

# The impact of growth

The evolution of medical knowledge and changes in the disease profile prompted the establishment of specialized facilities

Ricardo Aguiar

**L**ithium, a substance that has been used to treat bipolar disorder for decades, may play an important role in the prevention and treatment of Alzheimer's disease (AD). Headed by researchers Wagner Gattaz and Orestes Forlenza, the Neuroscience Laboratory at the Psychiatry Institute (IPq), which is part of the University of São Paulo (USP), has recently shown that lithium may attenuate the evolution of AD. A study of elderly patients with bipolar disorder, which is a serious mental illness associated with a high risk of developing dementia, has shown that the prolonged use of lithium affords protection against such an outcome.

“For patients treated with lithium, the risk of developing AD was five times lower than for those who were not,” says Gattaz. “Their risk went back to roughly the same level as the risk for people who don't have bipolar disorder. Add-

ing small amounts of lithium to the water supply may help in the prevention and treatment of mental illnesses, including AD.”

In addition to investigating the neuroprotective role of lithium, Gattaz is also studying schizophrenia. Years ago, his group detected some 300 genetic mutations that might lead to development of the disorder. According to the psychiatrist, these data have brought a more realistic understanding of the disease.

The IPq has also contributed to the understanding and treatment of other mental disorders, like obsessive-compulsive disorder (OCD). The group led by Euripedes Constantino Miguel used neuroimaging techniques to find evidence that different forms of treatment—like cognitive behavioral therapy and the use of antidepressants—have distinct and complementary effects on the brain. Another finding was that the results of treatment with





Architectural sketch of the USP Psychiatry Institute building

medication and with psychotherapy are similar. What matters most, according to the researchers, is that the treatment be continuous. By tracking 158 people with OCD for two years, it became clear that the longer the treatment, the more their symptoms receded.

#### THE MIND

In addition to producing world-class scientific research, the IPq has also been praised for its patient care. In 2014, it became the first psychiatric hospital in Brazil to receive certification from Brazil's National Accrediting Organization, in recognition of the excellent quality of its services.

The IPq traces its roots to Juqueri Psychiatric Hospital, founded and directed

by Francisco Franco da Rocha in the late nineteenth century. The University of São Paulo School of Medicine (FMUSP) gave some of its courses in psychiatry there.

Rocha's successor was Antonio Carlos Pacheco e Silva, who took over the hospital in 1923. With the collaboration of Benedito Montenegro, then director of FMUSP, and Jorge Americano, university president, Pacheco e Silva convinced the state government to construct the building that now serves as IPq headquarters.

When the IPq was instituted as a modern university psychiatric center in 1952, Pacheco e Silva overcame prejudice and brought serious cases of mental disorder closer to the general hospital. The facility was governed by Pacheco e Silva's belief that psychiatry should be grounded

not only on descriptive diagnoses but also on knowledge and research of the brain's organic and biochemical properties. The hospital model was quite different at that time, based on lengthy inpatient stays for those with serious mental illnesses like schizophrenia and manic-depressive psychosis. The range of treatment options was relatively limited.

Thanks to the development of psychopharmacology and biological psychiatry, shifts occurred in the diagnostic and therapeutic approaches to mental disorders and also in the focus of research. The IPq now treats a wide array of disorders, such as those involving mood, anxiety, eating, sleep, and sexuality. Moreover, the specificity of treatment for each problem is much greater.

Inpatient stays are also not as lengthy and efforts are made to link hospitalization to outpatient treatment.

The institute's research lines are broad in scope, heterogeneous, and respect the complexity of the phenomena associated with mental illness. This includes recognizing the biological, psychological, and social aspects that must be taken into account within the specific framework of each phase of life.

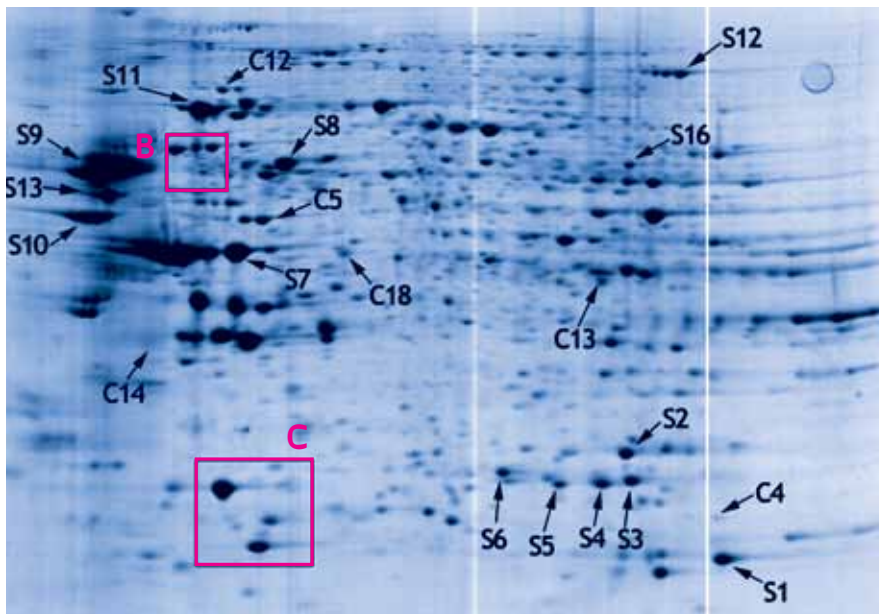
## CHILDREN

While the IPq changed and evolved in step with changes in medicine and society, the same is true of the Children's Institute (ICr). Founded in 1976, the ICr traces its roots to the Department of Internal Medicine's Pediatrics Service, then headed by Antonio de Barros Ulhoa Cintra, one of the founders of FAPESP and a former USP president. Eduardo Marcondes, then chief of the Pediatrics Service at the Hospital das Clínicas, is considered the principal founder of the ICr.

In its first years, the ICr primarily treated cases of diarrhea and malnutrition, which were the main causes of infant mortality at that time. In the 1970s, this rate stood at around 60 to 80 deaths per thousand live births in Brazil. The 1980s saw advances in the treatment of dehydration caused by acute diarrhea through the contributions of Giuseppe Sperotto, of the ICr.

Although Brazil's infant mortality rates are still higher than those of other countries, the figure had dropped to 15 deaths per 1,000 births by 2013. Today, infant deaths in the first year of life are chiefly a consequence of perinatal conditions, birth defects, and chromosomal abnormalities. In keeping with changes in the profile of childhood illnesses, the focal point of care and research at the ICr is currently on patients with serious, complex, and rare diseases (rare diseases are those affecting one in every 2,000 people). "This shift in focus was a deliberate decision by the ICr in recent years," says pediatrician Magda Carneiro-Sampaio, current chair of the facility's board of directors.

During the course of the 1960s and 1970s, the ICr was the birthplace of almost every pediatric specialty in Brazil, and it became the only service in Brazil designed to care for children and adolescents with hard-to-diagnose diseases.



Each point in the image represents a clump of proteins in the brain of someone with schizophrenia: schizophrenics produce more of the proteins identified by the letter 's'

One of the institute's distinguishing features is that it has specialists in 17 medical areas, all trained in pediatrics. "This means our patients are always cared for by pediatricians," Carneiro-Sampaio adds.

The facility also has a children's surgery service, founded by Virgílio Carvalho Pinto in the 1960s. Its emphasis has been on the correction of complex congenital malformations of the digestive, urinary, and respiratory systems as well as on procedures to separate conjoined twins. The experiences of this group, currently coordinated by Uenis Tannuri, have helped transform the ICr into Brazil's leading center for organ and tissue transplants in children.

One of the projects now underway at the ICr, in collaboration with the Heart Institute (InCor), involves DiGeorge syndrome, a serious genetic disorder that affects one in every 4,000 newborns. Along with congenital heart defects, these children present defects of the thymus, an organ essential to the development of the immunological system. "The thymus is an organ that has been greatly overlooked in research," says Carneiro-Sampaio. "We are working to improve our understanding of how this organ functions in children and to raise pediatricians' awareness of the diseases associated with it." To this end, the ICr proposed that November 22 be declared DiGeorge Syndrome Day, because the

disorder is the result of a microdeletion on chromosome 22 at position 22q11.2.

The ICr is also concerned with early prevention of chronic illnesses that appear only in adults or the elderly, like osteoporosis. It is possible to learn from family history whether a child has a risk of developing the disease, which usually only appears after the sixth decade of life. Children and adolescents at risk can thus be counseled to follow eating and lifestyle habits intended to forestall the problem in the future.

Quality of care is one of the hallmarks of the ICr, and the Child-Friendly Diagnosis program is an example of this. Launched in 2012, the program aims to reduce the amount of blood drawn from children for test purposes, children's exposure to exams that use ionizing radiation, and orders for anesthesia. "We want the institute to be cutting-edge in research but without neglecting the safety and well-being of our patients and their families," says Carneiro-Sampaio.

## REHABILITATION

A fundamental part of the treatment of many syndromes, including those seen at the ICr, is rehabilitation. DiGeorge syndrome, for instance, causes speech problems that can be ameliorated with suitable treatment. Providing rehabilitation for patients with different medical conditions and conducting research



are the goals of the Institute of Physical Medicine and Rehabilitation (IMREA).

Initiatives centered on physical medicine and rehabilitation began with the foundation of the National Rehabilitation Institute (Inar) in 1958. In its earliest days, Inar offered rehabilitation services primarily to the victims of car accidents, which were frequent at that time. Since 2000, IMREA has been strengthening its role as a rehabilitation facility that places priority on caring for patients with spinal cord injuries, cerebral palsy, and disabling pain, as well as for amputees.

The institute's lines of research revolve around neuromotor evaluation and control. For example, studies assess new approaches to rehabilitation and investigate the biological mechanisms involved in this process. This research led to the establishment of the Center for Advanced Studies in Brain Injuries, motivated by the hypothesis that a better understanding of brain plasticity and of new rehabilitation technologies will result in better treatment.

The IMREA is also part of the Research, Innovation, and Dissemination Center for Neuromathematics, which is

committed to disseminating evaluation and intervention techniques and systems in the area of rehabilitation and to establishing tighter controls in clinical trials.

"In this sense, if we know the best protocol for each patient, we'll be able to make his treatment more effective," says Linamara Battistella, coordinator of IMREA's Center for Clinical Trials.

#### CANCER

The youngest of FMUSP's eight institutes is the São Paulo State Cancer Institute (Icesp), which opened its doors in May 2008. Giovanni Guido Cerri, full professor of radiology, coordinated implementation of the institute and took the positions of director general and chair of its board.

The field of oncology had actually emerged earlier at FMUSP, in 1981, when Ricardo Brentani became the first professor of an oncology class at a Brazilian university. Two years later, he also became director of São Paulo's Ludwig Institute for Cancer Research, then operating out of the former A.C. Camargo Hospital, which became affiliated with the University of São Paulo in the 1990s. Now as the A.C. Camargo Cancer Cen-

ter, the facility emphasizes research and graduate studies.

Established by Brentani in 2005, the FMUSP Oncology Center unified in one setting the practice of oncology, which had previously been split among the various specialties at the Hospital das Clínicas. Brentani was a member of Icesp's first advisory council, although he was never directly involved in the institute's operation.

Icesp came into being with the prime goal of providing care for cancer patients in the state of São Paulo, but it was soon reorganized to encompass teaching and research as well. Its chief lines of research are in epidemiology, molecular oncology and biomarkers, and goal-directed therapy. Its aim is to improve diagnostics and to develop and refine treatments.

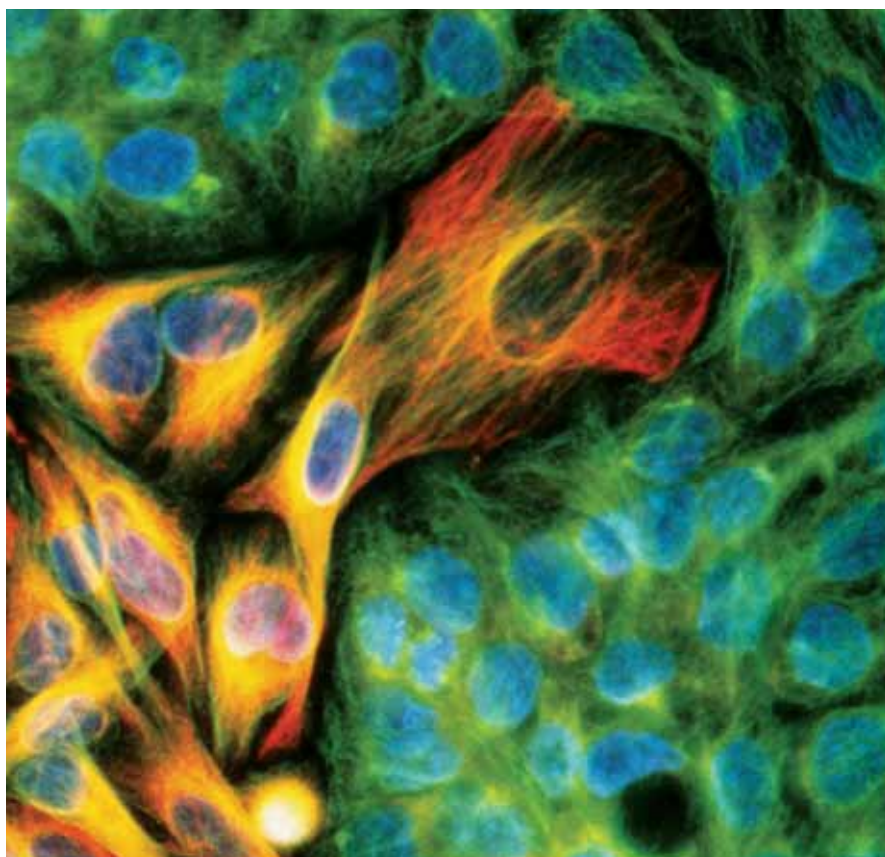
One of its current projects, led by researcher Roger Chammas, seeks to understand why some tumor treatments fail. Chemotherapy and radiation therapy can manage to destroy a tumor, for instance, but they leave open space in the tissue, which is often occupied by new tumor cells instead of healthy ones.

"We're researching ways to avoid this repopulation by tumor cells and to boost treatment effectiveness," says Chammas. "Since the blood vessels inside tumors are often abnormal, one of the ways of doing this is to increase vascular tonus to make it easier for the drug to reach its target. Pre-clinical trials have shown that it can be helpful to modulate vessel function."

Chammas stresses that the cancer research conducted at USP is diverse and of great value to national production. Studies are underway across all campuses of the university in fields like physics, chemistry, and pharmacy. "We have more than 100 groups engaging in cancer-related lines of research at USP," Chammas says. "This means the university has been involved in about two out of every three scientific papers produced in the field in Brazil over the past five years."

Another of Icesp's fundamental roles is to aggregate this formerly scattered research and to facilitate communication among researchers in the field

"When USP turns 100, I want to look back and see that Icesp served as a meeting point for all of the university's cancer research groups, generating groundbreaking knowledge and applying it ethically to the diagnosis and treatment of cancer patients," says Chammas. ■



Tumor cells (orange) occupy the space between skin cells