



Jules Hirsch

Straight talk with... Jules Hirsch

On 26 October 1910, nine years after the oil baron John D. Rockefeller opened the first research facility in the US devoted exclusively to experimental medicine, the Rockefeller Institute for Medical Research in New York (now Rockefeller University) admitted the country's first research participant in a hospital dedicated completely to clinical studies. Conceived as a place where patient care and laboratory investigations of disease would complement each other, the hospital was home to the development of methadone treatment of heroin addiction and the discovery of autoantibodies in rheumatoid arthritis and lupus, among other findings. The hospital also served as a model for dozens of other clinical research centers, including the US National Institutes of Health's own Clinical Center, which opened its doors in 1953.

Emeritus professor Jules Hirsch, a metabolism researcher who joined Rockefeller in 1954, has had a front-row seat for more than half of Rockefeller University Hospital's 100-year history, including four years as the hospital's physician-in-chief and 12 years heading up its institutional review board. As the hospital gears up to celebrate its centennial anniversary later this month, **Roxanne Palmer** sat down with Hirsch in his office at the Upper East Side hospital to discuss the clinical center's impact on biomedical research and education.

What do you see as the most important legacy of the Rockefeller University Hospital?

Its most important legacy is the demonstration that clinical research can be a very useful endeavor in understanding human disease. For example, a hundred years ago, the first patient who was admitted to the hospital had a bizarre inflammatory illness now known as subacute bacterial endocarditis—basically, he had a group of streptococcal infections that ultimately damaged his heart. Since then, most of the significant findings that now prevent or cure subacute bacterial endocarditis occurred in

laboratories right here. Studies of the immune reaction that leads to tissue destruction and heart failure were carried out at this hospital, as were some of the earliest experiments with antibiotics. Nowadays, if this patient arrived at any hospital, the chances are he would be cured and walk out.

Beyond therapies, were there also important discoveries made in basic biology?

Yes, many. In just one example, Rufus Cole, the first director of the hospital, showed that the bacterium that causes pneumonia had a small capsule about it and that the presence or absence of the capsule was very important in determining whether pneumococcus was virulent or not. A young bacteriologist was then brought to the lab to begin studies of the chemistry of the capsular material. His name was Oswald Avery, and in 1944 he showed that the transforming factor was a very unusual polysaccharide, a substance called deoxyribonucleic acid. This demonstration that DNA is the genetic material in bacteria became the single most important experiment in the birth of modern molecular genetics.

Before the creation of the hospital, was there such a thing as a clinician-scientist in the US?

This occurred occasionally in a doctor's lab, but there was no single central institution on American shores where this could happen.

How has the hospital shaped university medical schools around the country?

The people who came to the hospital were young physicians like the Arrowsmith of Sinclair Lewis' story—which, by the way, includes a description of the Rockefeller Institute; it's called the "McGurk Institute" in the novel. They came imbued with the notion of understanding disease and doing research. Over the years, they became the most important faculty members of American medical schools. So much so, in fact, that by 1940 half of the chiefs of medicine in American medical schools were Rockefeller Hospital alumni.

How did the hospital factor into your own work with fat metabolism?

We had patients that we could keep for many months and study their metabolism after weight loss. We found that individuals who had lost weight had really marked changes in the histology of fat cells, which ushered in further detailed studies of what hormones were being made in the adipocytes [fat cells]. Without the observation in the hospital, it would not have been possible to get this far.

What ongoing studies are happening at the Rockefeller University Hospital now?

Times have changed, and now there are a lot of outpatient and fewer inpatient studies. But there are important studies in progress in the hospital, with the use of dendritic cells in vaccines and studies of the treatment of HIV.

What do you see as the role of research hospitals today?

The observation of human disease as a starting point is not so popular anymore. The general feeling now is that, if the DNA code is the same in plants and animals as it is in humans, why study humans if all of these things can be studied in simpler organisms? Basic biological research has very much enriched medicine, but it's my personal belief that there's still much to be learned from the observation of sick human beings, particularly in areas of research that require behavioral interventions, like obesity. We seem to know a lot about obesity, except how to stop it.