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HOMEOPATHY: A FRONTIER IN MEDICAL SCIENCE
EXPERIMENTAL STUDIES AND THEORETICAL FOUNDATIONS

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TEXT without figures

Chapter 6

6. HOMEOSTASIS, COMPLEXITY AND HOMEOPATHY: THE LAW OF SIMILARS

The relationship between the concepts expounded in the foregoing chapter and the homeopathic medicine may not be directly self-evident, but is very profound and far-reaching: homeopathy presents itself as an approach which expresses a distinct preference for the "subtle" as opposed to the macroscopic, for homeostatic regulation as opposed to intervening drastically on some single factor modified by the disease, the equilibrium of the body as opposed to the organ; in a certain sense the preference is for information as opposed to more material aspects. The very law of similars itself, the cornerstone of homeopathic theory, is founded upon analogical-empirical rather than upon logical-inductive reasoning.

Homeopathy can only be understood within the context of the paradigm of complexity. In this chapter we are going to attempt to analyze the relationship between complexity and homeopathy without, however, laying any claim to solving all the questions raised by homeopathy, but confining ourselves, for the time being, to discussing the law of similars as defined by Hahnemann and the effect of small doses of pharmacologically active substances. In other words, in an attempt to shed light on such an intricate issue, we have decided to leave aside for the moment the problem of infinitesimal doses, which will be dealt with later (Chapter 7).

Here, homeopathy will be treated as *a therapeutic approach which uses compounds at low doses administered according to a rationale which differs from that characteristic of allopathy*. The justification for such a procedure is to be found in the very history of homeopathy, where the pivotal concept for both the founder and the various schools over the years has always been *the law of similars rather than the problem of dilutions*, and in its present-day practice, where we see that a substantial proportion of the drugs sold as "homeopathic" remedies effectively contain ponderal doses of substances of mineral, vegetable or animal origin. All the preparations containing dilutions lower than 20x or 10c belong to this category.

Using this type of approach, the possible mechanism of action of homeopathic remedies can be addressed without necessarily having to take as gospel truth the famous concept of the "memory of water," which understandably may be at variance with the tenets of current biomedical reasoning.

In a nutshell, then, the basic hypothesis considered here is as follows: *a homeopathic drug works by providing information commensurate with the complexity of the organism with which it interacts.* This hypothesis is illustrated in detail and step by step here below.

6.1. Mode of action of homeopathic drugs

The possible mechanism of action of a homeopathic remedy is to be sought within the sphere of the regulation of complex homeostatic systems. It is therefore necessary to refer to what we have already said about the characteristics of the functioning of homeostatic systems (Chapter 5, Section 4). By way of an initial approximation we shall attempt to consider the essential phenomena of the variations in homeostasis and the regulatory impact of homeopathic intervention. Thereafter, the model will be enriched with variants and its possible applications will be discussed.

Given a homeostatic system such as the one described in Figure 8 (Chapter 5, Section 4), we will consider how it is modified when a perturbation of a pathological type comes into play which shifts the equilibrium excessively towards *A′* (Figure 21). The variable *A* may thus be regarded as the normal condition and *A′* as the pathological condition, in the sense of an excessive oscillation of the parameter considered. Another possibility is that *A′* is a pathological event in the sense of the presence of biochemical alterations coming from the outside, i.e. *A′* is of exogenous origin, such as a foreign antigen or a toxic molecule: the subsequent chain of events does not change. At this point *A′* produces an enhanced signal *a′* which then brings about very marked activation of the regulatory system. We have seen that, following an increase in the signal *a′*, the specific receptor system is *primed*, i.e., to simplify things, it exposes a greater number of receptors for *a′* (see the homologous priming phenomenon mentioned above in Chapter 5, Sections 2.1 and 6.2).

Figure 21. Diagram of the modifications induced by an external perturbation in a homeostatic system. The starting situation ("controlled imbalance") is that described in Figure 8. The perturbing condition is posited as being that which acts upon the effector system *A* --> *A′* or directly upon *A'*, leading to an excessive increase in that parameter. With an increase in the signal *a′* , the regulatory system is activated and reacts by attempting to restore the lost equilibrium. For the receptor dynamics illustrated in this model, see also the text.

The primed regulatory system increases its activity by producing more of the signal *r*, which, in turn, will force the effector mechanisms (*A′*--> *A*) towards the normal condition *A*. In this initial phase of the disease, the body reacts logically and efficiently in the direction of equilibrium and healing. For instance, if *a′* is a molecule "judged" to be abnormal in terms of quality or quantity by the "immune" regulatory system, the system will produce more receptors for *a′* (in this example, antibodies and T lymphocyte receptors) and more *r* signals (interleukins, cytokines, interferons) which in turn prompt the effector system (phagocytes or complement) to restore normal homeostasis by eliminating the excess of *A′* and re-establishing the condition *A* (healing).

In this initial stage of the disease, which might be regarded as perfectly "physiological," other phenomena worthy of note occur: the first of these is the onset of symptoms. The signals regulating the homeostatic systems are generally endowed with substantial redundancy and pleiotropicity, in the sense that they are capable of activating multiple systems in various ways. Thus, *a′* will manifest itself by producing some symptom or other depending upon the systems it activates. It has already been said (Chapter 5, Section 1) that *symptoms are usually linked to the activation of endogenous systems rather than to the direct effect of the etiological agent*. The symptoms thus stem from "side" effects produced by *a′* activating the specific homeostatic systems. In the diagram presented in Figure 21, not only do symptoms appear caused by *a′*, but also symptoms caused by other signals (*r*), produced by the regulatory system. Referring once again to the previous example, an increase in *a′* and *r* may cause symptoms stemming from activation of the immune system, linked to the "side" effects of antibodies, complement, or cytokines (fever, leukocytosis, fatigue, sleep, and other manifestations).

With reference to classic homeopathic theory, as outlined in paragraph 63 of the *Organon* (see Chapter 2, Section 3), it may be said that the effects of signal *a′* (Figure 21) correspond to the "primary action," whereas those of signal *r* correspond to what Hahnemann called the "secondary action" of the remedy, which is believed to be of a "life-preserving nature."

A second event worthy of note, contemplated in Figure 21, is the onset of a new sensitivity related to exposure of new receptors by the regulatory system for substances other than *a′*. This event, too, belongs to the category of "priming" events (heterologous priming) and, in general, to all those modifications of receptor sensitivity and homeostatic system compensatory activity, related to pathological conditions and dealt with in some detail above (see, particularly, Chapter 5, Section 6.3 and Figure 15). The homeostatic systems involved in reactive regulation are thus altered not only specifically by the etiological agent, but also according to a broader spectrum of specificities. This, too, has been clearly demonstrated in many conditions: the interferons produced as a result of a viral or bacterial infection induce a greater resistance to other viruses, other bacteria and even tumor cells; a treatment with barbiturates induces an increase in the activity of microsomal systems in the liver which may serve to offset the effects of other drugs and toxic substances with greater efficacy; when leukocytes come into contact with endotoxins they are also sensitized for other bacterial products such as formylpeptides; when the main hepatic detoxification system (cytochrome P450) is activated by the chronic intake of toxic substances its ability to metabolize other substances is enhanced. There is thus a certain degree of broadening of the spectrum of specific sensitivities in a regulatory system activated during a disease.

After this initial reactive phase, if the perturbation of the homeostasis continues, the regulatory system may undergo a major change in status: it adapts to the altered conditions, progressively suppressing the sensitivity for the persistent, abnormally increased signal (Figure 22). This adaptation enables the system somehow to "survive" with the disease, which otherwise would require an excessive expenditure of energy (continual activation of both the *A* --> *A′* and *A′* --> *A* mechanisms) and excessive problems in terms of symptomatology. From the molecular point of view, the cells reduce the receptors for *a′* to the point where they disappear altogether, or they reduce their affinity, or they produce a decrease in communication with the effector systems (in our case, the production of *r*). By and large, this phenomenon is specific at receptor level: that is to say, it is the *occupied* receptors which disappear, whereas the others remain or even increase in number. In other words, the desensitization tends to be agonist-specific (though, obviously, exceptions and variants are possible in terms of combinations of groups of different receptors, cell states of overall exhaustion of all activities, etc.).

Figure 22. Disorder in a homeostatic system due to persistence of the perturbation. It is postulated that the perturbing condition is severe and long-lasting, such as to produce a strong, constant increase in the signal *a′* despite the efforts of the regulatory system. In these conditions, the regulatory system may adapt by reducing the sensitivity to *a′* with major consequences for the evolution of the disease process.

By reference to this basic model, which by the very nature of things is necessarily highly simplified, we are in a position to postulate the mode of action of the homeopathic remedy (Figure 23). It *activates the regulatory system via receptors other than those for* a'*, but which produce the same effect, namely that of restoring production of the signal* r *and thus of bringing about activation of the compensatory mechanism A′* --> *A*. The homeopathic drug is therefore thought to act in lieu of *a′*, to which the system is no longer sensitive as a result of adaptation.

Figure 23. Schematic and highly simplified representation of the possible way by which a drug with a "homeopathic" mode of action (h) may reactivate the regulatory system and the homeostatic circuit.

On what do we base such a hypothesis? It rests on the fact that the homeopathic drug necessarily has to interact with the regulatory system concerned, because it has been identified precisely on the basis of its *ability to cause symptoms similar to the disease, i.e. symptoms similar to those caused by the mediator a′ via activation of the regulatory system.* It is clear that, if it is true that most of the symptoms in a pathological condition are due to activation of homeostatic reaction systems, it should be possible somehow to "reproduce" the activation of these same homeostatic systems by administering a compound which "reproduces" the symptoms of the disease. Theoretically, in the healthy, nonperturbed system, symptoms of the disease may be produced by the administration of *a′* and *r*, or of a substance which activates the

regulatory system via receptors other than those for *a′*. In the diseased system, *a′* is already present in large amounts and effectively causes the symptoms, but, if the mechanism of receptor adaptation comes into play, we may find ourselves in a situation whereby the regulatory systems become "paralyzed," prove inefficient, and are themselves unbalanced. Since, however, the regulatory system conserves other sensitivities in the disease state, and indeed probably accentuates them, if other sensitivities are brought into play through other signals, the system can be reactivated. *By subjecting the regulatory system to a signal* "*similar*" *to a′ (in the sense that it causes similar symptoms), the response r is elicited and thus a return to normal homeostasis.*

The *similarity* is therefore between the symptoms caused by the activation of reactive mechanisms by the disease process in the patient and the symptoms caused by activation of the same reactive mechanisms in a healthy subject by a biologically significant external agent (in this case, the homeopathic drug).

The hypothesis put forward here is based essentially on the following points:

a) In the dynamic progression of a disease process, *specific homeostatic regulatory systems may break down or be blocked* following excessive stimulation or as a result of the interference of other pathological factors (metabolic and nutritional problems, toxic factors, heterologous desensitization, neurohormonal disorders, water-electrolyte imbalances, or simply as a side effect of high-dose drug therapies).

b) As long as the disease process does not lead to excessively profound and irreversible impairment of the regulation systems, *this blockade can be by-passed using different receptor sensitivities* (for exogenous or endogenous substances) which the perturbed systems themselves conserve or even accentuate.

c) The identification of suitable substances for reactivating the homeostatic systems *specifically* blocked in a given disease process is hard to achieve *with precision* in any single patient by using the conventional scientific approach, on account of the complexity, variety and multiplicity of the systems involved and because of the dynamic and changeable nature of diseases.

d) The homeopathic approach, particularly through the use of analogy (law of similars) *makes it possible to get nearer to identifying substances capable of interacting specifically with the homeostatic systems involved* in the disease process in each individual case.

At this juncture we feel obliged to quote Hahnemann, who was the first to gain a real insight into this therapeutic approach (forgiving him, of course, for indulging in hyperbole): "The curative power of medicines, therefore, depends on their symptoms (*), similar to the disease but superior to it in strength, so that each individual case of disease is most surely, radically, rapidly and permanently annihilated and removed only by a medicine capable of producing (in the human system) in the most similar and complete manner the totality of its symptoms, which at the same time are stronger than the disease. As this natural law of cure manifests itself in every pure experiment (**) and every true observation in the world, the fact is consequently established; it matters little what may be the scientific explanation of how it takes place; and I do not attach much importance to the attempts made to explain it. But the following view seems to commend itself as the most probable one, as it is founded on premises derived from experience. (...) As every disease (not entirely surgical) consists only in a special, morbid, dynamic alteration of our vital energy (of the principle of life) manifested in sensation and motion, so in every homeopathic cure this principle of life dynamically altered by natural disease is seized through the administration of a medicinal potency selected exactly according to symptom-similarity by a somewhat stronger, similar artificial disease-manifestation" (*Organon*, paragraphs 27, 28 and 29).

The purpose of this presentation here is to provide a model which explains the effect of homeopathic drugs in terms of molecular and cellular biology. This theory is based on an extremely simplified - perhaps oversimplified - model, but this is necessary in order to pinpoint the central concept, around which a whole series of other problems can be identified, which will be dealt with here below.

(Footnotes

(*) That is, those which the medicines are capable of causing in healthy human subjects.

(**) What Hahnemann means by "pure experiment" is one conducted by trying out the remedies in healthy subjects and in patients.

6.2 Discussion of the model presented

The theories and models outlined in the foregoing section do not lay any claim to being the only explanation of the action of a homeopathic drug, but are merely a first sketchy attempt at a hypothesis, which is undoubtedly due to be supplemented with new insights and new concepts in the future. The theory offers a frame of reference within which various aspects need to be clarified and a number of corollaries, extensions and variants need to be discussed.

6.2.1. Aggravation

From the diagram in Figure 23 we see that the administration of the homeopathic drug may cause symptoms related to reactivation of the regulatory system. Though the doses are low, reactivation therapy is, however, capable of producing effects which in some way match the disease, or which may appear as an acute exacerbation of the symptoms. In point of fact, activation of the regulatory system entails the production not merely of signals directly aimed at restoring homeostasis, but also of signals which are transmitted to systems which produce symptoms. This is a well known fact in homeopathy, so much so, indeed, that it has been termed "homeopathic aggravation." It is the price that has to be paid for the removal of the adaptation system.

It is also conceivable that, if the present disease is the outcome of a succession of pathological events, the regression of the last event may be accompanied by the recurrence of previously disappeared symptoms. In this sense, homeopathic therapy leads the patient to experience in reverse order the history of

the particular disease or even of his or her pathological history in general, according to a process which may bear some resemblance to psychoanalytical therapy. A similar concept has also been proposed by other investigators [Laplantine, 1986].

6.2.2. Further degrees of complexity

The diagram in Figure 23 (Chapter 6, Section 1) needs to be amplified in view of the fact that homeostatic systems are integrated with one another in complex networks. This interplay underlies one of the main insights of the homeopathic approach. It is clear, in fact, that, in the presence of a practically inextricable network of intertwined homeostatic systems, it is not possible, in any single case, to know sufficient details of the state of each such system to be able to apply effective pharmacological remedies. For example, in the course of an infectious disease, we may know that the thermoregulatory center is altered and institute therapy aimed in such a way as to restore its normal equilibrium (e.g. antipyretic therapy), but at the same time we have no means of knowing the status of the thirst and hunger centers, the macrophagic activity of the spleen, the hepatic synthesis of various mediators of the complement and antiproteases, the influence of the patient's psychological state on regulation of blood pressure or the patency of the airways, the relationship between the various lymphocyte subpopulations, the levels of growth factors in the blood, and thyroid and adrenocortical function, to mention but a few. Even if we were in a position to know these details through appropriate analyses, there is no guaranteeing that we would then be able to implement therapies coordinating all the various imbalances in order to help the patient's body to restore biological order. In most cases, then, there is no alternative but to resort to therapies combating the etiological factors or the symptoms. The regulatory systems, in fact, are too complex for us to be able to act at this level (which, however, is the very heart of the dynamics of a disease process).

This then is what the progress made by homeopathy is all about: realizing that such a degree of complexity exists in the informational disorder associated with the disease and discovering the main way of getting round the problem, namely the empirical-experimental method based on the law of similars. In point of fact, in this way *we have two sets of complex, integrated information*: the set regarding the drug and the one about the patient. It is true that little is known about *which* molecular and cellular alterations take place and particularly about the intimate relationships between them (their "*internal essential nature*," as Hahnemann puts it), but such alterations and such degrees of complexity somehow express themselves as

symptoms, which can be observed and documented. On comparing the patient's symptoms and those of the drug, two complex images are brought face to face, the expression of two reactive "patterns," which, if they match, must necessarily refer to the same or similar regulatory systems in the "internal sphere" of the body.

The drug thus "uses" the same systems (which we can even admit we do not know) as the disease. This is a typically *analogical* way of proceeding (what the doctor is basically seeking in the repertorization of the symptoms is an analogy between the patient and the drug), but, on the basis of what we have said, it would also appear to be a logical way of proceeding. The homeopathic approach does not mean that reason gives up the ghost in the face of inextricable complexity, but adopts a realistic attitude towards it. The complexity is accepted as a basic fact of life, but, by knowing a number of general rules (nonlinearity, feedback, integration, analogy), we can make up for our ignorance of the details.

The action of the homeopathic remedy presents itself as highly specific in terms of information. This specificity is based in the first place on the nature of the drug in itself, i.e. on the *low dose* (as a rule, the lower the dose of a drug, the more likely it is to be specific because it acts on the very few highly sensitive targets) and on its *active ingredients*, which are usually multiple and combined in various ways (cf. the vastness of the homeopathic pharmacopoeia, especially of vegetable and animal origin, and the subtlety of the distinctions between apparently very similar drugs such as plants belonging to the same family, to mention but a single example).

The specificity, however, is based not only on the nature of the drug because seemingly very simple drugs are used in homeopathy (mineral salts, metals), but is guaranteed above all by the particular symptom-based individualization procedure. This procedure enables the right remedy to be identified for the largest number of symptoms present and thus for the largest number of homeostatic systems impaired.

The homeopathic drug acts better, the more complex the system and the more subject it is to subtle regulatory dynamics. The use of such a drug as an enzyme inhibitor is unthinkable, and those investigators who have attempted such experiments have reported negative [Petit *et al.*, 1989] or poor and uncertain [Harisch and Kretschmer, 1988] results. The experiments described in Chapter 4 indicate that research is revealing that it is easier (or rather, less difficult) to achieve positive results with homeopathic dilutions when the experimental systems consist in animals or isolated organs rather than in cells or enzymes.

Homeopathy has a pharmacopoeia comprising a whole host of substances stemming from the animal, vegetable or mineral realms. Most of these substances (again, quite apart from the question of high dilutions) are extracts from raw materials, and not purified or synthetic molecules. This adds a further degree of complexity with regard both to the interpretation of their effects and to research in this field. On the other hand, according to the basic "logic" of homeopathy, this could hardly be otherwise. If it is true that diseases present complex dynamics, no action to restore equilibrium can be implemented without adopting a complex approach. In the optimal therapy, many different receptors have to be reached simultaneously in a dynamic, specifically targeted manner, some of which will be activators and others regulators, both in the psychic and physiological spheres. The homeopathic pharmacopoeia offers a vast choice of remedies with differing characteristics. The only or, at any rate, by far the most important clue to negotiating this maze of complexity is the similarity of patient and drug symptoms.

It is quite astonishing to find that the animal body presents multiform receptors capable of receiving information from any number of elements present in other animal organisms, in flowers, in the roots of plants, and in a variety of minerals. Often these elements are poisons if used at high doses, which indicates their very substantial reactivity with biological systems.

What is the sense of this "matching" of information from sources within and outside the body, which effectively proves damaging or therapeutic according to the doses? The reasons for this are to be found in the evolution of living creatures: poisons came onto the scene as the products of plants and animals that used them to advantage for defensive and offensive purposes; to achieve these aims they had in some way to "mimic" substances present inside the target organism, otherwise there would have been no specific interaction and thus none of the biological damage intended. Accordingly, poisons and toxins, precisely because they are what they are, are "similars" of certain structures, receptors, enzymes, or signal molecules already present in the body, probably as mediators of physiological functions.

On the other hand, in terms of evolution, we can readily understand why the complexity of the remedy (by this we mean a medicine which comes to hand or is discovered in nature) has evolved along with the complexity of the organism to be treated: living creatures have learnt, often to their cost, but in an increasingly expert manner, to "recognize" what is useful in the environment for therapeutic purposes. Those forms of life with a broader, more versatile and more flexible set of receptor apparati (the receptor is the

mirror of the signal) have adapted better to changing environmental conditions. According to this view of things, those forms of life which, when subjected to endogenous or exogenous stress and thus affected by a great variety of diseases, developed receptor apparati capable of recognizing specific substances (foodstuffs, plants, oligoelements, vitamins, *inter alia*) or other signals (light, heat, magnetic fields) present in the environment and useful for restoring normal homeostasis, have had a major evolutionary advantage.

In a word, it could be claimed that the law of similars, as applied in the field of complexity considered here in this section, and particularly with reference to what was said in Chapter 5 with regard to chaotic networks, is tantamount to an attempt to *increase the connectivity* of homeostatic regulatory systems, by introducing into the systems themselves *targeted information* which is of an *adequate degree of complexity and subtlety*, precisely because it has been identified on the basis of a vast array of information stemming from the symptoms. According to the reasoning which has led us here, increasing the *flow of information* which passes into the complex dynamic systems may serve as a guide for restoring their disrupted or dysregulated relationships and thus for redirecting them towards their original functions. In a word, the homeopathic stimulus is aimed to put a specific *form* of order (*in-"formation"*) into chaos.

6.2.3. Individualization

The conceptual frame of reference outlined here enables us to grasp one of the cornerstones of the homeopathic approach, namely the fact that one and the same disease can present different, peculiar symptoms in different subjects and may require different treatments. To this aspect, i.e. the individualization of the prescription, homeopaths have always accorded paramount importance.

The same disease may result from alterations of a great variety of homeostatic systems, with subtle differences for the individual patient, depending upon his or her genetic make-up, age, previous medical history, type of diet, and other intercurrent endogenous factors. The "typical" symptoms of a disease, that is to say the "diagnostic" or "pathognomonic" pointers, according to the conventional view, are the same in all subjects suffering from the disease (e.g., the high temperature of influenza, the headache of migraine, the jaundice of choledocholithiasis). These symptoms are of little significance in homeopathic individualization, where they are called "*local*" or "*common*" symptoms, whereas much greater importance is ascribed to those symptoms which differ from one individual to another with the same disease. These latter symptoms are called "*peculiar*" symptoms.

For instance, two subjects with influenza may both have a high temperature, but one may sweat and not the other; one may be in a state of prostration and the other agitated (*Belladonna* and *Aconitum*, respectively). Perspiration and prostration are peculiar symptoms and guide the homeopathic physician in his choice of remedy.

The importance accorded to the peculiar symptoms, within the framework of the theory expounded above, is justified on the basis of the fact that they reflect both the patient's *physiological homeostasis,* regardless of the disease, and the mode of reacting, *the way the body chooses to face up* to the disruption of homeostasis currently under way. It should be recalled that all homeostatic systems are interconnected, with the result that the modulation of one cannot fail to have an impact on the others. In the example we have given, it would seem clear that the imbalance of other homeostatic systems (thermoregulation, general cenesthesia) "conditions" the influenza. It is only by "conditioning" these systems pharmacologically that the particular subject can be helped by a homeopathic treatment.

The *disease*, from the homeopathic standpoint, is not identified either with what the patient complains of or with what he or she is conventionally accustomed to considering as such, but rather it embraces a broad spectrum of interrelated pathophysiological changes. It is common experience for homeopathic practitioners to observe that, in patients who present with organ diseases or diseases located at skin level, the therapy induces improvements in the psychological sphere, or in other diseases which have been present for some time and which the patient had not regarded as treatable. This happens because, by targeting the treatment at the patient's peculiar symptoms, one is operating at a much deeper level than that apparently involved on the basis of the symptoms currently experienced.

6.2.4. Importance of small doses

To reactivate the regulatory system impaired by the disease process, *small doses* of a substance acting at receptor level may suffice. The impaired system, indeed, may be hypersensitive, having a greater number of receptors and a heightened sensitivity at postreceptor (transduction) level. This fact accounts for something which was illustrated by Hahnemann and confirmed by the various schools of homeopathy: to cause the symptoms of the disease in healthy subjects you need higher doses of the remedy than those required for patient remission. On the other hand, considerations of this type also hold good for various nonhomeopathic drugs; aspirin, for instance, lowers the patient's temperature only when it is pathologically high; it does not lower it if it is normal; the thermoregulatory system becomes sensitive to aspirin only if it is operating abnormally.

The fact that the homeopathic remedy may act at low doses is also important because in this way we avoid:

a) The remedy used having toxic effects, seeing that many substances used in homeopathy are fully fledged poisons in their own right when used at high doses.

b) The actual receptors for the drug on the regulation system become saturated and thus lose their efficacy for the reasons explained above apropos of receptor dynamics (Chapter 5, Section 6.3).

Within the context of complexity, the issue of doses makes even more sense and appears even more interesting than would appear to be the case merely in the light of receptor dynamics in the classic sense. The sensitivity to small doses of drug is not explained solely in terms of the increase in numbers of receptors, as might appear from a simplified view of the phenomenon, as proposed in the diagrams in Figures 21-23. If it is true that homeostatic systems are governed by the "laws" of complexity, where chaotic dynamics may easily arise and where order (information) and tendency to disorder (entropy) coexist in a state of controlled imbalance, then also their pharmacological manipulation is subject to laws of nonlinearity. When a homeostatic system oscillates between order and disorder, between positive purposefulness and self-damage, or between the option of attacking the disease and that of saving a state of tranquillity, it is in a situation of great "precariousness" and "uncertainty" as regards the possible solutions adopted. This is the point which in mathematics is termed the "bifurcation point" or "symmetry break" point [Nicolis and Prigogine, 1991].

The borderline between what is considered defense and what is considered offense represents a watershed along which the body finds itself "undecided" in critical phases. At this point even the slightest piece of "exogenous" information, if properly directed and thoroughly understood, may be the crucial factor for the system in tipping the scales in favor of one or the other of two opposite attitudes (in our case, to simplify things, adaptation or reaction, receptor expression or their down-regulation, immunity or tolerance, coagulation or fibrinolysis, etc.). It might be postulated that to produce a regulatory effect the drug doses necessary will be all the lower, the more delicate and subtle the choice the system is called upon to make. In other words, in a system which can take on various different configurations or operate at different levels of activity, the intensity of the exogenous stimulus prompting the choice will be lower, the greater is the degree of "freedom" of the system itself.

What is meant here by "freedom" is the possibility of taking on different alternative configurations. In the behavior of complex systems, this may correspond to the possibility of shifting between different attractors, or between attractors of different degree of chaoticity. At one extreme there is maximum freedom, as in the case of a system oscillating through spontaneous and chaotic fluctuations, while at the opposite extreme we have a wholly deterministic system subject to precise controls and periodic behavior. As we have seen, biological systems and the human body as their maximum expression carry both characteristics (chaos and determinism) within themselves and therefore can be regulated both by "drastic" measures (high-dose drugs, enzyme inhibitors, surgical interventions, ionizing and excitatory radiation, to mention but a few) and by "subtle" measures (homeopathy, acupuncture, psychological and cultural factors, low-frequency electromagnetic fields, and many others).

According to this hypothesis, it would be utterly out of the question for a homeopathic remedy to act at atomic level or on simple molecules. If we want to split the nucleus of an atom (a relatively simple and highly - though not entirely - deterministic system), we must use an extremely large amount of energy, furnished only by special particle accelerators, and it cannot be done using any chemical substance, however powerful and concentrated it may be. If we want to split a cell, we have to use fairly hefty radiation, though the rays emitted by any run-of-the-mill cathode ray tube will suffice, and the splitting can also be done by acids, alkalis, or toxins at adequate concentrations. If we want to kill a man, this can be done with minimum doses of poison affecting only a minimal part of the body, e.g. the cardiac conduction system, or the

respiratory center. A man can also be killed - and it happens - by a shattering piece of news (minimum energy in physical terms, maximum informational significance).

In conclusion, then, we would say that *the more complex a system is, the less energy is needed to alter its behavior and structure*. We shall come back to this point when dealing with high-dilution homeopathy (Chapter 7, Section 5.2).

6.2.5. Inhibitory or antagonistic effects

An important aspect which, for the sake of simplicity, has not been previously discussed, but which must be part and parcel of the model, has to do with the possible inhibitory effect of the drug at low doses. Clearly, what we are talking about here is the effect of biologically active substances on homeostatic control systems and therefore the context is the one we have already extensively illustrated regarding the complexity of receptor dynamics (see Chapter 5).

The binding of a molecule to its receptor produce an effect which schematically may be of the stimulatory or inhibitory type, according to which transducers are activated by the receptor and according to the possible interaction of the molecule with other molecules (forms of synergism and antagonism). Within the frame of reference we are dealing with here, then, we should not neglect the possibility that a homeopathic drug may act not so much as an *activator* of the homeostatic system (action contemplated by the model in Figure 23), but rather as a *regulator* of the homeostatic system.

This point is very important because, if things were only as outlined in Figure 23, the action of a homeopathic-type measure would make sense only when the regulatory system is completely dys-regulated, in the case in point by the receptor adaptation which leads to the lack of, or to an inadequate counterreaction to the disease. If things were exclusively in these terms, it would be impossible to understand how a homeopathic drug would be able to act in the early stages of diseases, when the regulatory system is still very efficient and, indeed, in a state of hypersensitivity or hyperactivation. In these early stages, the responsiveness of the regulatory system is intact, and it would make no sense to give the system a further stimulus, "similar" to the endogenous physiological one. This might only aggravate the disease and the symptoms, introducing an additional pathogenetic factor.

By contrast, the homeopathic and homotoxicological experience refers to therapeutic effects obtained also in the initial stages of the diseases, effects which may be regarded essentially as a reduction of symptoms, achieved with medium to high doses of natural drugs. Obviously, we are not talking here about suppression of the type caused by allopathic drugs, particularly if used at high doses as enzyme inhibitors, but this reduction of symptoms is nonetheless a form of suppression. When the regulatory system functions optimally, it is this system itself which leads to restoration of the homeostatic balance (healing), and the doctor's action can be no more than an attempt to reduce the subjective symptoms and any complications due to excessive expression of the endogenous reaction (including the occurrence of the blocking of the regulatory system itself).

What conceivable form can the regulatory action of a homeopathic drug take? Theoretically, such action can come about via two main mechanisms:

a) *Binding or interference with receptors for endogenous activating mediators*. It has been said that, in healthy subjects, a homeopathic drug causes symptoms similar to those it is capable of curing in sick individuals. To explain this apparent paradox we may postulate that the drug in question is molecularly "similar" to the endogenous mediator (*a'* in Figures 8, 22 and 23) so that, if administered to a healthy subject, it pursues the same line of action as the mediator: causing symptoms similar to the disease and activating the regulatory system.

In sick individuals, on the other hand, *where the endogenous mediator is already present* in large amounts, the presence of a "similar" might express itself as an inhibition of the effect of *a'* through some form of *competition or interference at receptor level,* in a manner cognate to the well known mechanism of drug antagonism in conventional pharmacology. For this to happen, it is not necessary for the drug to be present in high doses because, if it is a "similar," it may show a much greater degree of affinity than the endogenous mediator in interfering with the receptors.

b) *Binding to receptors coupled to inhibitory systems*. Another possibility of moderating the unwanted action of the regulatory system is by activating receptor systems which, once occupied, exert an inhibitory or repressive effect on the cell, on the tissue, or on the global functioning of an organ. Many receptors of this

type exist (e.g. the opioid receptors in the C.N.S., the adenosine A_2 receptors in blood cells, and the H_2 receptors on mast cells). If a homeopathic medicine interacted with such receptors, activating them, we might expect effects such as an immediate reduction of the extent of the symptoms or other disorders.

At this point, it might well be objected that action mechanisms of this type cannot be called homeopathic, inasmuch as they are receptor manipulation phenomena used in many well established allopathic therapies (cimetidine, beta-blockers, calcium antagonists, and so on). This objection is tenable only within the framework of a schematic preconception that there is some kind of insurmountable iron curtain rigidly separating homeopathy and allopathy. We have already expressed the opinion that many modern therapies are steadily approaching homeopathic principles, in the sense that the precise targets of drugs are being increasingly specified, molecules increasingly similar to naturally occurring substances are being used, and synergisms are being exploited with, as a result, the maximum possible reduction of doses.

6.2.6. Relationships with other therapies

Homeopathic therapy is thus a therapy of reactivation or regulation, unlike other forms of therapy which act on different levels of the pathological process (Figure 24). Most of the therapies currently employed are based either on intervention before (against the etiological factors) or after the fact (against the symptoms). Another type of intervention is replacement therapy, which is necessary when a decisive pathogenetic element in the disease is the lack of some factor, such as a hormone, vitamin, or body organ (transplants). In addition, there are also receptor therapies (cf. cimetidine, antihistamines, etc.) which are based essentially on blockade of the response of the reactive system. The homeopathic approach is quite singular, in that it rests on the endogenous systems.

Figure 24. Possible levels at which various types of medical and pharmacological intervention act upon the homeostatic system.

According to the diagram in Figure 24, there are well established therapeutic procedures in modern medicine which act in a homeopathic-like way. Immunostimulants such as interferons, cytokines and bacterial extracts act via this mechanism, though at a slightly more aspecific level. However, here too, we find certain differences. In fact, while in this case the therapy is very specific (precisely targeting the receptors of the allergen), the effect is based more on the suppression of sensitivities than on the exploitation of alternative sensitivities. Actually, the question is subtler because there is evidence that the induction of tolerance in the immune system is not merely an effect of receptor suppression (this might apply to high-dose tolerance), but also an *active response* involving activation of suppressor lymphocytes. In this sense, then, specific immunotherapy might embody a number of elements resembling the action of the homeopathic drug in activating the regulatory system. It is likely that a closer examination of current practice will show that many other drugs used today work on the basis of a mechanism which is at least partly homeopathic.

Even a number of treatments of nonpharmacological type may act as activators of the regulatory system: for instance, hyperbaric oxygen treatment is used in the therapy of refractory skin ulcers. It is likely that such therapy does not work merely because it supplies oxygen to the tissues (this happens only during the brief period of treatment), but because, by virtue of the production of oxygen free radicals, it rekindles the inflammatory process serving the epithelial and connective tissue repair mechanism. Physical therapies such as marconitherapy or magnetotherapy (used in conventional medicine, particularly in orthopedics, cf. Chapter 7, Section 2) may act in a similar way. Finally, the relief of musculoskeletal pain by subcutaneous injection of distilled water should be mentioned: this effect, also called "counter-irritation" or "hyperstimulation" analgesia, is due to the mechanism of "diffuse noxious inhibitory control" (DNIC), referring to a widespread inhibition of the input from nociceptive afferents to dorsal horn cells [Byrn *et al.*, 1993].

In principle, homeopathic therapy is not at odds with other forms of therapy, and, indeed, may actually integrate the latter. This is a crucially important point, which has played a pivotal role in the history of homeopathy as a form of alternative medicine. It may perhaps be understandable that Hahnemann, in his day and age, when medicine had practically nothing scientific about it, should advocate his approach as the only

rational and effective one (see, for instance, the notes on paragraphs 22 and 25 of the *Organon*, in which he defines allopathy as an "irresponsible murderous game with the life of the patient"). Today, however, such an attitude obviously appears anachronistic, in that, from the therapeutic standpoint, it would be desirable to be able to use all such measures as contribute towards restoring human health. For example, it is quite clear that reactivation of the regulatory system fittingly accompanies removal of the etiological factors (environmental prevention, diet, abolition of intake of toxic, allergogenic and carcinogenic substances).

Thus, one can see no reason why homeopathy cannot be combined with antibiotics in cases of bacterial disease. In this latter eventuality, the only objection which could be raised (apart from the problems raised by antibiotics already known to allopathy) is that, if we administer antibiotics when it is not strictly necessary, the regulatory system is not given the chance to function naturally and thus to sensitize itself with a view to an enhanced later response.

Somewhat trickier is the issue of the relationship between homeopathy and drugs acting via symptom suppression. In theory, a combination of the two should not be contraindicated, except, obviously, in the case where suppressor drugs are used at doses that block the functioning of the very system at which the homeopathic drug is aimed. The problem is that, effectively speaking, most of the symptoms are produced by the regulatory systems (see Figures 2 and 21) and that most of the drugs that suppress symptoms (e.g. analgesics, antiinflammatory drugs, spasmolytic agents, bronchodilators) are not very specific in biochemical and biological terms. Consequently, interference with the regulatory action of the homeopathic drug is highly likely.

Another drawback has to do with the fact that suppression of symptoms, though desirable from the patient's subjective point of view, may cause problems in terms of homeopathic *methodology*, because it makes it very difficult for the doctor to get his bearings in the choice of remedy. This is therefore a problem of a methodological type which - who knows? - may conceivably be solved by homeopathy, once the concept has taken root that *some* symptoms (for example, pain) can be removed, while others remain and can be used for homeopathic repertorization.

Lastly, as regards the relationship between homeopathy and other forms of therapy, one fairly banal, but by no means negligible fact is worth stressing. The availability of immediately effective drugs (e.g. antibiotics for infections, antipyretic agents for high temperatures, antihistamines for allergies, sedatives for anxiety, bronchodilators for asthma) tends, almost inevitably, to condition the doctor's activity, diminishing the importance of investigating the causes and of hygienic and preventive measures. Regardless of his or her good intentions, the doctor, under the weight of a heavy workload and pressing patient demands, will be inclined to resolve the symptoms with drugs of immediate efficacy rather than worrying about the underlying causes. Problems of the same ilk are invariably associated with human activities as a result of technological developments: innate faculties and capabilities atrophy owing to disuse.

The homeopathic approach, far from being an alternative to the use of effective drugs when needed, may be of help in tackling this problem because the method entails a shift in the focus of attention from the disease to the patient. For example, it is known that there are people who are prone to frequent infectious episodes, particularly of the upper airways as a result of chills, changes in climate, stress, contact with infected people in particular social settings (schools, barracks, hospitals). It is also well known that, in most cases, no precise biochemical or genetic cause can be pinpointed for such an increase in susceptibility to infection. In these cases, it is clear that the immediate cause of the infection is microbial, but also that the "terrain" - in the case in point, a certain degree of immunodeficiency - plays a decisive role. The use of antibiotics, though resolving the condition if the disease is bacterial, makes it "superfluous" in practical terms to ask oneself why the subject presents such an abnormal risk of infection. Thus, there is a risk of solving the immediate problem well, while leaving the long-term problem unsolved or relegating it to the sphere of possible spontaneous healing. Devoting attention to the "terrain" in these cases would be a more logical and more effectively preventive approach.

6.2.7. Limits of homeopathy

One logical consequence of an analysis of the models presented is also a clearer delimitation of the possible fields of application of homeopathic treatment, this being a subject which is rarely considered, precisely because of the lack of a theoretical frame of reference. Of course, the homeopathic approach, like any other form of medical therapy, presents itself as the only possible approach in certain cases, as an optional

treatment in others, and as useless or perhaps even damaging in others still. Though admitting that, being a "global" approach (see below), some kind of effect will always be obtained, our model rules out the possibility that homeopathy can *resolve* the condition in cases such as the following:

a) In diseases in which the genetic component is preponderant, or rather, in the genetic component (meaning a permanent variance of the genetic code) which is present, to a greater or lesser extent, in almost all diseases.

b) Diseases in which there is an excessively accentuated or irreversible organic type defect, such as, for instance, cases of advanced arteriosclerosis, infarct-associated necrosis, slipped disk, etc.

c) When the etiological factor remains and strongly prevails over the reactive systems: in these cases, though the regulatory system is reactivated, the disease cannot be cured owing to persistence of an excessively intense *A --> A'* perturbation (see Figure 22).

d) When the regulatory system is impaired in such a way as to present no receptors and produce no signals: it might be supposed, for instance, that the efficiency of the various reaction systems declines in the elderly (homeopathy, in fact, is said to be more effective in children) or in subjects taking toxic substances or narcotics.

The logical consequence of this is that homeopathic therapy, based essentially on analysis of the symptoms and on the use of small doses of remedies, cannot be recommended, when there is a well-founded suspicion that we have to do with one of the above-mentioned conditions. To give just one example, precordial pain of sudden onset with characteristics suggestive of angina or infarct precludes an exclusively homeopathic approach and calls for an electrocardiogram and blood-chemistry tests at the very least to substantiate the diagnosis. Concepts of this sort appear only too self-evident today, and the need to integrate homeopathic practice and conventional medicine, tailoring the therapy to the diagnosis, is acknowledged also by modern homeopaths [see, for example, Tetau, 1989].

As far as tumor therapy is concerned, this is an intermediate case. The law of similars, at least in its "classic" form, proves hard to apply in cases in which gross localized anatomical alterations, such as in neoplastic growths, are overlooked by the homeostatic system in general and themselves become the main pathogenetic mechanism of the disease. Moreover, in this type of disease, as we have seen earlier, there is a genetic pathological component (mutation or translocation or insertion of oncogenes) which does not fall within the province of the disorderly functioning of homeostatic systems, but rather figures among those lesions which are practically irreversible on the molecular plane. It is impossible to see how small doses of any drug whatsoever can act on the genetic plane in an extensive cell population. Nevertheless, an approach based on principles analogous to the law of similars and aimed at activating the body's endogenous defences is not only feasible, but also positively desirable. In view of its importance and complexity, this issue will be dealt with in a later section (Chapter 6, Section 5).

Another objective limit to the possibility of effectively applying the homeopathic method may be the practical difficulty encountered in analyzing all the symptoms the patient complains of and attributing the right degree of importance to the various symptoms. In this case, this is not merely a theoretical problem, but also a question of applicability. While it is true to say that homeopathic theory holds that the same drug that causes the symptoms of the disease should be used, in actual fact *diseases are dynamic processes and symptoms often change with great rapidity*. Even the regulatory systems themselves can find themselves in a good response phase or in the phase of pathological adaptation (see Figures 22 and 23, respectively). In the same disease, drugs which are potentially active in one phase may be different from those which are active in another phase. At this stage, the new picture, theoretically, should call for another drug.

In conclusion, then, the activity of the homeopathic practitioner proves highly demanding on account of the continual changes in the clinical picture as a result of the developing course of the disease and the effect of drugs. For this reason, homeopathy, however plausible and useful it may seem in theoretical terms, is hard to apply in practice, requires a great deal of study, very substantial experience and a fair measure of inspired guesswork, and presents all the well-known problems of standardization and reproducibility in the clinical research field.

6.3. The law of similars at pharmacological and pathophysiological level

6.3.1. Considerations on the scientific validity of homeopathy

When tackling the problem of defining the pathological process in relation to the complexity of homeostatic systems, we admitted that the intimate nature of disease is essentially unknowable and, consequently, that the empirical approach adopted by homeopathy in search of remedies for the diseases themselves is essentially legitimate.

This, however, should not lead us to believe that it is pointless to seek an explanation for the action of a homeopathic drug on the basis of its specific pharmacological properties targeting determined pathophysiological mechanisms. Given a remedy identified empirically on the basis of the global approach advocated by homeopathy (that is to say, the complex of symptoms produced by the remedy), it is always possible to work backwards, from synthesis to analysis, seeking to break down the problem of the mechanism of action by considering, on the one hand, the active ingredients of the homeopathic drug and, on the other, specific informational and regulatory disorders of the likely target systems in the body.

Many homeopathic remedies were initially proposed and studied against a total lack of knowledge as to the possible active ingredients which the extracts and initial dilutions contained and, what is more, against a total lack of knowledge as to the possible molecular, cellular and pathophysiological disorders that such remedies were supposed to cure. Today, the situation is quite different and, on the basis of current scientific knowledge, we are in a position to make many connections which previously were unthinkable. One important concept emerges from these connections: at least some of the actions exerted by homeopathic drugs on organs and systems can be explained on the basis of their active ingredients. In this section, we intend to offer a number of examples of such concepts, without being able or desiring to deal in any way systematically with a topic of such vast scope.

The law of similars, as formulated initially by Hahnemann, was based on the similarity of symptoms, and the reasoning outlined in the foregoing section is aimed at demonstrating its substantial validity. However, precisely from what we have said it emerges that the need to resort to the analysis of symptoms is related essentially to ignorance of the intimate pathophysiological mechanisms involved in the disease. This ignorance will never be definitively overcome, owing to the complex nature of the pathological phenomena in most cases, particularly as referring to the complete analysis of the *individual patient.* According, however, to the reasoning behind the models outlined here, it is to be assumed that, if the mechanism or mechanisms of the disease were known, to achieve effective regulatory intervention it would not be necessary - indeed it would not be enough - to resort to analysis of the symptoms, inasmuch as a knowledge of the relevant biochemical. laboratory, molecular and cellular parameters and of their causes is more scientifically reliable and precise.

Assuming that a similar body of knowledge was achieved in an individual case, at this point Hahnemann's symptom-based approach would be integrated in a thoroughly and unequivocally scientific form of homeopathy. This is precisely what is happening in the field of immunotherapy, with the use of the so-called *biological response modifiers (BRM)*, vaccinations and desensitizing therapies, and even in homotoxicology itself. A factor is used which activates the function of the homeostatic system at a fairly well-known molecular level. It is thus readily predictable that *the principles of homeopathy, though not recognized as such, will increasingly pervade scientific medicine, paralleling the increase in scientific knowledge regarding endogenous regulatory systems.*

This should not prompt homeopathy supporters to fear the total "absorption" of classic homeopathy in scientific medicine because many aspects of diseases, in those areas where complexity predominates, will by the very nature of things elude description in molecular terms. In this sense, it is also likely that homeopathy may be a kind of outpost, or pilot experience, for medical research. Homeopathy, in fact, increasingly provides an enormous reservoir of empirical observations, clinical cases, and theoretical speculation built up over what now amounts to two centuries. This experimental and clinical knowledge might open up and suggest to a careful observer new lines of study of those complex regulatory mechanisms which we are gradually coming to understand in their dynamic aspects.

Also within the framework of the homeopathic world, however, we encounter tendencies to rationalize the law of similars according to the viewpoints of contemporary science, finding applications for it at cellular and molecular level [cf., for example, Boiron and Belon, 1990]. Thus, for instance, the *isotherapeutic* approach has been developed, whereby the etiological agent is used in a homeopathic preparation: dilutions of pollen to treat hay fever, dilutions of *Herpesvirus* to treat herpes infections, dilutions of *Candida* to treat candidiasis (needless to say, these are sterilized preparations) and similar therapies. It has also been seen that animals intoxicated with arsenic have been treated with dilutions of arsenic [Cazin *et al.*, 1987], which

indicates that the similarity was sought and found at the level of the etiological agent. At another level, the similarity may be found in organs or cells: we need only consider the protective effects of phosphorus on liver damage, or the effects of phytolacca on lymphocytes and of histamine on basophils, described in Chapter 4.

There are those who propose, at least as a working hypothesis, the "homeopathic" use of allopathic drugs [Dawley, 1988]. The rationale behind this, at any rate from the homeopathic point of view, lies in the fact that precise, detailed toxicological studies have been conducted for the majority of the modern drugs in use today, i.e., in practice, their overdose effects are known. These effects could be compared to a homeopathic "proving." Thus, according to homeopathic reasoning, it should be possible to obtain therapeutic results using diluted, dynamized preparations of the allopathic drugs in two situations:

a) In patients with symptoms similar to those notoriously caused by the drug in healthy subjects.

b) In patients presenting such symptoms as adverse effects of the drug administered at high doses. In practice, this is a modern version of isopathy, or at any rate an approach that should be pursued with all due attention, also in the light of the widespread occurrence of iatrogenic diseases.

The scientific soundness of homeopathy, or at least of some of its aspects, stems from the possibility that many issues can be tackled according to the tenets of current pharmacology and can be subjected to experimental and analytical review. Whereas, on the one hand, this type of therapy, as a global, integrated approach to disease, will always present areas that are essentially unknowable and unsoundable, on the other hand, it is also true to say that many specific problems can be rationalized and clarified.

References to specific drugs and substances mentioned in the following sections can be found in other works [Goodman Gilman *et al.*, 1980; Guermonprez, 1985; Evans, 1989; Brigo, 1990; Kent, 1990].

6.3.2. The history of nitroglycerine, a homeo-allopathic drug

To illustrate the relationship, also in the course of the history of medicine, between homeopathy and conventional pharmacology, it is interesting to note the history of nitroglycerine, which was originally studied as a potentially therapeutic agent by a homeopathic practitioner, C. Hering [Goodman Gilman *et al.*, 1980; Fye, 1986].

Hering tried the substance on himself and on his friends (synthesized not long before that for completely different purposes) over the decade from 1840 to 1850. This was the period which witnessed the birth of the great materia medicas, in whom the results of experiments on an infinite number of mineral, vegetable and animal substances were accumulated and assembled. Hering revealed that the main effects of the ingestion of nitroglycerine (which the homeopaths called *glonoine*) were headache, tachycardia and sense of precordial oppression, in addition to a very unpalatable taste. However, he did not ascribe any great importance to the cardiovascular symptoms and did not include nitroglycerine among the remedies for chest pain, leaving it mainly as a remedy for headache [Hering, 1849]. Perhaps this "oversight" was due to the fact that angina pectoris was a fairly rare disease or, at least, was rarely recognized as such at the time [Fye, 1986]. These early studies, however, are the basis for many other subsequent experiments conducted both by homeopathic and nonhomeopathic doctors, leading in 1879 to the discovery of the efficacy of nitroglycerine in angina pectoris.

This example shows that in-depth analysis of the mechanism of action of homeopathic drugs may bring homeopathy itself closer to conventional scientific medicine, whereas the latter may draw upon the empirical discoveries of homeopathy.

Other examples illustrating the fact that the two approaches are not basically in contrast can be derived from a consideration of what may be regarded as the *active ingredients* of homeopathic preparations in the classic pharmacological sense of the term. As we shall see from the following examples, examination of these active ingredients demonstrates that there is a *biochemical logic* in the use of these remedies, which, at the very least, hints at the reasons why certain drugs have certain effects on precise targets (this phenomenon is also named *biological tropism*).

6.3.3. Belladonna, Hyoscyamus and Stramonium

These are three plants of the *Solanaceae* order containing alkaloids with parasympatholytic activity: atropine, present mainly in *Atropa belladonna* and scopolamine mainly in *Hyoscyamus niger* and in *Datura stramonium*. They are extensively used in the homeopathic pharmacopoeia. According to the law of similars, these plants should be expected to be effective in syndromes with *parasympathetic blockade symptoms*, and, according to their pharmacological composition, the three remedies should present several similarities. Both of these assumptions are adequately corroborated.

According to classic pharmacology and toxicology [Meyers *et al.*, 1981; Goodman Gilman *et al.*, 1992], the effects of atropine drugs can be summarized as follows:

a) *Effects on the vegetative nervous system (VNS)*: mydriasis, dry mouth, tachycardia, postural hypotension, urinary retention and difficulty with micturition, and constipation. All these effects (except for constipation) are listed in the "pathogeneses" (list of symptoms caused in healthy human subjects) of homeopathic materia medicas. Mydriasis, dry mouth, tachycardia with a hard solid pulse and difficult micturition are characteristically present for all three plants.

b) *Effects on the central nervous system (CNS)*: drowsiness and depression, then delirium, hallucinations, sensory hyperexcitability and, with massive doses, convulsions and respiratory depression. In homeopathy, the three plants are indicated in various sleep disorders including *drowsiness* (sometimes accompanied, paradoxically, by inability to drop off to sleep), sleep too deep for arousal or agitated sleep with nightmares.

What distinguishes these three *Solanaceae*, however, in the homeopathic pathogeneses is *delirium* which is a furious, violent manifestation in all three: the patient tends to hit out, bite and tear; it is accompanied by visual hallucinations of men, ghosts, animals, and monsters. *Hyoscyamus* differs from the other two in the verbal excitement with shouting, singing, imaginary disputes or continuous incomprehensible muttering, and in the exhibitionism it produces.

Hyperesthesia is characteristic only of *Belladonna*, while impaired perception is frequent with *Hyoscyamus*. Another important coincidence of effects in toxicology and homeopathic pathogenesis is represented by the *convulsions*, which are present with subtle differences in the pathogeneses of all three *Solanaceae. Belladonna* acts better in the feverish convulsions of infancy. *Hyoscyamus* acts on those accompanied by automatic movements of scratching or plucking (carphology), which, moreover, are often triggered by swallowing (eating or drinking). *Stramonium* causes violent contractions of one or more muscle groups, particularly the muscles of the nape of the neck, in those experiencing its effects. As far as *respiratory depression* is concerned, the homeopathic action is more controversial, considering that *Belladonna* and *Hyoscyamus* can cause both a slowing and an acceleration of breathing, whereas *Stramonium* has no effect. Atropine and scopolamine are also known to have stimulating effects on the respiratory centers.

c) *Effects on extravascular smooth muscle*: whereas, for the CNS and VNS, the coincidence of effects in toxicology and homeopathic pathogenesis is almost total, there is a difference in the effects of homeopathic dilutions of these solanaceous plants on extravascular smooth muscle, where the coincidence can be observed not with the overdose (toxicology) symptoms, but with the ponderal therapeutic use of atropines.

These latter drugs are used in traditional therapy as spasmolytics, e.g. in hepatic and renal colic or in spasms of the gastrointestinal tract. Such indications coincide perfectly with those of *Belladonna* in its homeopathic dilution. *Hyoscyamus*, on the other hand, is used by homeopaths in spasms affecting the eyes (nystagmus) or the eyelids (blepharospasm) or bronchial muscle (spasmodic cough). In healthy subjects, *Stramonium* causes, and therefore cures, violent tics of the face and body as well as a spasmodic constriction of the muscles of the pharynx and esophagus which impedes swallowing. At the present time it is difficult to comment on such behavior on the basis of the law of similars (which would involve inversion of the effect) and of our pharmacological knowledge. However, the action of atropine on Oddi's sphincter is also unexpected: the latter contracts as a result of the action of the sympathetic fibers, while the parasympathetic fibers relax the sphincter; this, despite the fact that atropine inhibits sphincter spasm. One plausible explanation of these apparent discrepancies is to be found only if we consider the fine regulatory mechanisms at receptor and post-receptor level (presence of multiple types of receptor for the same substance, active or inactive state of the receptors, agonist and antagonist effects of the homeopathic remedy), which are topics we have already touched upon at some length in other sections (Chapter 5, Section 4, Chapter 6, Sections 1 and 2).

d) *Effects on perspiration and thermal regulation*: according to classic pharmacology, the atropines can cause suppression of perspiration, with consequent hyperthermia and redness of the skin, particularly in children. It comes as no surprise that, in homeopathy, *Belladonna* and *Stramonium* and, less often,

Hyoscyamus are used in childhood for the treatment of fever of rapid onset accompanied by signs of parasympathetic inefficiency, mydriasis, dry mouth, and facial flushing and congestion, regardless of bacterial or viral etiology. It should be noted, however, that the feverish conditions of *Belladonna* present red, dry skin only initially, later followed by a characteristic and copious perspiration.

6.3.4. Chemical groups present in plants with a spasmolytic effect: polyenes and coumarins

An example of the possible rationale underlying the use of homeopathic remedies is provided by the study of the active ingredients present in a series of plants used with spasmolytic and analgesic indications, though the relationship with conventional pharmacology is less clear than in the previous example. Among these plants, the most representative is *Matricaria chamomilla (wild chamomile)*, the common chamomile, which, in homeopathy, has a spasmolytic, analgesic, antiinflammatory and sedative action. The classic disorders in which it is indicated are unbearable pain, neonatal and infantile flatulent colic with foul-smelling diarrhea, intolerable dysmenorrhea, certain types of fever and otitis, and a number of convulsive syndromes. Bringing it down to three words, we are talking about inflammation, spasms, and hyperesthesia.

In the case of chamomile, the entire flowering plant is used, from which the mother tincture is obtained according to the international standard procedures [Brigo, 1990]. The most interesting constituents are: an essential oil containing chamazulene, a proazulene (matrizin); a polyene dicycloether; a number of polyphenols; coumarins and flavonoids.

Particularly worthy of note is the combination of *coumarins* (products containing a C=O carbonyl group) and *polyene derivatives* (with several C-triple bond-C acetylene groups). This combination is found not only in chamomile, but also in other plants used by homeopaths in convulsive syndromes: *Cicuta virosa* (water hemlock) contains coumarins (umbelliferone and scopoletol) and polyacetylene derivatives (cicutol and cicutoxin); *Oenanthe crocata* contains numerous polyacetylene derivatives and a carbonylated derivative, a ketone, latifolone or crocatone; *Artemisia vulgaris* (mugwort) contains a polyacetylene derivative with a ketone function, artemisia ketone. This type of combination thus appears to be a constant feature of many plants with an anticonvulsive effect. It should be noted that the homeopathic use of such plants seems to be directly related to their very similar chemical composition, despite belonging to very different families from the botanical point of view. *Cicuta* and *Oenanthe* are *Umbelliferae*, while *Chamomilla* and *Artemisia* are *Compositae*.

The polyene derivatives are to be found in two groups of plants:

a) Those with a homeopathic action in the convulsive syndromes: *Cicuta virosa* (spasms in hypertension, epilepsy), *Oenanthe crocata* (epilepsy), *Aethusa cynapium* (convulsions of newborns unable to tolerate mother's milk and suffering from gastroenteritis), *Artemisia vulgaris* (menstrual or peripuberal epilepsy), or, in any event, in various diseases with spasms: *Chamomilla* (in certain convulsions), *Conium maculatum* (tremors, esophageal spasms), and *Grindelia* (dyspnea, bronchoconstriction).

b) Those with a homeopathic action on the inflammatory process and on hemostasis: *Chamomilla matricaria*, *Arnica montana* (traumatisms, ecchymoses, toxic-infectious syndromes), *Bellis perennis* (traumas, ecchymoses, hematomas), *Echinacea angustifolia* (suppuration, abscesses), and *Erigeron canadiensis* (traumatic hemorrhages, ecchymoses).

Lastly, we should mention those plants with carbonyl function derivatives other than coumarins: *Strichnos nux vomica*, *Strichnos ignatii* (strychnine and brucine, indole alkaloids), *Moschus moschiferus* (muskone, an aromatic ketone), *Anamirta cocculus* (picrotoxinin, a highly oxygenated sesquiterpene with several ketone groups), *Crocus sativus* (an essential oil with carbonyl derivatives from safranal and isophorone), *Castoreum* (acetophenone, a ketone), *Ambra grisea (*dihydro-γ-ionone, a volatile compound with a ketone function), *Valeriana officinalis* (pyrryl-α-methylketone and the dipyridylmethylketone, an alkaloid called the "main" alkaloid), *Oenanthe crocata* (crocatone, a polycyclic ketone), *Actea racemosa* (carbonyl of the ester function of actein), *Sepia officinalis* (double carbonyl of sepia-melanin I and II, a black pigment), *Artemisia cina* (santonin, a sesquiterpene lactone), *Gambogia* or *Garcinia hanburyi* (numerous compounds with a carbonyl function including benzophenone), *Cephaelis ipecacuanha* (carbonyls of ipecoside, an azotized heteroside), and certainly several others.

All these plants, when diluted and dynamized and then administered to healthy human subjects in the so-called homeopathic pathogeneses, produce symptoms related to spasms of smooth or striated muscle fibers (in very different areas of the body), and in many of these the presence of such symptoms is essential for the

prescription of the remedy (e.g. *Nux vomica* or *Ignatia* or *Moschus*), while in others it is secondary (e.g. *Sepia*). A fair number of these (*Ignatia*, *Moschus*, *Castoreum*, *Ambra grisea*, *Actea racemosa* and *Valeriana*) are indicated for subjects with a hysterical temperament who manifest changeability of humor, loquacity, paradoxical behavior, and frequent fainting.

The fact that several plants share similar components such as the carbonyl and acetylene groups and that it is these components which at least partly explain the pharmacological effect strongly suggests the existence of a non-casual biochemical and pharmacological basis for the effects of homeopathic drugs.

6.3.5. Ipecac or Cephaelis ipecacuanha

This plant is a *Rubiacea* native to Brazil and Central America, but which is also cultivated in India and Malaysia. The part of it used is the dry root which contains 4-5% of minerals, 30-40% of starch, an allergizing glycoprotein, a tannin (ipecacuanic acid), 1.1% of ipecoside (an azotized heteroside with an isoquinoline ring) and 2-3% of isoquinoline alkaloids, the most important of which are emetine, cephaeline and psychotrine.

Ipecacuanha syrup is used in therapy as an emetic, particularly on account of its *emetine* content, which toxicologically causes:

a) Gastrointestinal symptoms, such as diarrhea, nausea, vomiting and cramping abdominal pains, due to its direct action on the intestinal musculature.

b) Neuromuscular symptoms, such as weakness, pain and stiffness of the skeletal muscles, particularly those of the neck and the extremities.

c) Cardiovascular symptoms including hypotension, tachycardia, dyspnea and ECG abnormalities.

This justifies the homeopathic use of *Ipecac* in diarrhea syndromes, especially if accompanied by nausea, and also in the most disparate syndromes where nausea of central and not gastrointestinal origin is experienced. It may be noted here, in support of the rationale underlying the use of homeopathic remedies by analogy with the pharmacological knowledge, that the specific indication for *Ipecac* is not nausea of gastrointestinal origin, which is characterized by a dirty tongue and is improved by vomiting, but only that where the tongue is clean and moist, salivation is copious and the attacks of nausea are not improved by vomiting. This observation was made by homeopaths back in the last century, long before such nausea could be defined as *central* and, above all, long before it was known that there is a chemoceptor trigger zone in the medulla oblungata and that emetine acts precisely at this level. Furthermore, emetine hydrochloride in a homeopathic dilution is generally preferred to the dry root *in toto* if the diarrhea and nausea are accompanied by hypotension and tachycardia, which are toxic manifestations of emetine and not of the extract of the dry root *in toto.*

Another rational comparison of the use of ipecacuanha in the conventional vs. the homeopathic pharmacological traditions can be done at the level of the respiratory tract. In fact, this vegetable drug is undoubtedly active as an expectorant, but its use has been substantially limited by the presence of the appreciable side effects mentioned above (nausea and vomiting); it was present in a number of antitussigenic preparations and was used at times by asthma sufferers who were unable to tolerate potassium iodide. The homeopathic use of this plant is fairly similar, and is prescribed in respiratory tract diseases with cough, dyspnea, bronchospasm and bronchial hypersecretion; yet, to stress once again the global action of homeopathic drugs, it is particularly indicated if the bouts of coughing are accompanied by nausea or if nausea and diarrhea figure frequently in the patient's medical history.

Summarizing the tropism of *Ipecacuanha* and referring back to the previous chapter, it can be said that *Ipecac* has a distinct spastic tendency in its effects on both the gastrointestinal and respiratory tracts. From the biochemical point of view, this is probably due to the presence of several carbonyl groups in the ipecoside.

6.3.6. Anthraquinone derivatives and diarrhea syndromes

Another example confirming the link between the constituent vegetable active ingredients and the actions of the homeopathic remedies obtained from these plants is provided by the plants used as laxatives both in the popular tradition and in modern pharmacology. These are a liliaceous plant, *Aloe ferox,* a leguminous shrub,

Cassia angustifolia, or senna, and two *Polygonaceae*, *Rheum officinalis* or rhubarb and *Rumex crispus.* These plants all contain anthraquinone derivatives (aloin and rhamnosides of aloin) the laxative action of which is well known; in homeopathy, the action of these plants on the large bowel is confirmed, though obviously with inversion of the effect. In fact, all these plants are characterized by action on diarrhea syndromes, especially *Aloe*.

6.3.7. Coffea

Originating in the highlands of Abyssinia, the coffee plant was introduced into numerous tropical regions of Asia, America and Australasia. In homeopathy green coffee is used, that is to say the coffee bean stripped of its coverings, as it presents itself prior to torrefaction, which produces the aroma. For this reason the remedy is called *Coffea cruda.* In the green coffee bean some 3-4% of minerals can be measured, mainly calcium phosphate and sulphate; citric, malic and oxalic organic acids; carbohydrates and glycosides (over 50% of dry weight); lipids (from 10 to 15%); abundant acid phenols (from 5 to 10%), the most important of which is chlorogenic or 3-caffeoylquinic acid; scopoletol; azotized compounds including serotonin amides and particularly caffeine (from 0.6 to 3%).

Of all these compounds the most interesting and intensively studied is undoubtedly *caffeine*. Caffeine, like theophylline and theobromine, is a purine-based methylated xanthine derivative. Its best known pharmacological action is stimulation of the CNS: in experimental conditions it induces an increase in ability to sustain intellectual effort, a reduction in reaction time and a better association of ideas. However, after ingestion of 1 g (15 mg/kg) or more of caffeine, corresponding to plasma concentrations of more than 30 μg/ml, insomnia, restlessness, excitation and hyperesthesia occur. Another effect of caffeine on the CNS is stimulation of the bulbar respiratory centers, probably because it raises sensitivity to CO_2 stimulation; this action, however, is encountered much more often when respiratory function has been depressed by certain drugs, such as opioids. One last effect on the CNS is nausea and vomiting.

The cardiovascular system is also subject to the action of caffeine. Doses greater than 400 mg, i.e. approximately 5 cups of coffee, increase the sinus rhythm, the formation of ectopic impulses and the cardiac contraction force.

Lastly, caffeine is capable of stimulating both acid and pepsin gastric secretion and the secretion of catecholamines.

To explain the therapeutic effects of methylxanthines, reference is frequently made to their ability to inhibit the phosphodiesterases for cyclic nucleotides. Pharmacological studies, however, clearly show that the therapeutic concentrations do not coincide with those necessary to bring about an increase in cyclic AMP. On the other hand, methylxanthines act as competitive antagonists on the adenosine receptors at concentrations which fall very comfortably within the therapeutic range. Adenosine is actively involved in numerous local regulatory mechanisms, especially at CNS synapsis level; for example, adenosine inhibits the release of neurotransmitters from the presynaptic structures and reduces the neuron discharge rate; in addition, it induces dilation of the coronary and cerebral blood vessels and slows down the activity of cardiac pacemaker cells.

In homeopathy, *Coffea* is used in three main conditions:

a) The most frequent is *insomnia*, and particularly that due to cerebral excitation with continual hyperideation; the subjects for whom it is usually prescribed are agitated, excitable and inclined towards euphoria. In the materia medicas they are described as “full of ideas and quick to act.” Thus, the homeopathic therapeutic use appears to coincide with the toxic effect of caffeine on the CNS at ponderal doses.

b) A second indication is *hypersensitivity to pain* and of all the senses, particularly the sense of hearing, in view of the fact that any pain is aggravated by noise. Some authors claim, however, that this sensitivity is due not so much to caffeine as to the chlorogenic acid contained in green coffee [Guermonprez, 1985].

c) The third indication is a condition of *hypersympathicotonia* which also embraces tachycardia and tachyarrhythmias. This latter indication of *Coffea* in homeopathic dilution may also be compared with the action of caffeine at pharmacological doses on the myocardium.

6.3.8. Active ingredients and inverse effect

The indications outlined above are only a few examples of how, taking homeopathic empiricism as our starting point, a line of study akin to modern pharmaceutical reasoning can be pursued. Of course, a broader-ranging effort of analysis and experimentation would be necessary to provide systematic documentation of the soundness of these concepts.

Table 6 schematically summarizes the possible relationship existing between active ingredients in the preparation, the "homeopathic" effect and the biological and biochemical action of the active ingredients themselves.

The result is a significant demonstration of how, once we admit the possibility of inverse effects, the homeopathic effect can be viewed in terms of an action pharmacologically targeted at one or more physiological systems: *the biological effect of the active ingredient is* "*similar*" *to the homeopathic indications of the remedy itself*. Considering the fact that many homeopathic remedies were identified and applied empirically long before their targets at pathophysiological level could be understood, the relationships illustrated here provide surprising "*a posteriori*" evidence of the soundness of the homeopathic empirical tradition. It goes without saying, of course, that the examples given here constitute only a small, indicative part of a field which is extremely vast and highly complex, inasmuch as homeopathic remedies, often being of vegetable origin, contain a multiplicity of active ingredients.

Table 6. R*elationships between a number of active ingredients of homeopathic remedies and their possible pharmacological effects.*

Drug	**Homeopathic indications**	**Active ingredient**	**Biological effects**
Apis	Edema Pomphi Itching	Melittin	Activates mast cells
Phytolacca	Lymphadenitis Pharyngitis	Mitogenic pokeweed	Activates lymphocytes
Nux vomica	Spasms Hyperesthesia	Strychnine	Blocks post-synaptic inhibition
Ipecac	Nausea Vomiting	Emetine	Activates spinal chemoreceptors
Silica	Chronic inflammation	Silica	Activates macrophages
Opium	Drowsiness Euphoria Constipation	Morphine	Mimics endorphins and enkephalins
Belladonna	Mydriasis Dry mouth Agitation	Atropine	Blocks muscarinic and cholinergic receptors

Iodum	Tachycardia Anxiety Hot flushes	Iodine (via thyroid hormones?)	Activates metabolism
Coffea	Insomnia Hypersensitivity Sympathicotonia	Caffeine	Increased cAMP Adenosine antagonist

6.4. Considerations on autohemotherapy

In our account of the variants of homeopathy (Chapter 2), mention was made of autohemotherapy as a particular form of isotherapy performed with the patient's own blood. It consists in withdrawing a certain amount of the patient's blood, treating the blood with ozone or homeopathic drugs, and re-administering it to the patient, usually by the intramuscular route [Kief, 1988; Kirsch, 1989; Kief, 1991]. Other authors make high homeopathic dilutions (30c or 200c) of patient's blood in distilled water and give it *per os* [Richardson-Boedler, 1994]. Since in this section we do not deal with high dilutions but are interested in the application of the *similia* principle in this particular sector, the topic is discussed considering the use of whole blood or of blood used at low dilutions, i.e. containing putative active principles in molecular form.

As can be seen, the procedure is technically simple, but what is not clear is its efficacy, its mode of action, its indications and its contraindications. We cannot review here all the problems, some of which serious, which make this modality a subject of much debate and indeed a questionable practice. The procedure is interesting because it may provide a valid example of an "interface" between homeopathy and problems within the domain of modern immunology. Autohemotherapy is based on the homeopathic principle: administering to the patient something which contains active ingredients of the disease, in this case autologous blood.

Here we shall consider a number of hypotheses as to the possible mechanism underlying the therapeutic procedure termed autohemotherapy, particularly when this is applied to the treatment of allergies. The mechanism of action of autohemotherapy may be interpreted in the light of the most recent advances in knowledge regarding immunological homeostatic systems, most notably in the context of the idiotype network theory.

Up until the mid 'sixties the reactions of the immune system were viewed in terms of the ability to recognize and eliminate, through the antibody (B lymphocytes) or cellular (T lymphocytes) response, non-self antigens, largely originating outside the individual, or antigens deriving from abnormal modifications of endogenous substances. Following the discovery of anti-antibody antibodies, it was appreciated that the interplay between antigens, antibodies and cells of the immune system is a far more complex matter.

Credit is due above all to N. K. Jerne, the 1984 Nobel Prize-winner for Medicine, for constructing a model (the *idiotype network*) to explain these interactions. According to this theory, which is universally accepted today [Jerne, 1974; Male *et al.*, 1988; Golub, 1984; Blaser and Weck, 1982; Perelson, 1989], the antibodies, as proteins, are themselves antigens and thus an antibody (antibody-1, or "Ab1"), directed specifically against a certain foreign antigen (in our case, for instance, an allergen) presents a particular structure (*idiotype*) in its variable part called Fab (Fragment antigen binding), and this idiotype may evoke the formation of specific antibodies (*antiidiotype*, or "Ab2") (Figure 25).

Figure 25. Schematic representation of the formation of antibodies to a foreign antigen (Ab1) and of antiidiotype antibodies (Ab2 and Ab3). Solid lines = stimulation of the system or production of antibodies; dashed lines = blockade of the antigen or idiotype regulation. For the sake of simplicity, the antibody is represented as univalent (i.e. binding an antigen with only one region).

These antiidiotype antibodies in turn evoke the formation of anti-antiidiotype antibodies, or "Ab3." Ab1, Ab2, and Ab3 are produced in different (decreasing) amounts in the course of a normal immune response.

We do not know what the effective degree of "ramification" of the system is, but it would not appear to go beyond Ab3 or Ab4 [Male *et al.*, 1988].

On this basis, various mathematical models have been developed in order to be able to make quantitative predictions regarding the behavior of lymphocyte clones during the immune response [Perelson, 1989]. On analyzing immune dynamics (e.g. the trend of the production of a certain antibody) by these means, it has been seen that it always presents oscillations in which the concentrations of idiotype and antiidiotype antibodies fluctuate inversely with peaks recurring roughly every 80 days. If. however, a number of parameters of the system-model are changed, even only slightly (such as, for example, the rate of formation of new B cells in the spinal cord), the fluctuations become irregular or even aperiodic (chaotic). An interesting point is that such substantially irregular oscillations have also been found in experimental immunizations in the rat [for a review see Perelson, 1989].

Since the antiidiotypes recognize and bind to Ab1, they have a physicochemical structure "*similar*" to the allergen (which also binds to Ab1) and represent, so to speak, the "*internal image*" of it produced by the body (see Figure 25).

The fact that the antiidiotype (Ab2) is in many respects similar to the original antigen has already been exploited by immunologists to produce vaccines which are used when the administration of the original antigen is inadvisable for reasons of safety (e.g. particularly dangerous viruses). In this case, the patient who receives an antibody resembling the pathological antigen will produce anti-antiidiotype antibodies (Ab3) which will be similar to Ab1 and thus will furnish a certain degree of protection against the antigen we are seeking to induce immunity to. Another possible application, still, however, at the experimental stage, is the use of antiidiotype antibodies in autoimmune diseases [see, for example, Verschuuren *et al.*, 1991].

This whole series of interactions does not have the pathological significance of the known anti-antibody antibodies present in autoimmune diseases, but appears to perform important regulatory functions. In fact, the binding of an antibody to the idiotype of another antibody may have a number of major consequences, namely:

a) The neutralization of the possibility of binding the "natural" antigen (or allergen), by masking the recognition site.

b) Elimination of the aggregate antibody complex by the phagocyte system.

c) Blockade of the receptors for the antigen on B lymphocytes, these being receptors which notoriously present the same idiotype as the antibody that the cell will produce; thus blast cell formation, cloning and maturation of the B plasmacell line specific for that antibody are also blocked.

d) It cannot be ruled out that a strong antiidiotype response may even lead to the elimination of the lymphocyte clones through cytolysis or apoptosis, with the result that a state of permanent desensitization might be expected.

Though the theory was originally proposed in terms of interactions between antibodies and B cells, it now also embraces T cells, which present antigen-specific receptors on their surfaces. T-lymphocyte receptors also present a variable part which therefore expresses a particular idiotype, which can be recognized and may interact with an antiidiotype receptor on the T cells or with an antiidiotype antibody. Inclusion of the T cells makes the interpretation of the possible physiological functions of the system enormously more complex. There are, in fact, various types of T lymphocytes, the main ones being those of the *helper* type (which increase the immune response) and those of the *suppressor* type (which inhibit it). There is evidence that idiotype-specific cells of both helper and suppressor type can be formed.

The interactions at idiotype network level, both of B and T cells, are very important in the regulation of processes controlling both the quantity and quality of the immune response. Malfunctioning of the idiotype network forms part of the mechanisms causing the onset of autoimmunity: since a certain amount of autoimmune reaction is also present in the healthy body, it is the idiotype networks (and more specifically their "*connectivity*") that govern the transition from innocent to aggressive autoimmunity [Kumar and Sercarz, 1991; Cohen, 1991; Varela and Coutinho, 1991].

Other experiments, conducted in the mouse [Kelsoe *et al.*, 1981; Blaser and Weck, 1982] have shown that injection of idiotype has modulatory effects on the immune system depending upon the dose injected. For example, 10 μg of antibody suppress the production of anti-antibody, whereas 10-100 ng stimulate it. It has also been seen that it is easier to obtain suppression in young animals than in adults [Male *et al.*, 1988].

The induction of T cell mediated suppression can be explained by the fact that the idiotype injected binds with T suppressor cell receptors and stimulates them, inducing the proliferation of a clone of antiidiotype T lymphocytes. These cells then interact with and suppress B cells expressing the idiotype,

blocking the production of antibodies. There is experimental evidence that B cells, antibodies and T cells have receptors with similar or identical idiotypes [Blaser and Weck, 1982]. It should be noted that, for the T-B interaction (in which cells of the macrophage series also participate) to be able to take place, recognition of the HLA group is also necessary. In other words, these mechanisms operate only between cells belonging to the same HLA group.

What we have said here above refers to studies conducted on the normal IgG immune response. Evidence is available that the idiotype network also plays a role in the regulation of the IgE response, which is the most important (though not the only one) in the pathogenesis of allergic manifestations. In synthetic and necessarily simplified terms, the main pathogenetic factor in allergy, or type I immediate sensitivity, is excessive production of IgE antibodies in subjects who are particularly sensitive to given allergens. These antibodies then bind with their constant fragment (Fc) on the membrane of the circulating basophils and mast cells in the connective tissue, mainly subepithelial. When the allergic (sensitized) subject again comes into contact with the allergen, this binds to the Fab part of the cellular IgE and triggers the release of histamine and of other inflammation-promoting substances. According to the area where the reaction is maximal, there will be various manifestations such as urticaria, rhinitis, conjunctivitis, edema of the glottis, asthma, and diarrhea, and even anaphylactic shock if the reaction is generalized.

According to some researchers [Katz *et al.*, 1979], the formation of IgE is minimal in normal subjects and kept at low levels by a disactivation mechanism consisting in T suppressor cells and their soluble factors. Depression or malfunctioning of this disactivation mechanism might trigger sensitization whereas the stimulation of IgE-T suppressors might restore the state of health. Neuroendocrine mechanisms are also certainly involved in allergic reactions, if we consider, for example, that cortisone has a potent depressant effect on lymphocyte responses and that some nerve endings in connective tissue can release neuropeptides (substance P) which are capable in themselves of stimulating the mast cells to secrete histamine.

Going back for a moment to autohemotherapy, it can therefore be postulated that this procedure could enable us to intervene in the delicate equilibrium regulating the IgE response and thus the allergy. By introducing the patient's own blood by the intramuscular or subcutaneous route, critical factors are introduced into the network, which are vectors of specific information: antibodies, immune complexes and lymphocytes (especially T lymphocytes, which are the ones most commonly present in the bloodstream) bearing particular idiotypes. Aided by the inflammatory reaction caused by the blood in an extravascular site and, possibly, by the large amount of lipid material supplied by the erythrocyte membranes (that could work as an adjuvant), these factors may stimulate the production of antibodies (IgG or IgM) capable of neutralizing IgE, or may stimulate the production of idiotype-specific T lymphocytes capable of suppressing their corresponding IgE-producing B cell counterparts.

The administration route is of considerable importance. In fact, one possible objection to the hypothesis propounded here might be based on the fact that in autohemotherapy what is administered is the patient's own blood and thus something which is obviously already present throughout the immune system and tolerated as "self." This would therefore fail to explain an anti-idiotype response greater than the physiological one. One answer to this objection, hypothetically, may be that via the intramuscular or subcutaneous administration route the idiotype-specific factors (B or T receptors or antibodies) are expected to reach the immune system (lymph nodes) across the cortical sinus, which is the most appropriate route for it to be recognized, processed by the phagocytes and presented to the lymphocytes. As already discussed previously (Chapter 5, Section 6.1), by changing the introduction route of the antigen opposite effects can be achieved in the immune response.

Equally important may be a partial chemical modification of the antibody (or of the lymphocyte receptor) [see Sehon, 1982]. This modification, which transforms the "identical" into the "similar," might come about during the inflammatory response (intervention of proteases, formation of carrier-hapten processes, protein and proteolipid aggregates) as a result of the very presence of blood in an extravascular site. The transformation of the "identical" into the "similar" may be a mechanism for bypassing immune tolerance and inducing the anti-idiotype response.

In the context of this type of reasoning, an explanation may be found for the fact that, according to certain authors [Kirsch, 1989], on treating blood with ozone prior to reintroducing it into the body, earlier and more effective therapeutic responses are obtained. Ozone, a potent oxidizing agent, would make the idiotype (or the adjacent parts of the protein structure) slightly different from the naturally occurring idiotype, thus stimulating a much more intense response. In animal models of autoimmune diseases (experimental allergic encephalomyelitis) it has been seen that modification of no more than a single amino

acid in the protein inducing the autoimmunity (myelin basic protein) transforms it into an agent capable of preventing the autoimmunity itself [Smilek *et al.*, 1991].

The regulation of the formation of antibodies involves both helper and suppressor effects, and an alteration in the equilibrium between them may be triggered by an antiidiotype response. In this connection, it is significant that the formation of IgE is particularly susceptible to suppression by the antiidiotype. In some cases, concomitant suppression of the IgE response and activation of the response of other antibody classes have even been observed. This is important because the specific suppression of the entire immune system may be deleterious for defense against a pathogenetic antigen and its elimination [Blaser and Weck, 1982].

Among the possible mechanisms involved in autohemotherapy we would probably also be well advised to consider the "aspecific" reactions, namely those reactions which are not directly related to immunity to a certain substance. In a patient's blood, in addition to the antibodies and activated lymphocytes, there are many other components potentially endowed with biological significance. For example, cytokines, interleukin soluble receptors, and cytokine antagonists, are all highly active substances, even in small doses. It is plausible that, in every disease and at every stage of the disease, particular "constellations" of various compounds of this type are created for regulatory purposes. In other words, there is also a *cytokine network*. At this point, the use of blood of this type may prove very efficacious in regulating nonspecific responses. The inhibition of the degranulation of basophils *in vitro* by blood dilutions may be due to such effects [Sainte Laudy *et al.*, 1986].

Despite the fact that the foregoing considerations may conjure up suggestive intervention possibilities, we must make it quite clear that, owing to the complexity of the immune system, it is to date impossible to construct a model which enables us to establish with certainty what happens as a result of the introduction of autologous blood according to the autohemotherapy procedure. It is by no means easy to predict the response in the individual patient or even to know whether this procedure, which undoubtedly constitutes a "perturbation" of a delicate equilibrium embracing many components, may entail a risk of aggravating the patient's immunological status.

In a critical review of the problem, one point which can hardly fail to capture our interest is the fact that the clinical evidence is in favor of autohemotherapy, in that it shows a significant number of cures or improvements in allergic patients. What is more, no serious side effects have been reported, if we exclude the occurrence of fever syndromes. Since, however, the literature on this subject is fragmentary and for the most part not retrievable by consulting current texts of immunology, further and more detailed research is necessary. Particularly in the treatment of severe diseases of the immune system such as AIDS, where the use of autohemotherapy has also been proposed and experimented with (apparently unsuccessfully) [Garber *et al.*, 1991], it is absolutely mandatory to proceed with all due caution using reliable assessment procedures for evaluating the efficacy and harmlessness of such techniques.

In conclusion, then, it would be desirable to clarify the biological basis of a method which might, if properly known and conducted under strict surveillance, constitutes a valid approach in the management of various disorders of the immune system and of inflammation. Essentially, two main avenues of research could be explored:

a) Conducting large-scale strictly controlled clinical trials to establish the validity of the procedure and its adverse side effects, if any. In these clinical trials the investigators should take into account not only the subjective symptomatological aspect, but also the instrumental aspect (e.g. spirometric determinations in forms of asthma) and, above all, the laboratory aspect (antibody assays, assays of lymphocytes belonging to the various subclasses, all the relevant allergy tests).

b) Intensifying research into the biological basis of autohemotherapy, investigating, for example, whether the effect depends on administration of antibodies, or of lymphocytes, or other blood components (cytokines, immune complexes). Furthermore, animal models could be developed (particularly in mice) which are much easier to manipulate in experimental terms. Most of the studies on the idiotype network have, in fact, been conducted in mice, so much so indeed that many aspects of this theory in human subjects are purely hypothetical.

6.5. Homeopathic medicine and modern oncology

In this section we shall tackle the problem of possible new therapeutic approaches to tumors, not with the intention of providing indications for therapeutic practice (this would be both beyond the bounds of the aims of this book and beyond the sphere of competence of its authors), but with the intention of illustrating how complex the problem is and the possible contribution of the homeopathic approach in this field, at least from the theoretical point of view.

The giant strides made by oncology in recent years in the fields of surgery, radiotherapy and chemotherapy are there for all to see. Malignancies which until not so very long ago carried a thoroughly negative prognosis are now treatable and even curable today. At the same time, the necessary awareness and means of intervention have also increased as a basis for an effective prophylactic effort. Much, however, still remains to be done and to be understood before we can claim to be satisfied with the therapeutic measures available to medicine in the struggle against these diseases.

On the basis of our analysis of the situation in Chapter 5, Section 3, where we reviewed the basic elements of our knowledge of molecular pathology in cancer, we might be tempted to ask ourselves whether the dispelling of the darkness shrouding the pathogenesis of cancer allows us to project new and more effective therapeutic measures. Realistically, we are still a very long way from seriously capitalizing on such knowledge from the therapeutic point of view, though certain tendencies and lines of research now appear highly promising.

6.5.1. Problems related to possible therapeutic measures

The existence of various phases linked to epigenetic events (see the concept of neoplastic "*promotion*" illustrated in Chapter 5, Section 3.3) and to the intervention of exogenous and endogenous factors which control and promote tumor growth (see the concept of neoplastic "*progression*") partly modifies the notion of a tumour as a chance event, subject to the laws of probability and ultimately unmodifiable in its dynamics, unless through some form of destructive attack (surgery, chemotherapy).

The basic question is the following one: *if it is true that neoplastic disease is subject to a progressive dynamic trend, might there also be a regressive dynamic trend?* The recent studies on this issue enable us to give a partly affirmative answer, at least from the theoretical standpoint and on the basis of experiments in cell cultures. It would appear, in fact, that tumor growth is not inevitably progressive, not entirely uncontrollable, and not necessarily irreversible. Little can be done to modify the transformed gene (oncogene), but a great deal could be done to block its deleterious effects. Hope lies therefore in being able to act effectively at epigenetic level, as argued, for instance, by L. Sachs: "*The genetic abnormalities that give rise to malignancy can be bypassed and their effects annulled by inducing the differentiation that blocks multiplication*" [Sachs, 1989].

A number of theoretical possibilities of inducing tumor regression using means other than conventional radio- and chemotherapy or surgical approaches are the following:

a) *Immunotherapy*, consisting in potentiating the defenses of the host organism by administering immunotoxins (antibodies to the tumor, acting as vehicles for toxins), interferons and cytokines, or cells treated with interleukin 2 (LAK), or other natural or artificial immunostimulating agents such as bacterial extracts or polysaccharides (research here is breaking extensive new ground) [Uchida, 1993].

b) *Blockade of oncogene expression*, by means of the addition of appropriate agents such as interferons (α-interferon seems particularly important, above all because its efficacy in certain tumors has been demonstrated [Gutterman, 1994]) or antagonists of the tumor promoters, such as, for example, bryostatin, genistein or corticosteroids.

c) *Blockade of the protein production of oncogenes*, by means of the administration of antisense oligonucleotides specific for the oncogene or oncogenes involved, which would interfere with the mRNA and thus with protein synthesis in the tumor cells.

d) *Induction of cell differentiation,* by means of specific tissue-specific factors, hormones, vitamins (e.g. vitamin A, or vitamin D3), sodium butyrate, and other agents which would bring the cells to more mature stages, with consequent arrest of proliferation.

e) *Induction of expression of anti-oncogenes* (very important, but for the time being purely theoretical, since little is known about their products and their modes of regulation).

Among all these possibilities corticosteroids have been in use for some time now in the treatment of leukemia, but more recently there has also been the use of vitamin A (retinoic acid) and, particularly, that of

cytokines (such as interleukins, interferons, and tumor necrosis factor), because these agents have pleiotropic effects, acting both on the host and on the tumor. It would appear important to base the intervention not so much on a single cytokine as on a combination of two or more cytokines so as to be able to exploit their synergistic effects and thus reduce the doses and home in on the target or targets. From tests in cell cultures it would also appear that the combination of a cytokine (such as tumor necrosis factor) and a chemotherapeutic agent (such as adriamycin) makes it possible to use very low doses of both to overcome the resistance of the tumor cells to the treatment [Bonavida *et al.*, 1991; Taylor Safrit *et al.,* 1993]. In view of their importance, these lines of research are actively pursued with promising results.

The problems that hinder a simplified approach to the modulation of the neoplastic growth are multiple, and this is all the more true, if we consider the possible clinical applications. We can do no more here than merely touch upon a number of open questions:

a) Therapy with cytokines or with LAK cells has often been characterized by serious side effects and, moreover, appears effective only in a minority (albeit by no means negligible) of the tumors in which it has been tried.

b) The differentiation factors and the cytokines themselves may be mitogenic factors in some cancers, thus accelerating tumor progression.

c) The proliferation-inhibiting factors can hardly be expected to possess such a degree of specificity as to be able to inhibit only the tumor, and thus they may have immunosuppressive side effects (e.g. corticosteroids).

d) The antisense oligonucleotides (which theoretically would have the enormous advantage of selectivity) work in cell cultures, but only at doses that could hardly be used *in vivo*, where they would also be rapidly degraded.

e) In general it is difficult to predict the actual doses that reach the target cells, especially in the case of molecules with a poor tissue diffusion capability or which are not easily picked up by the receptors.

f) One last problem has to do with the fact that the trials with the new drugs must first be conducted in animals, despite the fact that, in this field, animal models are not always predictive of the outcome in human subjects.

What we have said thus far may suggest, by and large, that a disease as complex as cancer necessarily calls for a subtle, sophisticated, complex diagnostic and therapeutic approach, taking good care to individualize the treatment. Alongside the traditional strategy of “attack” (surgical, pharmacological or radiotherapeutic), which, as is well known, is capable today of resolving many cases of cancer, we may postulate that the identification of the various and multiple factors contributing towards cancer development may enable us to take efficacious remedial action for inducing regression, or at least for slowing down tumor progression.

Faced with all the various possible levels of dys-regulation in the system as a whole, we can hardly suppose that the reductionist approach will prove resolvent, whereby, knowing the molecular mechanism involved, we can then intervene with a specific drug, just as we can hardly suppose (and history demonstrates it) that pure empiricism will prove resolvent, whereby on the strength of continual trial and error a recipe will be found for curing cancer. It is, however, experience, scientifically based and methodically controlled, that will have the last word regarding the usefulness of a treatment. Faced with a problem of enormous complexity, modern biomedical science and the empirical approach, which often comes up with new and unexpected aspects of reality, can meet on common ground and integrate one another, each providing its own specific contribution.

6.5.2. The law of similars in oncology

In this context, what role can homeopathic medicine play? First and foremost, we should stress the serious danger posed by those methodological approaches which expressly claim to be an alternative to conventional medicine - aiming at its exclusion - on the basis of purely empirical or intuitive reference markers. Such approaches, which are perhaps less open to criticism in other fields of medicine where the patient’s life is not at stake, take no account of the biological reality or of the advances in scientific knowledge of cancer and therefore cannot fail to be inadequate in terms of results. It goes without saying that, in those cases where healing by allopathic means is reasonably possible, homeopathy can play no more than a secondary role. In the current state of our knowledge and experience, homeopathy cannot be considered as an antitumor

therapy, in the sense of being able to attack the tumor directly. In this field, there are no important, convincing studies, but there are theoretical objections regarding the efficacy of homeopathic remedies in resolving diseases involving the genetic component of the cell (cf. Chapter 6, Section 2.7).

In tumors, particularly when diagnosed at an advanced stage, the molecular, cellular and systemic alterations are so advanced and serious that the "similarity" between the symptoms of the remedy and those of the patient, as expressed in the classic version of the law, proves hard to detect and is barely applicable. In other words, since the identification of suitable remedies is supposed to be based on experiments with such remedies in healthy subjects, where they are supposed to cause symptoms similar to those of the disease, it is unthinkable that such experiments can be conducted in such a way as to cause tumors in healthy people. To this one might object that it is, in any event, possible to implement homeopathic therapy not aimed directly at the tumor, but at the overall complex of the subject's neuroimmunoendocrine characteristics, in an attempt to restore their equilibrium. This is undoubtedly true, but two major outstanding problems remain:

a) How can such characteristics be identified in a situation where the tumor has created such a severe and profound upheaval in the patient's body?

b) How can a treatment aimed at the fine regulation of homeostasis act within the context of such a strongly and progressively degenerating clinical and biochemical picture?

Having said this, it does not mean that we cannot express a number of general considerations on the subject, which is most certainly of considerable topical interest.

If the basic problem is at the informational level (genetic or epigenetic), it ought to be expected that, in theory, a good therapeutic intervention should consist in providing the system with the "right" information in a form that can be received and utilized at the level of the control system that has undergone a loss of equilibrium. In this sense molecules, too, are items of information (good or bad, as the case may be; for example, the viral oncogene is "bad news" for a cell!) and in this sense they are often used in therapy. Once we have excluded the possibility that the weak and complex information provided by homeopathic medicines can have any chance of defeating a tumor in its progressive phase, we have to ask ourselves whether or not the homeopathic approach can have a positive impact *on a number of aspects of the body's struggle against the tumor*.

As regards the contribution that homeopathy, and natural medicine in general, might perhaps be able to make in the field of modern oncology, one aspect which in the first place appears to be of particular interest is the study of a number of drugs of vegetable origin such as the extract of *Viscum album*, which first came to light in the empirical tradition and today have clearly and surprisingly (if we think of the way they were discovered) been shown in scientific studies to contain active ingredients of both immunostimulant and cytotoxic type against cancer cells [Koopman *et al.*, 1990; Gabius *et al.*, 1992a; Gabius *et al.*, 1992b; Kuttan and Kuttan, 1992].

The methodological approach of homeopathy and homotoxicology, however, is not only important for its ability to supply empirically identified natural remedies, but is worthy of note above all because it tends to provide an overall picture of the patient in his or her entirety and particular pathophysiological individuality, the essential programmatic and methodological characteristics being the painstaking, systematic effort to gather the greatest possible amount of information about the patient's state and history, together with the basic guiding concept that to be effective a treatment must aim first of all at treating the "host" or "terrain," i.e. at treating the patient before treating the disease.

In this connection, it is worth recalling that homotoxicological theory [Reckeweg, 1981] defines cancer as a dynamic process which is in a certain sense progressive vis-à-vis inflammation, when the latter has not been completely resolved (see also Chapter 2, Section 6). From the therapeutic point of view, homotoxicology has introduced the concept of "*regressive vicariation*," according to which stimulating the process of expulsion of "homotoxins" ("excretion phase") and inflammation ("reaction phase") with various biological means may constitute a way of preventing or combating the transition to degenerative or neoplastic phases of disease.

These concepts, though generic, appear to be consistent with modern cytokine therapies which, while being much more controllable and scientifically sound, are based essentially on the same biological principle: activating inflammation and immunity for the purposes of utilizing these systems to the full to attack the tumor. Using purified cytokines or mixtures of them, as is done today in a number of antitumor protocols is not *substantially* very different from the administration of the old B.C.G. (bacillus Calmette-Guérin, an attenuated strain of the Koch bacillus) or of the homeopathic nosodes (which are essentially extracts of tissues with pathological processes in progress and thus containing mixtures of cytokines in

addition to the etiological agent). Cytokines, in fact, are normally produced *endogenously* whenever the inflammatory reaction is activated.

From a theoretical standpoint, cytokine therapy is, in a certain sense, akin to the homeopathic approach. These molecules, in fact, are produced in the cancer patient and are responsible for a fair amount of the symptoms: we may recall, for example, the effects of the tumor necrosis factor, which causes lack of appetite, weight loss to the point of cachexia, fever, shock and a whole series of biochemical disorders. In small doses, the same molecule serves to activate the leukocyte antitumor defenses.

An even more marked degree of analogy with the homeopathic approach can be found in treatments aimed at providing specific immunotherapy for cancer. In this field there have been many attempts in the past, with very little success, but recently interest in this line of research has been rekindled thanks to new ideas and new experiments [see, for example, Chen *et al.*, 1992; Boon, 1993; Fathman, 1993; Dranoff *et al.*, 1993; Dalgleish, 1994]. Though this is not the place for a systematic analysis of such a vast and varied problem, some brief mention at least of the basic principle of this specific immunotherapy is worthwhile. What the various proposals have in common is the use of the cancer cells themselves, suitably treated in order to "unmask" their antigens so as to specifically stimulate the defenses against the tumor. A very interesting way of achieving this "unmasking" would appear to be to insert into the tumor cells by genetic engineering additional signals for the lymphocytes, which, in this way, may be able to "understand" that the tumor cells are extraneous to the body and thus give the go-ahead for rejection of the tumor. In other words, an attempt is made to "present" the tumor cells to the immune system, which previously failed to recognize the tumor, the purpose being to activate the reaction of the immune system.

The above-mentioned approach is a very sophisticated use of a "similar" in order to enter into the subtle information network of that complex homeostatic system known as immunity. The law of similars is transferred from the sphere of similarity between symptoms to that between cellular and molecular mechanisms. This is not entirely in keeping with classic homeopathic reasoning, which, for the reasons already discussed, programmatically seeks to focus upon the entirety and the complexity of the human being. The fact, however, that it does not fully comply with the law of similars does not mean that it conflicts with it. Rather, we might start thinking - without departing from the province of theoretical indications - in terms of intervention at various levels:

a) Fighting the tumor mass according to the conventional "allopathic" approach (surgery, chemo- and radiotherapy).

b) Regulatory measures on the biological plane and nonspecific immunotherapy (see previous section).

c) Specific immunotherapy using the tumor cells themselves.

d) An attempt to restore overall pschyo-neuro-endocrine homeostatic equilibrium by means of psychotherapy and/or the classic homeopathic approach.

The possibility of integration between conventional and complementary approaches to cancer treatment is also suggested by a recent survey in the *British Medical Journal*, which reported that in Britain a sizeable percentage (16%) of patients receiving conventional treatments for cancer also use complementary therapies, the most commonly used being healing, relaxation, imagination exercise, diets, homeopathy, vitamins, and herbalism [Downer *et al.*, 1994]. The study was not an attempt to investigate the efficacy of complementary therapies in these diseases, but rather to look at what proportion of patients used complementary therapies and at their satisfaction with these treatments. Apart from the difficulties caused by diets in some patients (weight loss, unpalatable nature of the diet, time and money spent preparing the food), patient satisfaction with complementary therapies was in general high, even without any hope of an anticancer effect. Benefits were mainly psychological, such as an increase in optimism and feeling emotionally stronger. Individual patients also reported physical effects, including less difficulty in breathing, reduced nausea, and increased energy.

As regards the above-mentioned study, it is worth stressing that even if the main outcome of such complementary therapy in cancer was of a psychological nature, it would in any case be an important result in this type of patient.

We can conclude, then, by saying that, despite all the inaccuracies related to the paucity of scientific research conducted in this field (a situation which is improving today), the homeopathic and homotoxicological approaches appear to integrate the modern concepts stemming from experimental oncology. Obviously, we should stress once again that the considerations expressed here remain within the province of theoretical speculation and that the intention is not to champion the actual usefulness of

homeopathic and homotoxicological remedies as a primary prescription in oncology. Any such usefulness, to our mind, has still to be demonstrated in practice by means of appropriate clinical trials.