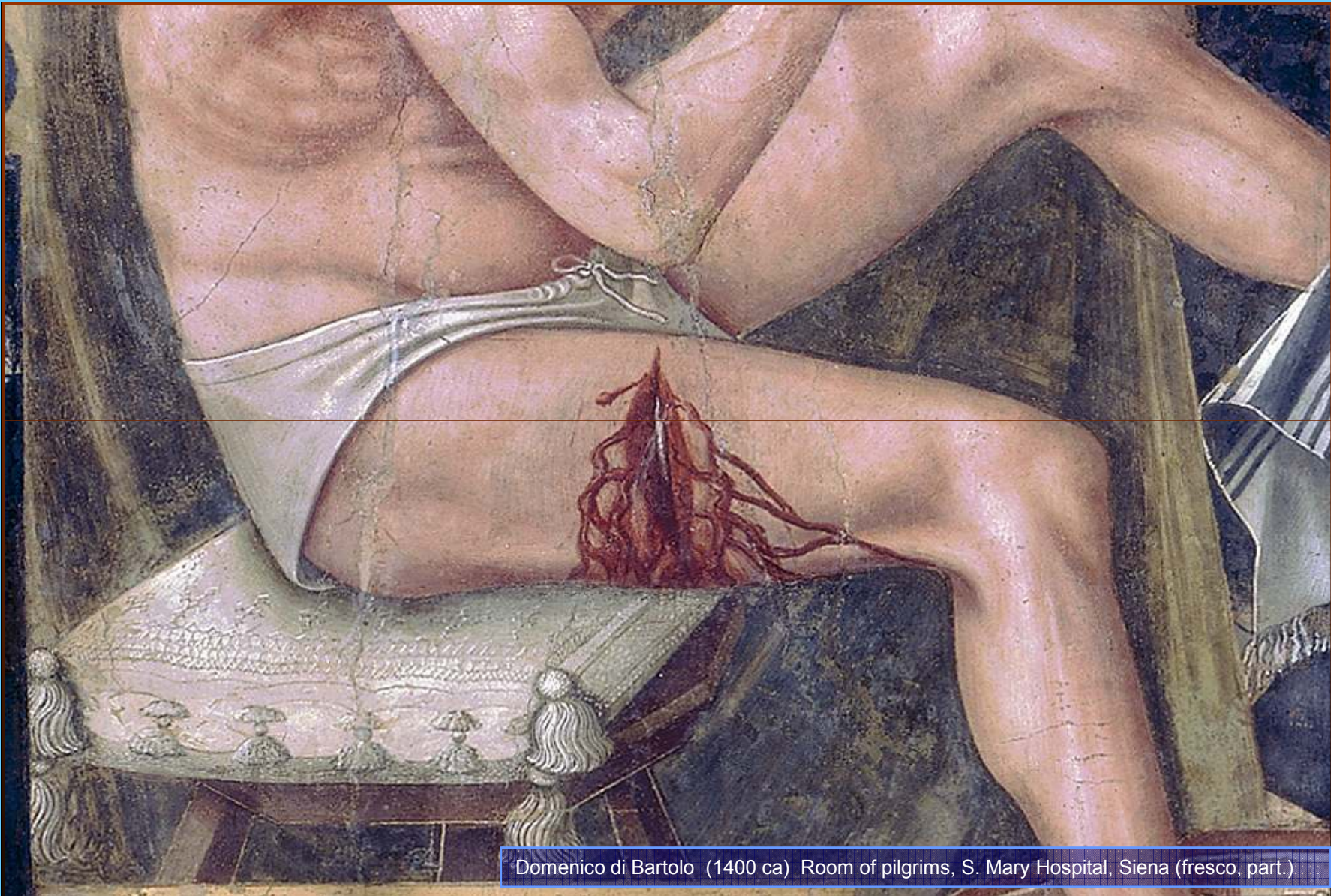
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Domenico di Bartolo (1400 ca) Room of pilgrims, S. Mary Hospital, Siena (fresco, part.)





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- These considerations lead us to our first conclusion: judging what is useful and what is damaging, on every occasion and in every aspect of disease, is by no means easy, in that it presupposes a knowledge of the "logic" of disease and normality, a knowledge of the language of complex systems (some of these systems are inflammation, immunity, neuroendocrine organizations, subtle metabolic regulatory mechanisms) rather than of the language of molecules.
- Disease is a problem of molecules, but also, in a different dimension, it is a problem of cells, of physiological systems and of the human being as a whole: if the molecular disorder is not compensated for by supramolecular systems, it is the latter that are responsible for the disease, and not the molecule. Disease is a problem of the individual, but it is also a problem of the environment: the individual is often the victim of a disease greater than him- or herself (e.g. violence, pollution, epidemics, misinformation by the mass media, social alienation, loneliness), and whoever reflects upon the real nature of diseases can hardly be satisfied with a reductionist explanation which fails to go beyond the latest biochemical consequences of these problems.
- If disease is an information disorder of complex systems, to get to the heart of the matter the molecular approach, which analyzes only one aspect of information, is necessary, but not enough. New approaches, new models, and new concepts are beginning to be introduced in biology in order to overcome this hurdle. It is not enough to understand the individual elements and try to put them together according to a computer-aided or cybernetic model: no-one believes any longer that the formulation of a precise, predictive model, capable of taking account of all the variables involved in a single cell, is remotely feasible, not to mention the even unlikelier construction of exact models for the functioning of organs or systems.





# DISEASE IS AN INFORMATION DISORDER OF COMPLEX SYSTEMS

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Peter Bruegel Senior (1525-1569) The triumph of the death, 1562





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- If we want to capture in a single image the whole crux of the problem of information regulation in vital processes, and thus also of its pathological aspects, it may be illuminating to refer to the model of an orchestra. The orchestra is the body, and the music is its life. In the orchestra, there is a material, "molecular" part, composed of instruments with a precise structure and of musicians with their receptive, elaborative, and motor capabilities. What matters most, however, is that the orchestra plays in harmony according to a program provided by the score and at a pace dictated by the conductor. A performance may prove unsuccessful because one of its material parts breaks (e.g. the strings of a violin, or the stool of one of the musicians), but it may also fail because the various musicians are in disaccord. The quality of the music the orchestra produces depends on conditions such as the quality of the instruments, the quality of the score, the skill of the conductor, and, above all else, the degree of unison and harmony between the members. If there should be interference due to some outside noise or disturbance, or if an orchestra is tired or distracted, there is a risk that the orchestra will play out of tune, and this risk is all the more serious, the less able the conductor is to keep the orchestra under control. If the music is seriously out of tune, or the conductor is weak, the flaw may involve the entire orchestra to the distinct detriment of the work as a whole.
- This example shows us that an information disorder can also arise as a result of subtle and not immediately perceivable deviations from the norm, which are then amplified and/or stabilized by adaptation and positive feedback mechanisms. In the healthy body this orchestra plays continuously in a coordinated manner. It is difficult to say whether there is a "conductor" because all the parts, including the brain, function properly, influencing one another reciprocally. If, however, the coordination is lost, i.e. the *connectivity* of a system as a whole and in relation to the rest of the body, certain subcomponents may oscillate in an excessive, unpredictable and pointless manner, thus generating localized disorders which may, however, be amplified. Oscillation thus becomes disorder and takes on the aspect of disease, in that it causes the emergence of substantial symptoms and damage. In a complex system, loss of communication and of connections means pathology; thus the major goal of the medical intervention is to re-establish proper communications, helping the self-organization process (healing) of the organism.

➤ [Full paper on disease as systemic information disorder](#)





# FROM THE CONCEPT OF DISEASE

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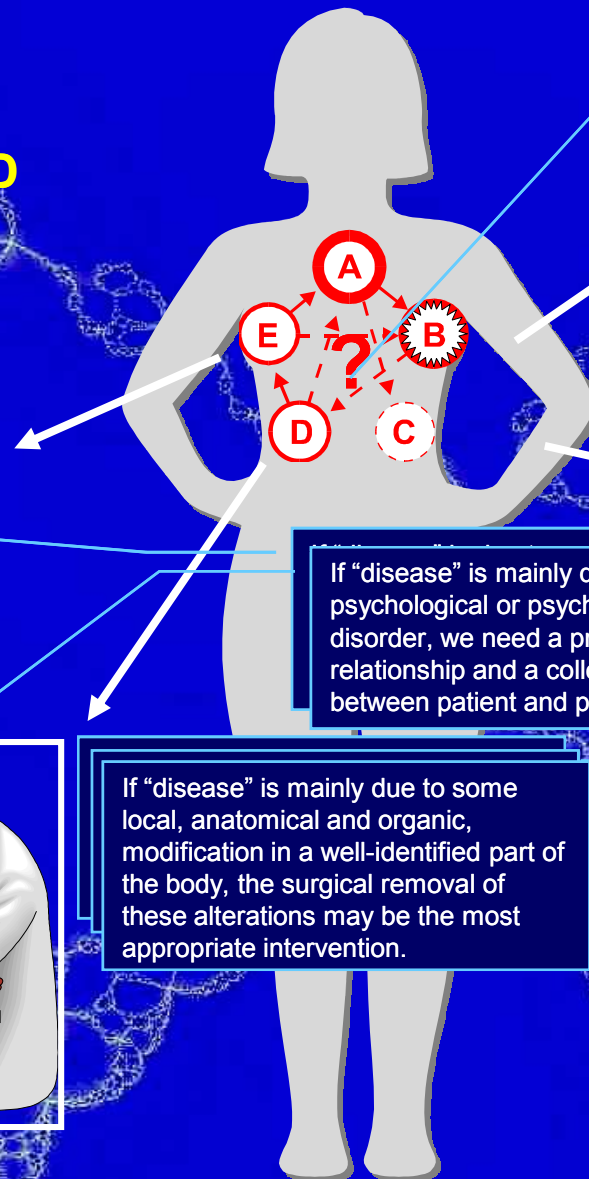
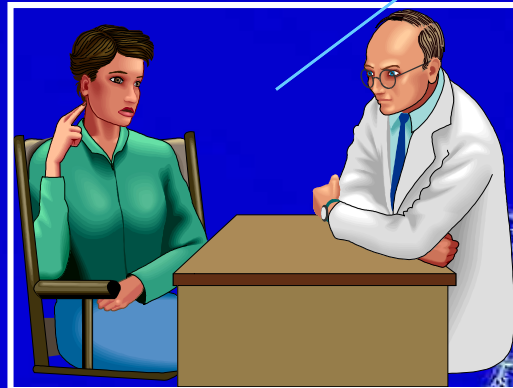
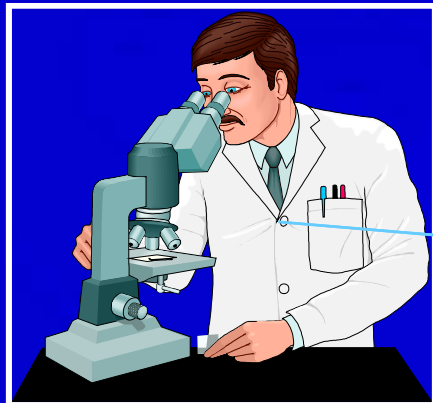
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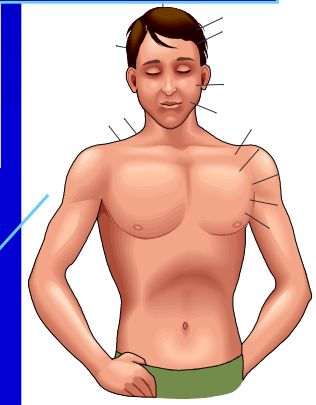
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## TO CLINICAL DIAGNOSTICS AND THERAPEUTICS

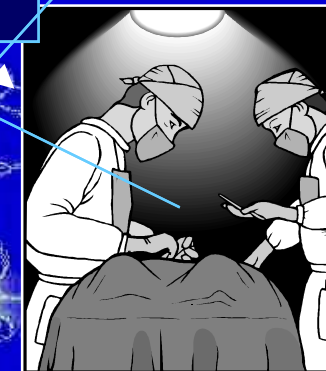


The concept of disease is central in any medical approach because it unavoidably determines (consciously or unconsciously) the diagnostic methods and the therapeutic interventions.



If "disease" is mainly due to some psychological or psychosomatic disorder, we need a profound relationship and a colloquium between patient and physician.

If "disease" is mainly due to some local, anatomical and organic, modification in a well-identified part of the body, the surgical removal of these alterations may be the most appropriate intervention.





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