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THERAPEUTIC DISEASE: A CONCEPT OF XIX AND EARLY XX CENTURY MEDICINE

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SUMMARY

The concept of therapeutic or antagonistic disease, i.e. a disease that interrupts or cures another and then spontaneously heals, had an ephemeral success in the XIX century and the first decades of the XX century. Some authors limited themselves to the careful collection of pertinent instances; others tried to go beyond the mere analysis and to develop practical applications, i.e. attempts to use a disease to cure another, only one of which, namely the electro-convulsive therapy, survives to date. In the long run, however, the concept proved of limited value and reduced applicability, and was abandoned. The origins of the concept of therapeutic disease cannot be traced down with certainty, since sporadic, matter-of-fact observations are already present in the most ancient Greek medical writings. However, the full theoretical development of this concept in a systematic form, and its intentional application to therapy occurred much later, and reached its height in two medical theories developed by German speaking authors: Hahnemann's homeopathy and Freud's psychoanalysis. A third theoretical elaboration of the same concept can be found in the writings of some French hypnotists, by and large in the same period, although hypnosis (at the time called somnambulism) is the heir of Mesmer's magnetism, a theory that did not originally imply the concept of therapeutic disease. In addition to the above theories, at the beginning of the XX century effective therapies based on the same concept were devised on a purely empirical basis: e.g. Wagner Jauregg's malaria therapy for syphilis, abandoned in favor of chemotherapy, and the several shock therapies for major psychoses, of which only the

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electro-convulsive therapy of Cerletti and Bini has survived. Were it not for these applications, the whole concept of the therapeutic disease would qualify as an interesting error in the pathway of medical thinking.

Introduction

The observation that a disease may sometimes cure another can be traced back to Greek medicine and followed through Roman and medieval times. Correctly interpreting the ideas of Greek physicians on the role of the curative diseases is often difficult because of the imprecise nosography and diagnosis. In some cases we have the impression that the reported event is coincidental; e.g.:

When the stools are bilious, they cease if deafness supervenes; when there is deafness, it ceases when bilious stools supervene[1].

In other cases we may confidently assume that the curative disease is but the conclusive manifestation of the spontaneous one, e.g.:

When the head aches and the pain is very severe, a flow of pus, water, or blood, by the nostrils, ears or mouth, cures the trouble[2].

In this case we may imagine that the pain was due to infection or inflammation, and that the emission of the exudates offered relief. Harris Coulter noticed that the ancient physicians interpreted emissions like the ones described in the latter quotation as the result of the "coction" of abnormal fluids[3]; if this interpretation were to be generalized, the concept of the curative disease should be better termed the curative evolution of one and the same disease. However, it seems to me that at least in some cases the relationship between the curative disease and the coction of pre-existing pathological humors is not obvious. Thus we may assume that the hypothesis of the curative disease was born in two slightly different and mutually confused versions. The first version, that we may call the therapeutic disease proper, states that a supervening disease, natural or iatro-

genic, can interfere with, and possibly cure, a pre-existing, unrelated one. There are clear cut instances of the therapeutic disease proper, e.g. the immune depression occurring in the course of measles may induce a temporary remission of allergic or autoimmune diseases like nephrotic syndrome. The ancient physicians may possibly have observed some such cases, even though the imprecise nosography of the time does not allow a clear identification of these cases from their reports. The other version, of the therapeutic evolution, suggests that a disease may transform, spontaneously or because of a therapy, into another, with a better prognosis. In either case, cure requires the substitution of the original disease with another.

With the great advancements of nosography that occurred through the XVIII and XIX centuries, the hypothesis that a disease may cure another could be reassessed with greater precision and acquired its systematic form in the hands of theoreticians and experimentalists; not all of them, however, proved to be right. The physicians became able to better distinguish between the therapeutic disease proper and the therapeutic evolution, and to rationalize their clinical implications. Indeed inducing a therapeutic evolution had often been a goal whose fulfillment was hindered by the scarce therapeutic measures available and the insufficient understanding of physiology, whereas causing a therapeutic disease proper had never been granted the same status, but had been practically resorted to in some empirical practices. Moreover a related concept lies at the basis of the successful practices of variolation and vaccination, whose aim was and is prevention rather than cure[4].

It is important to distinguish theoretical and fact-finding approaches, aimed at producing knowledge, from practical ones, eminently empirical and aimed at finding cures. Indeed, in some cases the therapeutic application was based on a poorly demonstrated antagonism between diseases, and the fact-finding approach was erroneous. A case in point is Meduna's convulsive therapy of schizophre-

nia, whose theoretical basis, i.e. a supposed antagonism between schizophrenia and epilepsy, was disconfirmed by later research. Nevertheless experimentalists were able to develop therapeutic protocols that in some cases proved effective, for example the use of malaria to cure neurological syphilis, or convulsive therapy for major depression.

In the present study, which is centered on the history of a concept, theoreticians will receive greater attention than empiricists. Theoreticians incorporated either the hypothesis of therapeutic disease proper or of therapeutic evolution in their medical theories, but usually not both: e.g. Hahnemann used the therapeutic disease proper as a founding stone of homeopathy, whereas Freud adopted the concept of therapeutic evolution in his theory of transference neurosis. Of course, the hypothesis of therapeutic disease is only a relevant detail of these theories, and any temptation to derive the whole of homeopathy or psychoanalysis from it should be resisted; thus I shall not discuss exhaustively either theory, but shall try to analyze the role of the hypothesis of curative disease within each of them. An interesting observation is that homeopathy is the most complete and extended theory produced by romantic medicine, and both Henry Ellenberger and Franz Alexander recognized a strong romantic influence in Freud's psychoanalysis[5]; thus it is tempting to speculate that the concept of the curative disease is linked, albeit not exclusively, to romantic medicine.

Samuel Hahnemann and the homeopathic therapeutic disease

Samuel Hahnemann, the founder of homeopathy, is probably the medical theoretician most strongly committed to the hypothesis that I called the therapeutic disease proper. He thought that a constant and permanent beneficial effect could be expected if the supervening disease were similar to the original one (i.e. homeopathic to it), whereas only a temporary and inconstant benefit could result if the two dis-

eases were dissimilar. The hypothesis first appears in Hahnemann's writings in 1796:

> *Every powerful medicinal substance produces in the human body a kind of peculiar disease; the more powerful the medicine, the more peculiar, marked and violent the disease. We should imitate nature, which sometimes cures a chronic disease by super adding another, and employ in the (especially chronic) disease we wish to cure, that medicine which is able to produce another very similar artificial disease, and the former will be cured: similia similibus*[6].

This short piece summarizes four key hypotheses of Hahnemann's theory (there are others, of course): (I) the effect of drugs is that of causing a iatrogenic disease; (II) the iatrogenic disease caused by a drug can replace a previously existing one, if the two are similar enough; (III) when the action of the drug ceases the iatrogenic disease will disappear and the natural one will not come back; and (IV) the "spontaneous" healing is sometimes (in later works often or always) caused by a similar mechanism. That homeopathic cures can occur naturally, in the absence of physicians and prescriptions is in keeping with the fact that many of Hahnemann's remedies can be found in every kitchen: e.g. table salt, garlic, onion, etc.[7].
Initially Hahnemann pretended that the beneficial effect of the iatrogenic disease induced by homeopathic remedies was a purely empirical finding; but in later works he elaborated a more general theory. We can follow the evolution of this hypothesis over Hahnemann's long career:

> *In order therefore to be able to cure, we shall only require to oppose to the existing abnormal irritation of the disease the appropriate medicine, that is to say, another morbific power whose effect is very similar to that the disease displays*[8].

> *In the living organism a weaker dynamic affection is permanently extinguished by a stronger one, which, though different in nature, nevertheless greatly resembles it in expression*[9].

In the latter quotation, dated 1842, the disease is called a "dynamic affection". This is due to the fact that Hahnemann had adopted vitalism as an all-embracing theory of physiology and assumed that diseases were perturbations of the living force. Both the living force and its perturbations he considered "dynamic", i.e. not linked to any material substrate. This is in itself quite an unusual elaboration of contemporary medical science that he supported with explicit references to gravity and magnetism as models of "immaterial" forces[10]; but we need not to discuss this subject here. In its final version, the theory of the curative disease included the following additional hypotheses: (v Points I to IV in the preceding page are indicaded using capital letters, thus v to vii should also appear in this page as V, VI and VII) diseases are "dynamic" perturbations of the immaterial, "spirit-like" vital force; they have no material basis; (vi) the vital force has no memory and, upon the pressure of the medically induced homeopathic disease it can be made to "forget" the original disease; (vii) the homeopathic remedy is capable of perturbing the vital force, thus inducing the curative disease, because it contains its own immaterial, dynamic force[11]. In 1799 Hahnemann, having noticed that the therapeutic effect of his remedies was scarcely influenced by dosage, started to experiment with his much contested procedure of serial dilutions[12]. Initially, dilution was intended to lower the toxic effects of his drugs, some of which were clear-cut poisons; but later Hahnemann justified this practice with the further hypothesis that dilution and mixing (succussion) were able to free the dynamic principle contained in the drug from its material envelope[13].

Both in the Medicine of Experience (1805) and in the Organon, the VI and last edition of which was completed in 1842, even though published posthumously only in 1922, Hahnemann further elaborated his theory of the therapeutic disease to include two other conditions: that of naturally occurring contemporaneous but dissimilar

diseases, and that of non-homeopathic iatrogenic diseases. Also in these cases interactions between the old and the new disease occur: basically, if the supervening disease, be it natural or iatrogenic, is weaker than the existing one, it is repelled and the patient is protected; if it is stronger the existing one is temporarily suspended but not cured and will at some point relapse[14]. It is perhaps interesting that the supervening disease in Hahnemann's examples is often either measles or smallpox; these diseases are indeed so characteristic that their diagnosis was certain even with the limited clinical information that the physician could gather in the XIX century, and are known to induce a transient depression of immunity that may cause temporary relief of some symptoms (e.g. allergic or autoimmune).
The empirical bases of Hahnemann's idea were and are flimsy, and the judgment of similarity or dissimilarity between diseases was superficial and arbitrary, based only on the symptoms, since he refused the current nosography and the then rising science of pathology:

> *The curative virtues of medicines thus depend on their symptoms being similar to those of the disease, but stronger (par. 12 to par. 26)*[15].

> *... human diseases are nothing but groups of certain symptoms ...*[16]

Hypnosis as an iatrogenic variant of hysteria

Hypnosis is the heir of Franz Anton Mesmer's animal magnetism, as beautifully reconstructed by Ellenberger[17]. Although Mesmer's magnetism is often quoted by Hahnemann to support the view that pathogenic and therapeutic influences on the human organism are immaterial and "dynamic"[18], it was not, at its beginning, an elaboration on the theme of therapeutic disease. Mesmer thought that diseases were due to the anomalous distribution of the supposed magnetic fluid in the body and that the physician could correct this condition by means of his own magnetism and with the help of metal magnets.

Magnetism was recognized as a psychological, rather than physical, phenomenon by Amand Marie Jacques de Chastenet (Puységur), a French disciple of Mesmer, and renamed somnambulism; the name of hypnosis was only adopted after 1840. By then several authors had remarked that the personality induced in the course of hypnosis resembled that of hysteric patients. Since hysteria was at the time the main indication for hypnotic therapy, it was but a short step to suggest that hypnosis was an iatrogenic variant of hysteria and that hysteria was a spontaneous hypnosis. This hypothesis was implicitly made by several authors, and was adopted and publicized by Jean Martin Charcot. The essential observation, as reconstructed by Henri F. Ellenberger[19], was that hysteria-like symptoms could be induced or removed in patients under hypnotic state. The hypnotists assumed that it was possible to substitute hypnosis for hysteria, in this way bringing the natural disease under the control of the physician. Once this substitution was made, the role of the therapist was to gradually reduce the symptoms and to restore the control of the patient over his/her own emotions. Charcot's hypothesis gradually faded into oblivion, perhaps also because of the decline of the frequency of hysteria diagnoses in the XX century; it never evolved to a full medical system comparable to Hahnemann's homeopathy or to Freud's psychoanalysis.

Freud's transference neurosis

Sigmund Freud hypothesized a specific type of a medically induced therapeutic evolution capable of transforming one disease into another, that he called the transference neurosis. I cannot trace precisely the origin of this concept within Freud's writings: transference is present since the very beginning of Freud's elaborations on hysteria and evolves gradually into transference neurosis.

Freud named transference the peculiar and sexualized relationship that is established between the neurotic patient and his or her therapist. That in some cases the patient may fall in a sort of Platonic

sexual engagement with his or her therapist was by no means new: it had been already observed by the scientific commission lead by Bailly that king Louis XVI of France had appointed to investigate the merit of Mesmer's magnetic therapies[20]. The possible sexual involvement of the patient with his or her therapist had been also noticed by Charcot, one of Freud's early mentors, who used hypnotism to treat hysterics, and Freud had supposed that Anna O. had dreamily fallen in love with her hypnotist, his senior colleague and friend Joseph Breuer[21].

In the course of his successive elaboration, Freud came to the conclusion that the transference is the re-enactment of the Oedipus complex, i.e. the platonic and incompletely conscious sexual fantasies of any boy or girl with his/her opposite sex parent. The full elaboration of this hypothesis, as presented in the 27th lecture of the Introduction to Psychoanalysis[22] is as follows: the oedipal wishes are painful and generate psychical conflicts in the baby because love for the opposite gender parent is associated to hate and fear of the same gender parent. This conflict is the more or less "physiological" infantile neurosis and is solved by elaboration of the oedipal fantasies that become integrated in the personality of the boy or girl. The incomplete elaboration of oedipal sexual fantasies causes the boy or girl to repress them in the unconscious. Strictly speaking, what is repressed is the representation of the Oedipal drive, rather than the drive itself which is structurally unconscious; the repressed representations cannot be integrated into the structures of the personality and remain as "fixations" throughout adulthood. Any experience that may recall the repressed is felt as painful and requires further (secondary) repression; neurosis is the condition of an adult whose ability to interact with the environment is severely damaged by numerous and grave fixations and secondary repressions.

In Freud's theory the infantile neurosis is a physiological condition rather than a disease, and a necessary step in the formation of person-

ality. The true psychiatric disease is the consequence of the incomplete healing of the infantile neurosis, whose remnants are active in the unconscious of the adult, and betray the anomalous formation of the personality of the patient. This hypothesis suggests that the adult neurosis as such is incapable of further evolution and can neither spontaneously heal nor be cured, since its roots lie in the remote past of the patient. The psychoanalyst is supposed to be able, by his or her unconditioned listening and careful questioning, to induce the regression of the patient to his or her infancy. The infantile neurosis can thus be experienced again, with the analyst playing the role of the patient's parents, because of transference: this is the so-called transference neurosis. The psychological conflicts that could not be solved during the infantile neurosis, and would never by themselves resurface explicitly in the adult neurosis, are thus given a second chance to heal in the transference neurosis.

It is quite hard to discuss the transference neurosis since it only occurs in the fantasies of the patients (or perhaps in Freud's) and cannot be described in any more objective terms than Freud's figurative and almost poetical prose. It seems fair to state that Freud's transference is an important, if not completely original, clinical intuition on the relationship between the neurotic patient and his or her therapist, and that the transference neurosis is more a *façon de parler* than a real nosographic entity. Nevertheless, in Freud's theory, transference neurosis is an artificial disease that can only occur under the peculiar circumstances of the psychoanalytic setting, and fully qualifies as an iatrogenic therapeutic evolution: it is the infantile neurosis of an adult patient.

The paradoxical concept of the "physiological disease"

Both Hahnemann's and Freud's medical theories suggest that some diseases are not only very common or ubiquitous, but necessary to the course of a healthy life. This peculiar hypothesis is strictly related to that of the therapeutic disease and is much different from the trivial ob-

servation that some pathological conditions are frequent. Hahnemann thought that diseases are induced not only by drugs but also by food, and indeed the distinction between foods and drugs in his writings is either faint or absent[23]. This, of course, is a consequence of the dynamic nature of disease and the equally dynamic forces contained in foods and drugs. Freud's physiological diseases are the neurosis and the sexual perversions in the infancy that are not only ubiquitous, but necessary steps of the evolution of personality. Some Freud's followers have extensively elaborated on this unlikely concept, to propose that every psychiatric disease of adulthood is the re-proposition of a condition that is physiological during the infancy, e.g. Melanie Klein's schizophrenic and depressive positions of the baby.

The empiricists

In the last decades of the XIX century and in the first of the XX nosography could be greatly refined and rationalized thanks to the discoveries of microbiologists, physiologists and geneticists. Infectious diseases could be diagnosed and classified with certainty, because of the identification of the causative microorganisms; genetic diseases were put on a firm empirical basis by Garrod's pioneer studies; and the physiological functions and diseases of endocrine glands were described by several authors. As a consequence of these studies, diagnosis at least in some cases became objective rather than subjective, and some hybrid or spurious diseases (e.g. typhoid-malarial fever) were recognized as non-existing.

Since a basic, even though possibly incomplete, nosography is a necessary requisite for any evidence-based study on real instances of therapeutic or antagonistic diseases, it is not surprising that this idea underwent a re-evaluation on a strict empirical basis at the beginning of the XX century. In 1900 Sir Humphry Davy Rolleston published a study on the subject, entitled "On the antagonism of some diseases, and the curative effect of one disease on another, real or reputed"[24]. In his study

Rolleston, after remarking how easily a disease may be mistakingly assumed to cure another, discussed three possible ways in which a real antagonism between diseases can be established and proposed some pertinent examples. The first condition in Rolleston's list is "one disease mechanically protecting against or curing another" and the main pertinent example is the reciprocal interference between mitral valve stenosis and pulmonary tuberculosis. In Rolleston's collection of case histories not only the two diseases rarely occurred together, but the lungs of patients suffering of mitral valve stenosis appeared to be free of tuberculosis also in patients who presented this disease in other organs. The second item in the list, "acute disease may cure pre-existing disease", is perhaps the most interesting to the present analysis, since it essentially coincides with Hahnemann's elaborations. Rolleston is able to quote only a limited number of instances, among which is noteworthy the case of erysipelas temporarily interfering with cutaneous or subcutaneous tumors, which he attributes to a direct effect of the bacterial toxin. Another interesting example is that of typhoid fever curing worm infestations of the intestines. The third and final item of the list, "the possibility of a chronic disease protecting chemically against secondary infections", is by the author's admission "highly hypothetical" and only one uncertain example is quoted, namely that of the possible protection that Graves' disease would offer against tuberculosis.
In no case Rolleston claimed that a disease can really cure another: the antagonism is limited to two less straightforward outcomes, i.e. a disease may offer partial protection against another, so that suffering of both is an unlikely event, or a disease may induce the temporary remission of another. An interesting observation that leads us to our next case of therapeutic disease is the following:

> *In some instances it is said that an acute disease like pneumonia or typhoid fever may so interfere with the evolution of the second stage of syphilis that the latter is postponed for several months ...*[25]

Rolleston was not the first to notice the interference between febrile diseases and syphilis: the observation had already been made by others and is especially interesting since this antagonism was exploited by Julius Wagner-Jauregg who described the malaria therapy of luetic dementia. Wagner-Jauregg summarized the history of his discovery that malaria may induce a remission of paralytic dementia (a manifestation of neurological syphilis) in the lecture delivered when he was awarded the Nobel prize for medicine in 1927[26]. He claimed to have observed remissions of the otherwise unrelenting progression of luetic dementia after intercurrent febrile diseases since 1887. Among the febrile diseases apt to induce remissions of dementia he names malaria and erysipelas. In 1890 he started experimenting on the effect of fever induced by subcutaneous injection of Koch's tuberculin coupled to mercurial preparations. Although his initial results were promising, the remissions were of unpredictable duration, and relapses were common; thus he switched to malaria in 1917. Meanwhile Paul Ehrlich had discovered the antiluetic drug Salvarsan (arsphenamine; 1908) and its improved derivative neoSalvarsan (in 1912). Malaria proved to be more effective than tuberculin, and the coupling of malaria and neoSalvarsan better still; thus this became the standard therapy adopted not only by Wagner-Jauregg and his co-workers, but by many neurologists from several countries.

In his Nobel lecture, Wagner-Jauregg discussed at length the advantages and disadvantages of tertian malaria as a febrile iatrogenic disease, and remarked the following points: (i) a therapy (quinine) existed that allowed the physician to effectively stop medically induced malaria, whereas infections of bacterial origin (e.g. streptococcal) might prove fatal; (ii) although the agent of malaria at the time could not be cultured, large institutions hosted a sufficient number of patients to allow transmission of malaria by means of subcutaneous injection of the blood from an infected patient. I may add that malaria does not confer permanent immunity and thus it was suitable also in the case of luetic

patients who had already suffered of malaria in the past; this would not be the case with several bacterial and viral infections.
Malaria therapy of luetic dementia had a significant success for a couple of decades, and was gradually abandoned as the widespread use of neoSalvarsan, and later of penicillin, coupled to the improvement of diagnostic procedures, made early and effective treatment of syphilis widespread and sharply cut down the frequency of its late manifestations. Malaria therapy had not been proposed as a therapy of early syphilis, but only for its late neurological forms, and fell into disuse as these became rare because of effective early treatment.
Wagner-Jauregg's work on neurological syphilis stimulated another (and as far as I know last) attempt to use a disease to cure another: the convulsive therapy of major psychoses experimented by Ladislas von Meduna in 1933-34. Meduna had been impressed by Wagner-Jauregg's research on malaria therapy, and by Nyiro and Jablonszky's finding of a negative correlation between schizophrenia and epilepsy in whose case series patients suffering of the latter disease rarely contracted the former, and schizophrenics who experienced a convulsive episode often had a remission[27]. Meduna, on the basis of the hypothesis that "between schizophrenia and epilepsy there exists a sort of biological antagonism"[28], started experimenting on schizophrenic patients several drugs capable of inducing a convulsive episode. Initially he found that camphor was effective, but later he switched to cardiazole (pentylenetetrazole). Since at the time there was essentially no effective treatment of psychoses, convulsive therapy was applied to numerous patients with different diagnoses and proved more effective for depression than for schizophrenia. Retrospectively one may notice that Meduna's hypothesis contained two major flaws: first and foremost, the original findings were of poor statistical quality and were later proven wrong; indeed it is today accepted that epilepsy and schizophre-

nia present a positive, rather than negative, correlation[29]. Second, the similarity between epilepsy and cardiazole-induced convulsive crises is superficial, and Meduna's assumption that the latter had the same hypothetical antagonism with schizophrenia as the former was unwarranted.

Other so-called "shock therapies" were in use at the time for schizophrenia, e.g. Sakel's insulin coma therapy (ICT); however in these therapies the concept of the antagonistic disease did not play a prominent role. Indeed Sakel attributed the positive effects of ICT to metabolic effects of insulin and hypoglycemia, and considered less relevant that coma could be associated to a convulsive episode[30].

As a consequence of the successes of the treatments developed by Meduna and Sakel, the Italian psychiatrists Ugo Cerletti and Lucio Bini started experimenting with electrically-induced fits. Cerletti and Bini's electro-convulsive therapy (ECT) proved safe and effective and rapidly replaced Meduna's cardiazole, especially because it could be administered under anesthesia and curare-induced myorelaxation. The introduction of safe and effective antipsychotic drugs after 1945 reduced the clinical indications to ECT, a practice that had been criticized because of ideological reasons and that required hospitalization of the patient. ECT remains nowadays the last resort for severe, drug-resistant depressive episodes. Although Cerletti did acknowledge Meduna's convulsive therapy as an inspiration, he did not mention explicictly the concept of therapeutic disease[31], a sign that the hypothesis was being dropped at the time. It is consistent with this view that Cerletti also acknowlegded Sakel's ICT as a precursor of ECT, in spite of the fact that Sakel and Meduna proposed different and conflicting explanatory hypotheses for their therapies[32].

The definitive fall of the hypothesis of the therapeutic diseases coincides with the great discoveries of pharmacology in the late thirties and thereafter: it was obviously safer to treat a patient with a drug than with a disease.

Decline and fall

Meduna was the last physician to adopt the hypothesis of therapeutic disease, which was abandoned afterwards, and gradually disappeared from the medical literature. There are several plausible reasons for the decline of the hypothesis: (i) better drugs were being developed, that made the idea of curing a disease with another scarcely appealing; (ii) studies like Rolleston's had demonstrated that the real instances of therapeutic disease are rare and often have an unsatisfactory prognosis (i.e. the therapeutic disease is often a grave one); and (iii) the medical thinking had changed. The last point may deserve some consideration: Hahnemann had thought that every external intervention on the human body is pathogenic, and results in disease. Since he did not consider the possibility of "neutral" or "healthy" influences, it came as a necessary conclusion that the only possible cure was through an iatrogenic disease. In less than half a century Hahnemann's idea had become strange and odd to his followers, and was either misunderstood or explicitly abandoned. The British homeopath R. Hughes at the end of the XIX century was among the first to question that the main or only scope of drugs is to cause a disease[33] and tried to reformulate the hypothesis within the framework of the then more plausible theory of the protoplasm[34]. Modern homeopaths seem to have entirely forgotten Hahnemann's hypothesis and usually maintain that the reason why a drug causing symptoms similar to those of the patient has curative power is that symptoms are "viewed as attempts on the part of the body to heal itself."[35], thus the drug would recruit to a greater extent than the disease the same self-healing forces or processes. This hypothesis, that does not involve the therapeutic disease, contrasts not only with Hahnemann's original hypothesis, but also with other aspects of his theory, e.g. with the observation that only some symptoms are reactive, while others are "primary", i.e. due to the perturbation of the life force itself[36]. While secondary symptoms

can be assumed to represent "attempts of the body to heal itself", primary symptoms cannot.

Homeopathy was the medical theory most strongly committed to the hypothesis of the therapeutic disease, and the most resistant to new scientific discoveries; in other fields of medicine the hypothesis was dropped more easily; e.g. the effectiveness of malaria therapy for syphilis was confirmed beyond doubt, and its molecular bases were discovered[37], but Salvarsan, and later penicillin, proved to be more effective and less dangerous, and gradually relegated malaria therapy to the history of medicine. The case of psychoanalysis is different from both those of homeopathy and academic medicine, since the discipline underwent an extensive re-elaboration and its principles became somewhat exchangeable, if not confused[38]. Freud's transference was reinterpreted in several ways and the concept of transference neurosis became blurred.

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