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BIOLOGICAL THERAPIES AT THE BEGINNING OF THE 20TH CENTURY: WHAT IS INNOVATIVE TODAY BECOMES OBSOLETE TOMORROW

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Abstract: The affirmation of Psychiatry, as a medical specialty, throughout the 20th century, was supported by advances achieved not only in terms of understanding aspects of psychology, but also the biology and clinical aspects of mental illnesses, which contributed to the development of therapeutic tools considered innovative for the time. By way of example, we highlight Wagner von Jauregg's malariotherapy in 1917, which earned him the Nobel Prize in 1927, Klaesi's prolonged sleep therapy in 1922, Alexander Fleming's discovery of penicillin in 1929, Sakel's insulin coma in 1933 and psychosurgery initially developed by Egas Moniz, which earned him the Nobel Prize in 1949. However, despite being used at that time, some of these therapeutic tools currently do not have any scientific validity in the treatment of mental disorders, meaning their use is now extinct.

Keywords: Psychiatry; Biological therapies; 20th century

INTRODUCTION

In the first years of Psychiatry's existence, hospitalization was the only treatment available for patients with serious mental illness. However, this did not translate into a change in the course of the disease and brought Psychiatrists feelings of anguish and despair, since their patients and their families could offer little more than comfort.

As a consequence, there was a progressive increase in the number of institutionalized mental patients and, simultaneously, a progressive degradation of the conditions of hospitalization. For example, there are descriptions of overcrowded wards, where patients came into contact with their own excrement and where a deafening noise could be heard permanently.

Naturally, all these factors contributed even more to the negative image of Psychiatry and, deep down, the reality of that time was

just one: there was no effective treatment for serious mental illness and there was no hope of recovery for these patients.

BODY OF TEXT

CONTEXT AND HISTORICAL EVOLUTION

In the first half of the 20th century, as a way of trying to find a solution to the growing problem of overcrowding in psychiatric hospitals and, simultaneously, to alleviate the suffering of patients and their families, psychiatrists began to look for alternative therapies that, despite being audacious, were they had a terrifying aura, as they seemed to be extremely radical and potentially dangerous innovations.

However, at that time, the risk associated with dangerous or radical treatment was often considered acceptable or tolerable, especially when compared to the possibility of being hospitalized for life in miserable conditions and without any dignity or comfort.

Regarding the biological therapies developed some of which will be described below, some led to dead ends and were abandoned, while others prepared the foundations for the revolution in drug therapies that would follow.

BIOLOGICAL THERAPIES DEVELOPED AT THE BEGINNING OF THE 20TH CENTURY

MALARIO THERAPY OR "FEVER CURE" BY JULIUS WAGNER VON JUAREGG

In the first decades of the 20th century, a peculiar form of psychosis, known as "general paralysis of the insane", was responsible for a large number of admissions to psychiatric hospitals.

This disease actually corresponded to an advanced and untreated form of syphilis, called neurosyphilis, in which the microorganism responsible for the infection lodges in the brain and produces symptoms similar to those manifested by patients with schizophrenia.

In this context, the primary role of Julius Wagner von Juaregg, a Viennese doctor and professor of psychiatry, stands out, who in 1883, during his internship at the psychiatric hospital, found that a patient had experienced a complete remission of her psychosis after having contracted an infection.

This fact aroused his interest in the relationship between fever and madness and, in this sense, in 1887, he wrote an article questioning the possibility of treating psychosis through fever.

Following up on this hypothesis, he developed an experiment where he infected patients with “general paralysis of the insane” with diseases that caused fever to test the effect of high temperatures on psychoses.

Thus, in 1890, taking advantage of the discovery of the German microbiologist Robert Koch, Wagner von Juaregg inoculated patients with psychosis associated with neurosyphilis with tuberculin, with the aim of inducing a febrile state (secondary to tuberculosis). However, despite achieving prolonged remissions, the toxicity associated with tuberculin eventually led to the interruption of these treatments.

Later, in 1917, as an alternative to tuberculin, he began injecting neurosyphilitic patients with the blood of soldiers returning from the First World War infected with malaria. A few weeks later, these patients presented episodes of fever induced by malaria and, subsequently, over time, they showed significant clinical improvements, such that some patients who previously behaved in strange and bizarre ways now seemed completely cured.

A year later, he presented his work, describing the effects of curing malaria. This fact constituted a historic moment for Psychiatry, as it contradicted for the first time the therapeutic nihilism that had dominated previous generations and questioned the possibility of treating psychoses.

The cure for malaria fever, developed in 1917, was the first successful physical therapy in Psychiatry and, despite having a mortality rate of 15% and not showing improvement in symptoms in psychoses that were not caused by microorganisms, it was worth the effort. Wagner von Juaregg the Nobel Prize in 1927, the first in the field of Psychiatry.

LONG SLEEP THERAPY BY JAKOB KLAESI

In the development of this therapy, the role of a recently graduated doctor from Edinburgh, named Neil Macleod, stands out, who used potassium bromide to induce a prolonged state of sleep in patients dependent on morphine and cocaine.

According to historical records, this doctor, when called to help a patient, resident in Shanghai, but who was staying in a hotel in Japan and who showed psychotic symptoms, and did not have nurses to help with transport, helped himself of the scientific knowledge acquired in his clinical practice and administered potassium bromide. The patient fell asleep and was later transported back to Shanghai. After a trip that lasted several days, she woke up without any sign of mental disturbance, remaining asymptomatic for at least two years.

“Bromide sleep” consisted of the administration of potassium bromide at a dose that led to a state of stupor for five to nine days, leaving the patient totally dependent and unable to perform any of their higher cognitive functions. When she woke up, the patient seemed completely recovered.

For the first time, there appeared to be a medicine that alleviated serious psychiatric illness. However, the use of potassium bromide ended up being supplanted by the synthesis of new, more effective substances such as sedatives and hypnotics, called barbiturates. These were better tolerated and acted at therapeutic levels lower than the toxic dose, allowing manic patients to calm down and restore sleep to melancholics and insomniacs.

Veronal, Medinal, Seconal and afterwards, Luminal were some of the most commercialized medicines.

Taking advantage of the growing use of barbiturates, in 1922, Jakob Klaesi, a Swiss psychiatrist working at a university psychiatric clinic in Zurich, began using an innovative combination of two barbiturates, marketed under the name *Somnifen*.

Of the 26 patients treated using prolonged narcosis, induced by *Somnifen*, between a quarter and a third improved significantly. However, 3 patients died as a result of pneumonia or circulatory failure, which represented a high risk of fatality.

Prolonged sleep therapy, considered in the early 1930s as the only useful treatment for acute psychotic illnesses, is inevitably associated with Jakob Klaesi who aspired to achieve a cure for schizophrenia through prolonged narcosis (*Dauernarkose*).

PENICILLIN DISCOVERED BY ALEXANDER FLEMING

In 1929, at Oxford, Alexander Fleming discovered, incidentally, that penicillin mold cultures inhibited the growth of bacteria.

This discovery had a huge impact on the treatment of bacterial infections at the beginning of the Second World War. However, the scarcity of penicillin production reserved its use only for military forces.

Only in 1943, John Mahoney, at the time a military doctor commissioned in the Public

Health Service of the United States of America and director of the *Venereal Disease Research Center of Navy Hospital on State Island* obtained enough penicillin to be used in the treatment of syphilis.

This experience, which began on the outskirts of American centers, far from a New York where psychoanalytic therapy reigned, achieved tremendous success, demonstrating excellent results in the treatment of this venereal disease.

Even in patients with neurosyphilis, who had severe mental symptoms, it was possible to observe a remission of psychiatric symptoms.

A cure for one of the main causes of mental illness was thus identified.

MANFRED SAKEL'S INSULIN COMA

Therapies that induce comatose states, such as insulin coma, constitute dangerous procedures that remain controversial to this day.

In the 20s of the 20th century, the role of Manfred Sakel, an Austrian doctor, who treated patients with morphine dependence using low doses of insulin stands out.

In this context, depending on the risk of insulin administration, it was not uncommon for patients to present complications such as hypoglycemic/insulin coma and it was this circumstance that allowed Sakel to verify that heavy consumers of morphine and opium, who initially appeared restless, and agitated, with behaviors similar to mentally ill people, later, after administration of higher doses of insulin that led to a state of coma, they woke up after a few hours more calm and accessible.

In this sense, in 1933, he presented the results of his experiment and sought to validate insulin shock as a cure for schizophrenia. According to Sakel, in Vienna, in his psychiatric clinic, remission rates of around 70% were observed. However, these results were ridiculed by peers.

Despite this, this therapy was widely disseminated in Anglo-Saxon countries, since British psychiatrists who looked suspiciously at sleep therapy saw insulin coma therapy as the first therapy that effectively managed to help patients.

According to the records, the treatment consisted of administering an increasing dose of insulin until the patient began to enter a state of “insulin drowsiness” and then passed into a state of “deep unconsciousness” where unwanted convulsions sometimes occurred. When a state of coma was reached, the patient remained under surveillance and after twenty minutes a glucose solution was administered, through a nasogastric tube or intravenously, which allowed the patient to recover from the state of consciousness to the state of coma. Improvement in psychiatric symptoms was observed after approximately 20 comas.

Despite presenting similar efficacy to sleep therapy, its danger and associated risk were considered inferior, which is why it was considered first-line physical therapy in Hospital *Mausdley*.

PSYCHOSURGERY OF EGAS MONIZ

In the first decades of the 20th century, psychiatrists envisioned the possibility of using brain manipulation as a therapeutic tool to treat the symptoms of mental disorders.

Following this line of thought, and sharing the beliefs of biological psychiatrists, in 1933, a Portuguese doctor named António Egas Moniz, a neurologist at the Faculty of Medicine of the University of Lisbon, considered that mental illness was a neurological condition and that it must be treated through direct intervention in the brain.

According to his reasoning, calming emotions was the key to treating mental illness, and therefore manipulating a certain part of the brain would lead to correction of behaviors and emotions. The only question

was: which area of the brain must be operated on?

In 1935, at a medical conference in London, he heard the observation of a neurology researcher who stated that patients, when they suffered damage to the frontal lobe, became emotionally subdued, but apparently maintained their ability to think.

With this idea in mind, he returned to Lisbon and began preparing his first psychosurgical intervention. The aim was to cause permanent brain damage to the frontal lobes of patients diagnosed with a serious mental illness. However, as he had no training in Neurosurgery, he recruited a neurosurgeon, named Pedro Almeida Lima, to perform the procedure that he would later call leucotomy.

The procedure, carried out under general anesthesia, consisted of perforating the skull, just above each of the eyes, inserting the needle of a special instrument, in the form of a syringe that he invented himself and which he called a leucotome, through the hole in the skull. Then, he pressed the syringe plunger and inserted a wire, with which he excavated a small area of brain tissue in the prefrontal region.

As at this time it was not possible to know the functional anatomy of the brain, Portuguese doctors decided to excavate six areas in each of the frontal lobes. If the results were unsatisfactory they would have to cut even more brain tissue.

The first leucotomy was performed on November 12, 1935 at the Santa Maria Hospital in Lisbon and in 1936, the results of the first twenty leucotomies were presented. Nine patients suffered from depression, seven from schizophrenia, two from manic-depressive psychosis and two from anxiety disorders. According to data released by Egas Moniz, seven patients had improved significantly, another seven showed relative improvements and six remained in the same condition. No

patient recorded a worsening of their clinical condition.

Naturally, this procedure was the target of criticism, mainly by José de Matos Sobral Cid, a renowned Portuguese psychiatrist, who condemned this technique, stating that patients were diminished with an evident degradation of their personality. Still, Egas Moniz's treatment, prefrontal leucotomy, was hailed as the miracle cure that allowed permanently agitated patients to become calm and obedient.

Following the promising results presented, leucotomies quickly spread throughout asylums throughout Europe and America and the results were evident to any visitor. The shrill noise present in the wards was replaced by a more pleasant whisper. Patients with aggressive behavior were now patients who didn't bother anyone.

In January 1946, an American neurologist named Walter Freeman, an admirer of Egas Moniz's work, considered that more patients could benefit from this surgical procedure. To achieve this, it had to be made cheaper and more accessible. He thus developed a new method of radical psychosurgery that could be used in clinics and doctors' offices.

The procedure, known as transorbital lobotomy, consisted of placing the tip of a thin surgical instrument, similar to an ice pick, under the eyelid and against the top of the eye socket, which was supposed to pass through the thin layer of bone and penetrate the brain.

Then, the tip of the instrument was rotated to create a lesion similar to that caused by Egas Moniz's leucotome.

In 1949, the Nobel Prize was awarded to Egas Moniz for the development of leucotomy as an important tool in the treatment of serious mental disorders. This was the second Nobel Prize awarded in the field of Psychiatry.

CONCLUSIONS OR FINAL CONSIDERATIONS

At the end of the 19th century, most medical specialties showed significant scientific progress. However, there was one specialty that remained stagnant, mired in failure, leaving psychiatrists distressed and patients without hope of any potential for recovery.

However, at the beginning of the 20th century, more specifically in the first half of the century, taking advantage of the most recent scientific knowledge about the biology and clinical aspects of mental illnesses, new biological therapies were being discovered and tested.

Even so, despite the exaltation and scientific value that was attributed to them at the time, and which in some cases even earned them the Nobel Prize, today the vast majority of therapies would constitute reprehensible practices, without any validity or scientific basis, and therefore That's right, they are currently abolished.

REFERENCES

- Lieberman, J. A. (2016). *Psiquiatras: Uma história por contar*. Lisboa: Temas e Debates- Círculo de Leitores.
- Pereira, J. M. (2023). *Doenças e Terapêuticas na Psiquiatria Portuguesa nas primeiras décadas do século XX*. Forte da Casa: Climepsi Editores.
- Saraiva, C. B., & Cerejeira, J. (2016). *Psiquiatria Fundamental*. Lisboa: LIDEL.
- Shorter, E. (2001). *Uma História da Psiquiatria- Da era do manicómio à idade do prozac*. Lisboa: Climepsi Editores.
- Material de apoio do Curso Pós-Graduado Online de Atualização em Psicofarmacologia na Prática Clínica, ministrado pela Sociedade Portuguesa de Psiquiatria e Saúde Mental, em 2021.