Karger Gazette

No. 71 Published October 2010 · Your complimentary copy

At the Cutting Edge

Swiss Pioneers in Science and Medicine

EDITORIAL

P.J. MEIER-ABT

Science and innovation have always been important pillars of the social, cultural and economic development of Switzerland. This is especially true for biomedical research, a field in which this small country has a long and successful tradition. Indeed, it is probably not an overstatement to say that Switzerland's current wealth and high standard of living would not have been possible without a continuous flow of biomedical discoveries and new life science technologies, together with their successful translation into medical practice.

This progress is surprising for such a small country as Switzerland. It is based on several factors including the stable and free political system, the periodic appearance of outstanding intellectual personalities and the creation of an increasing number of academic institutions over the past few centuries.

Some of the most creative and influential Swiss personalities to push forward biomedical research are featured in this issue of the *Karger Gazette*. Certainly many other individuals and innovations of equal importance could have been added, but the examples selected highlight a broad spectrum of Swiss contributions. Included are pioneering molecular studies (the discovery of DNA), groundbreaking progress in psychiatry (the concept of 'schizophrenia'), the development of surgical techniques and tools, innovative synthetic chemistry (the industrial synthesis of vitamin C), and the first steps into the area of nutritional health with the propagation of Bircher muesli. This issue also ventures into more controversial territory with a look at Ita Wegman, who founded anthroposophical medicine in Switzerland. Although the scientific basis of this system of healthcare remains a matter of debate, complementary and alternative medicine has become very popular and remains a huge challenge for the rational application of the principles of evidenced-based medicine.

It is important to remember that these outstanding individuals did not exist in splendid isolation. They were immersed in a culture that had for centuries stimulated research, through the consecutive foundation of five universities (Basel, Bern, Geneva, Lausanne, Zürich) and two Federal Schools of Technology (ETH Zürich and Lausanne). The oldest of these is the University of Basel, which was founded by Papal decree in 1460 and is celebrating its 550th anniversary this year.

During its long existence the University of Basel has hosted many influential and visionary thinkers. Among those to walk the halls of the university are Erasmus, the humanist and theologian, the famous Bernoulli family of mathematicians, Friedrich Nietzsche, the philosopher, and Carl Gustav Jung, the psychiatrist. Today, the region of Basel is one of the world's leading life science centers, hosting the headquarters of pharmaceutical giants Novartis and Roche alongside numerous other drug companies and research institutions. In this, Basel has profited greatly from its strategic location at the point where the borders of France and Germany meet Switzerland.

> The region of Basel has developed into one of the world's main life science centers

Although somewhat younger of age, the other Swiss universities also declared biomedical sciences as one of their priorities and gained international reputations in various research fields. Today, attempts are being made to bundle and coordinate tertiary education and sciences within a nationwide network of complementary research groups and strong interactions between the different Swiss universities.[1]

These developments reflect a trend in modern science away from individual researchers and towards research teams. Indeed, it is a debated issue whether the future of scientific research will be driven by outstanding single individuals, as in the past, or by teams and centers of closely interacting researchers and organizations. But it is certain that the times of Friedrich Miescher, who made his breakthrough discovery of DNA working alone in a converted kitchen, are behind us.

The Power of We

Great ideas springing from the great minds of singularly creative individuals will always remain a force of the utmost potency,

Article continues on next page

This issue features articles on:
- Friedrich Miescher • Albrecht von Haller
- Auguste Forel • Eugen Bleuler
- Carl Gustav Jung • Ludwig Binswanger
- Ita Wegman • Maximilian Bircher-Benner
- Theodor Kocher • Tadeus Reichstein
- Albert Hofmann

WELCOME

G. Karger

As a biomedical publishing house, it is the nature of our business to constantly look forward. Our journal editors select papers that push the frontiers of their specialties, our book authors try to anticipate the future in their fields and, as publishers, we are always looking for exciting new ways to get this information to you as quickly and easily as possible.

This relentless pace of change is part of what makes working in the biomedical sciences such a rewarding and fascinating experience. But once in a while we all need to take a breath and look back, to find some context in the past for the endeavors of today. For us here at Karger this year has provided that opportunity. In 2010 we are marking the 120th anniversary of our company and celebrating its exciting and vibrant history. Karger's story began when my great-grandfather founded the publishing house in Berlin at the end of the 19th century, but during the turbulent years of the 1930s the company relocated to Basel, in the northwestern corner of Switzerland.

Basel has been known since the European Renaissance as a leading center of the printing industry and has a tradition of fostering the universal transfer of knowledge that spans more than five centuries. Today, the city is globally renowned for its pharmaceutical industry. It is in this exciting, nurturing environment that Karger has flourished.

It therefore seemed appropriate to dedicate this issue of the Karger Gazette *to some of the historical personalities that have helped make this small European country such a powerhouse of biomedical thinking. This is no compendium, it is just a snapshot of some of the most interesting scientists Switzerland has produced. As the author Paul Eldridge wrote: 'History is the transformation of tumultuous conquerors into silent footnotes,' and in many cases we have had to relegate huge personalities to footnote status – and beyond.*

We hope that the pages of this issue will serve as a tribute to the past and inspiration for the future.

Gabriella Karger

Continued from cover

but those ideas must increasingly be channeled by others. The methodologies and technologies of modern biomedical research have reached such a degree of complexity that no single person can master them all. Today's scientists must rely on shared core facilities and borrow expertise from neighboring disciplines, which is, for example, particularly evident in the field of systems biology.

Modern biomedical science is mostly interdisciplinary and requires a translational research approach that reaches from the bench to the bedside and from the bedside back to the bench. The basic biologists and biomedical researchers who sit at one end of that spectrum have to be able to interact and communicate with the clinical scientists who sit at the other end in order to develop new diagnostic tools and individualized therapies. The necessity for disciplines to work together has been realized all over the world, and some leading Anglo-American centers of thought, such as the universities of Cambridge and Harvard, have created translational research institutes to gather biomedical researchers of various stripes in close proximity to each other.

> The era of the pioneering scientist working long hours alone in his laboratory is over

In Switzerland, the Swiss National Science Foundation has recently created new programs to better support translational biomedical research and many Swiss universities have created translational research networks in order to speed the application of new basic discoveries and medical technologies in clinical medicine. In addition, new forms of collaboration between academia and industry are increasing innovation as they strive towards implementing personalized medicine. A nationwide network of clinical trial units has also been created to further improve the quality of patient-oriented clinical research in all Swiss university hospitals.

The era of the pioneering scientist working long hours alone in his laboratory may be over, but that does not mean that individuals no longer matter. Organizations, networks, collaborations and research groups are only as good as the people in them. Inspiring young people to forge a career in biomedical research and spotting and promoting talented individuals is of huge importance in a small country like Switzerland, but in recent years this has proved more difficult than expected.

There is no doubt that Switzerland is a country that punches above its weight in international science. But like many other smaller nations, it must work ever harder to maintain this position in a globalized world. Promoting talented individuals at home and attracting leading researchers from abroad will be of fundamental importance to the future of Swiss biomedical science. In areas where it is falling short, the scientific community must be prepared to find answers to some tough questions, to ask whether salaries and support systems are sufficient and teaching and mentoring stimulating. If it does this, and the government and private companies continue to invest in people and infrastructure, then the outlook for Swiss biomedical science is promising.

[1] www.swissuniversity.ch

Peter J. Meier-Abt
Vice-Rector, University of Basel

Prof. Meier-Abt is Vice-Rector of Research and Talent Promotion at the University of Basel.

The river Rhine flowing through the center of Basel. The white building to the far right is the first seat of the University of Basel, which was founded in 1460.

Karger Gazette

The Karger Gazette is provided free to the biomedical community. It appears once a year and highlights a specially selected topic in biomedicine.

To subscribe to the print edition please write to:

S. Karger AG, P.O. Box
CH–4009 Basel, Switzerland
Fax +41 61 306 12 34
Email: gazette@karger.ch

PDF and printable version:
www.karger.com/gazette

Published by S. Karger AG, Basel.
Edited by Dagmar Horn (dh), David Paterson (dp) and Paul Lavender (pl)
Design by Erich Gschwind
Web design by Gabriela Bütschi

The views expressed in the articles are those of the authors and do not necessarily reflect those of S. Karger AG.

Picture credits

The following persons and institutions are gratefully acknowledged as sources or copyright holders:
Friedrich Miescher Institute Basel (p. 4)
Burgerbibliothek Bern (p. 5)
University Library Basel (pp. 6, 15)
Swiss National Bank (p. 8)
Ita Wegman Clinic, Arlesheim (p. 10)
Archiv des Medizinhistorischen Instituts, Universität Zürich, Bestand Bircher-Benner (p. 12)
Institut für Medizingeschichte, Universität Bern (p. 13)
Novartis company archives (p. 16)

The photo of A. Forel and the drawings of ants (p.8) are taken from the book *Le Monde Social des Fourmis* by A. Forel (Kundig, Genève, 1921-23). Despite intensive research the publisher could not locate the copyright holder of the figures, but however consents to compensate all legal claims as customary and appropriate upon receipt of relevant notification.

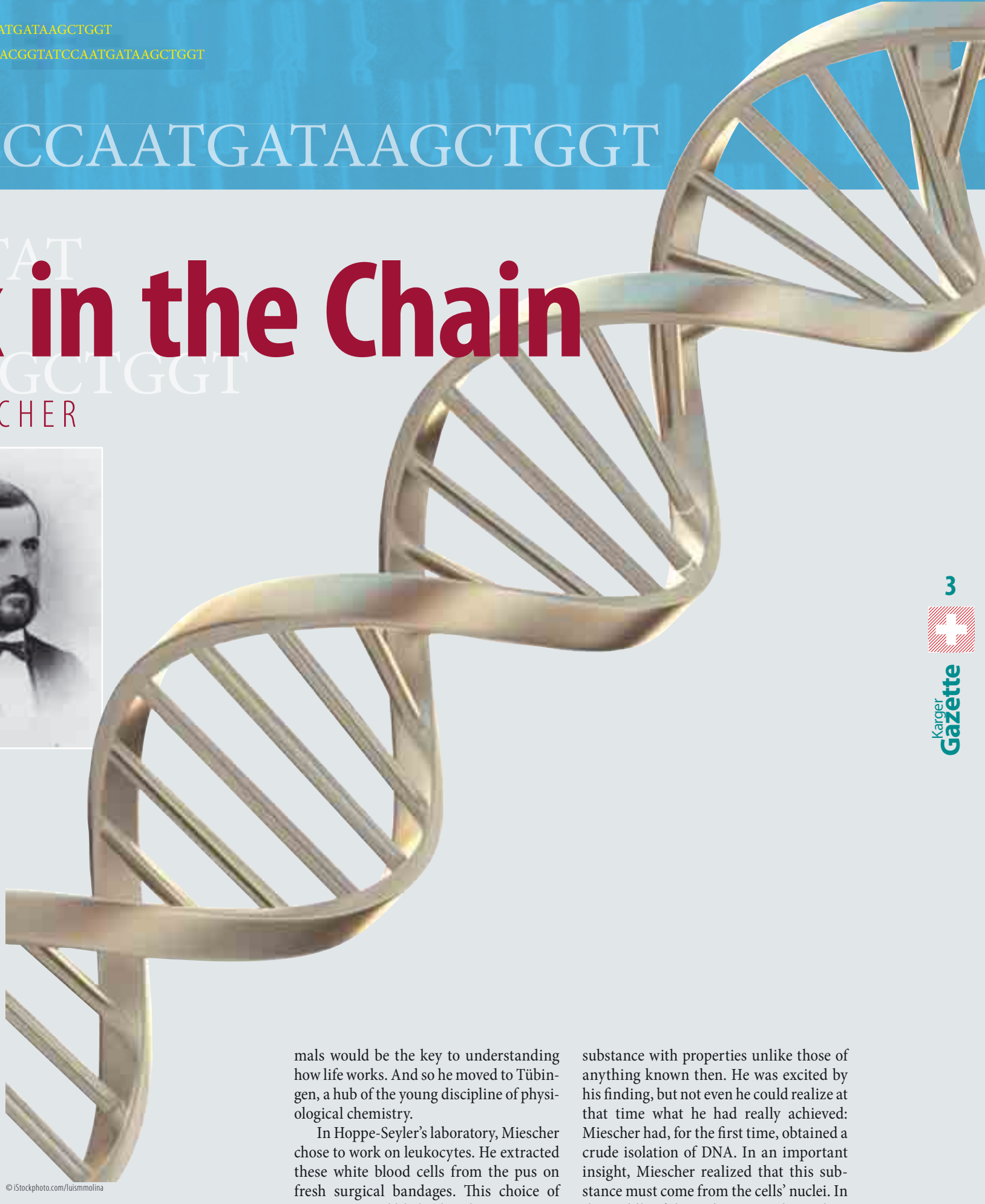
International Red Cross

Since the First Geneva Convention of 1864, the red cross on a white background has been recognized in law as a protective symbol for medical facilities in times of conflict. The symbol is a reversal of the colors found on the flag of Switzerland, which emphasizes the neutrality of medical services. Today, the symbol is in use by the Red Cross societies of 151 countries, with 32 others using the Red Crescent.

A Link in the Chain

FRIEDRICH MIESCHER

(1844–1895)



© iStockphoto.com/luismmolina

Working in freezing conditions in the converted kitchen of Tübingen castle, the physician Friedrich Miescher isolated the molecule we now call DNA. It was a monumental breakthrough for the life sciences – and it came courtesy of some pus-stained bandages and pig stomachs.

R. DAHM

It is a cold winter day in February. A young postdoctoral researcher training abroad writes a letter home. In it he describes what he has been up to in the laboratory, including an unusual observation he has recently made in one of his experiments. What seems like a commonplace occurrence in the life of any budding scientist was in fact a defining moment in the history of the life sciences. The year was 1869, the young postdoc was the Swiss doctor Friedrich Miescher, and what he related in his letter is one of the most far-reaching findings ever made: the discovery of DNA.

At the time, Miescher was working under the guidance of Felix Hoppe-Seyler, one the of great biochemists of his age. Their laboratories were located in the former kitchen and laundry of an ancient castle in the old university town of Tübingen in southwest Germany. Though picturesque, from today's point of view the laboratories would seem hopelessly inadequate with their sparse and primitive equipment. Nonetheless, in the 19th century this was a top location where Hoppe-Seyler and his colleagues were making groundbreaking discoveries on the chemical basis of life.

> Though picturesque, from today's point of view Miescher's laboratory would seem hopelessly inadequate with its sparse and primitive equipment

This was the reason why the young Miescher had chosen to work with Hoppe-Seyler. After finishing his medical studies in his native Basel, he had decided against a career as a practicing physician and instead chose to investigate the chemistry of living beings. Little was known of the molecules that comprise animals, plants or fungi at that time. Physiological chemists, as biochemists were called then, were mainly trying to classify and characterize the different proteins, lipids and other compounds they could isolate from different tissues or species. But it was still totally unclear what drove the processes of life.

Miescher was convinced that understanding the chemicals that make up animals would be the key to understanding how life works. And so he moved to Tübingen, a hub of the young discipline of physiological chemistry.

In Hoppe-Seyler's laboratory, Miescher chose to work on leukocytes. He extracted these white blood cells from the pus on fresh surgical bandages. This choice of source material likely played an important role in Miescher's ultimate success. Most of his contemporaries were analyzing the composition of tissues or entire organs, but by starting with a single cell type that could easily be purified, Miescher had the advantage of dealing with a simpler mixture of molecules.

> Miescher was convinced that understanding the chemicals that make up animals would be the key to understanding how life works

Having isolated the cells by carefully washing the bandages, Miescher subjected them to various procedures to separate their chemical constituents. Initially, he focused on the different fractions of proteins and lipids, which he isolated and tried to characterize. In one of his experiments he noticed something unusual: a substance that did not behave like any of the molecules known at the time.

In the letter he wrote on February 26, Miescher described his experimental findings: 'I could obtain precipitates that could not be dissolved either in water, acetic acid, very dilute hydrochloric acid, or in solutions of sodium chloride, and which thus could not belong to any of the hitherto known proteins.' Miescher had hit upon a substance with properties unlike those of anything known then. He was excited by his finding, but not even he could realize at that time what he had really achieved: Miescher had, for the first time, obtained a crude isolation of DNA. In an important insight, Miescher realized that this substance must come from the cells' nuclei. In the middle of the 19th century the nucleus was an enigmatic structure, and Miescher realized his discovery might provide a key to understanding it. But in order to characterize the new molecule better, he first needed to purify more of it.

He therefore developed a protocol to separate nuclei from the surrounding cytoplasm. To achieve this he washed the cells repeatedly over a period of several weeks with diluted hydrochloric acid. To avoid degradation of the material during long washes, he performed this step at 'wintery temperatures'. The exact conditions under which Miescher worked are unknown, but it is easy to imagine him in his laboratory, behind the thick walls of Tübingen's castle with the windows open to the cold winter and the temperature in his laboratory barely above freezing.

Miescher observed that nuclei isolated with this method behaved similarly to the unknown substance he had detected before, confirming that it did indeed reside within the nuclei. But the protocol did not yield enough of the novel substance to

characterize it further, so it was necessary for Miescher to develop yet another method.

Fortunately for Miescher, in 1868 the German physiologist Wilhelm Kühne had published a protocol that described how solutions containing the enzyme pepsin – which is secreted by the stomach to digest protein – break down the cytoplasm of cells, but not the nuclei. Miescher decided to expose his cells to pepsin to get rid of the cytoplasm. But to obtain the enzyme, he first had to rinse out pig stomachs with hydrochloric acid.

The new protocol finally brought success. As a first step, Miescher washed the leukocytes with warm alcohol. This broke the cells up and stripped off some of the cytoplasm. To remove the remaining cytoplasm, he then exposed the nuclei to his pepsin solution, which digested all the proteins. After a few hours, a fine gray powder sank to the bottom of his beaker. As before, Miescher shook this sediment with ether and washed it several times with alcohol to get rid of the lipids. In alkaline solutions, the sediment dissolved, but when he added acid, a wool-like precipitate appeared again. Miescher had finally obtained his first clean preparation of DNA for analysis.

Since he could precipitate the new substance by acidifying the solution, Miescher knew that it was an acid. His next step was to determine which elements it was composed of. In addition to carbon, hydrogen, nitrogen and oxygen – which are commonly found in organic molecules – he detected unusually high amounts of phosphorous, but little or no sulfur. This was in stark contrast to proteins and other molecules known at the time and the results convinced Miescher that he had indeed discovered a completely new type of molecule. He would later write: 'We rather have here entities sui generis [i.e. of their own kind] not comparable to any hitherto known group.' Since he had isolated the new molecule from the cells' nuclei, he named it 'nuclein'. Although the molecule has since been renamed, Miescher's original idea remains in today's designation: deoxyribonucleic acid.

Having found nuclein in leukocytes, Miescher began to search for it in other cells and tissues too. And wherever he looked, he found it: in kidney, liver, testes, nucleated erythrocytes and yeast cells. This led him to state later that nuclein 'will prove equal in importance to proteins'.

At this stage Miescher was clearly keen to publish his results. At the end of 1869, when Miescher had since moved to the University of Leipzig, he had finished drafting his first manuscript and was ready to send it to his mentor Hoppe-Seyler in Tübingen. In a letter to his parents dated December 23, 1869, he wrote: 'On my table lies a sealed and addressed packet. It is my manuscript, for whose shipment I have already made all necessary arrangements. I will now send it to Hoppe-Seyler in Tübingen. So, the first step into the public is done, given that Hoppe-Seyler does not refuse it.' Much to Miescher's disappointment, however, Hoppe-Seyler did refuse to publish his manuscript until he had a chance to verify Miescher's results himself.

Kitchen science: Despite being the converted kitchen of a former castle, Miescher's lab in Tübingen was considered cutting edge at the time. Perched on a hill overlooking the town, the 16th century castle was doubtless cold and draughty, but these 'wintery conditions' were exactly what Miescher needed to prevent degradation in his experimental materials.

This decision on Hoppe-Seyler's part does not so much reflect a lack of trust in Miescher's work. Hoppe-Seyler had just founded a new journal and Miescher was hoping to have his article included there. To warrant the reputation of his journal, Hoppe-Seyler had to ensure that only work of the highest standards would be published. As it turned out, Miescher's paper would provide exactly that, but to be sure Hoppe-Seyler had to confirm his student's results. Finally, nearly a year later, Miescher received a letter from Hoppe-Seyler to say that both he and another student of his had reproduced the results and that they would be included in Hoppe-Seyler's *Medicinisch-chemische Untersuchungen*.

Fishing for a Breakthrough

After a brief spell in Leipzig, Miescher returned to Basel where he became a professor at the university and resumed his studies on nuclein. There he discovered that sperm cells, with their large heads packed to the brim with nuclein, were an excellent source of DNA. In Basel, with its annual migration of salmon through the Rhine, Miescher soon recognized that male salmon are full of sperm as they swim upriver to their spawning grounds. He would frequently get up in the middle of the night and spend the early hours of the day on the riverbank catching fish for his experiments.

With this new source of nuclein, Miescher managed to purify much bigger quantities than he could produce in Tübingen. He used this material to perform some of his most accurate analyses of the properties of DNA. Miescher also worked hard to understand what role DNA played in the life of a cell. Even during his time in Tübingen, he had speculated that increasing the cell's DNA content might be required for cells to be able to proliferate.

Later, when working on the presence of nuclein in sperm cells and oocytes, Miescher also speculated on a role in fertilization and heredity, but ultimately rejected the idea. Instead he favored a function for nuclein in storing phosphorous inside the cell. It is tragic for Miescher that he came so close to uncovering the function of the molecule he had discovered. Ultimately though his thinking was trapped in his intellectual environment, and it fell to others to link DNA with heredity.

Based on the pioneering studies by Miescher and subsequent work by others, scientists had concluded by the mid-1880s that nuclein might be the molecule that stores hereditary information. But in the early 20th century scientists increasingly shifted their attention to proteins as the candidates for this function. DNA, with its composition of only four different building blocks, was seen as too simple to encode the complexity of life. Proteins on the other hand, which consist of 20 different amino acids, appeared better suited for this task. It was not until 1944 that experiments by Oswald T. Avery, an American molecular biologist, and his co-workers showed conclusively that DNA is the molecule that transmits genetic information. Finally, in 1953 James Watson and Francis Crick deciphered the double helix structure of DNA and, nearly a century after Miescher had discovered the molecule, the genetic code was cracked. Now scientists could, for the first time, decode the information contained in DNA.

Birth of an Icon

Friedrich Miescher died in 1895 with a feeling of not having fulfilled his scientific ambitions. But his discovery was the foundation upon which an entirely new discipline of biology was built: molecular genetics. Our understanding of how DNA works and our ability to manipulate it have since transformed not only the life sciences and medicine, but also pervaded numerous other areas of our lives. Modern forensic science would be unthinkable without DNA analyses; food inspectors use it to detect ingredients which are prohibited or to trace their provenance; it allows conservationists to check whether products contain materials from protected species; and even artists are now using DNA or its double-helical shape in their works. The molecule Miescher found behind the ancient walls of Tübingen castle truly has become the icon of the modern life sciences and one of the great symbols of our time.

Further Reading

Dahm R: Friedrich Miescher and the discovery of DNA. Dev Biol 2005;278:274–288.

Dahm R: Discovering DNA: Friedrich Miescher and the early years of nucleic acid research. Hum Genet 2008;122:565–581.

Dahm R: From discovering to understanding: Friedrich Miescher's attempts to uncover the function of DNA. EMBO Reports 2010; 11:153–160.

Maderspacher F: Rags before the riches: Friedrich Miescher and the discovery of DNA. Curr Biol 2004;14:R608.

Miescher F: Ueber die chemische Zusammensetzung der Eiterzellen. Medicinisch-chemische Untersuchungen 1871; 4:441–460.

Wolf G: Friedrich Miescher, the man who discovered DNA. Chem Herit 2003;21:10–11 and 37–41.

Ralf Dahm
University of Padova

Dr Dahm is currently Director of Scientific Management at the Spanish National Cancer Research Centre (CNIO) in Madrid and Visiting Professor at the University of Padova. He speaks and writes extensively on popular science.
www.ralf-dahm.com

FMI

Friedrich Miescher Institute for Biomedical Research

In the city of Basel, Friedrich Miescher's hometown, the memory of the pioneering physician is kept alive at the Friedrich Miescher Institute.

Founded in 1970, the institute is a crucial part of Basel's globally important biomedical industry. Now associated with the Novartis Research Foundation, the institute carries out fundamental research to understand what causes diseases at a molecular level.

Much of the institute's research is devoted to epigenetics, the study of how the expression of the same sequence of DNA is modulated by the cellular machinery to produce different phenotypes.

Susan Gasser, director of the FMI, sees this work as fitting for an institution named after the man who first speculated that DNA is the basis of heredity. She says: 'The innovative aspect of epigenetic research is very much in line with the pioneering spirit of Miescher, and the focus on genetic inheritance – and epigenetic modification of genetic inheritance – creates tight links to the famous Basler.'

The FMI aims to be 'intellectually daring' which, as Gasser puts it, means 'working at the frontiers of our knowledge, trying to link and apply novel concepts from different areas of expertise.'

The institute also donates the Friedrich Miescher prize, which is given each year to a particularly brilliant young researcher, as selected by the Swiss Society of Biochemistry.

irritable sensible brilliant

ALBRECHT VON HALLER

(1708–1777)

In the 18th century the salons of Paris and the coffeehouses of London buzzed with the big ideas of the European Enlightenment. But the Swiss intellectual Albrecht von Haller saw the limits of theoretical discussions. Devoting his life to rigorous methodological study, his results shocked the world and questioned long-held beliefs about the nature of the human body.

D. PATERSON

In 2008 the city of Bern unfurled the flags and banners for celebrations marking 300 years since the birth of one of its most famous sons, Albrecht von Haller.

Academic conferences were organized, a beautifully designed website appeared and word of Haller's life and achievements was spread through plays and exhibitions. Even Pascal Couchepin, then Swiss Federal President, was among the celebration's patrons, calling Haller 'one of the most distinguished Swiss scientists ever'.

The city was paying tribute to one of the most extraordinarily productive minds Switzerland has produced. Authors grasping for a suitable description of Albrecht von Haller invariably opt for 'polymath', though this barely does justice to a man whose intellectual stamping grounds included botany, anatomy, embryology and physiology, and who still found time to muse on poetry and religion and hold important civic offices in his hometown of Bern. It is not only the quality of Haller's work that is impressive, it is also astonishing for its quantity.

'Haller was indeed one of – if not the – most prolific scientific authors of all time,' says Hubert Steinke, a senior research associate at Bern University's Institute for the History of Medicine. 'He published approximately 50,000 pages of scientific works, mostly in a very precise and concise Latin.'

Illustration by C.J. Rollinus from Haller's book *Icones anatomicae* (1756)

Born the fifth child of Niklaus Emanuel Haller, a jurist, the young Albrecht was schooled in Bern before studying medicine at the renowned university in Tübingen (in what is now southwestern Germany). After graduating in 1727, Haller took to the road, turning up in London, Oxford and Paris, where he continued his medical studies, before heading to Basel to study mathematics under prominent mathematician Johann Bernoulli.

On his return to Bern he took up practice as a physician, while nourishing his passion for poetry in his spare time.

He published his *Essay of Swiss Poems (Versuch Schweizerischer Gedichte)* to great acclaim, and for a while it looked like his name was destined to end up in the annals of history under the section on poets.

However, in an unexpected move, in 1736 King George II of England – who also happened to be the Elector of Hanover – appointed Haller professor of anatomy, botany and surgery at the newly established University of Göttingen.

The following 17 years in Göttingen (now in central Germany) were a phase of immense activity for Haller. According to Frixione, writing in the *Journal of Neurology* in 2006, Haller was keen to turn the town into a center of advanced medical thought and he 'engaged in frenzied activity that included teaching, creating a library, installing clinics, laboratories and botanical gardens, as well as promoting the establishment of Göttingen's Royal Society of Sciences and editing its journal.'

It was during this period that Haller produced some of his most important scientific works. He published a massive flora of Switzerland, waded into the debate on Linnaean nomenclature with competing ideas (which were ultimately unsuccessful) and also published important works on anatomy. But it was his research in physiology that would cause the greatest impact, challenging long-held beliefs on the very nature of the human body.

> Haller showed that the body was not a passive machine guided by the soul but an active organism reacting to stimulations

At a time when hands-off theoretical reasoning was what passed for medical research, Haller saw that the only way to find out what was really going on in the body was through detailed methodological study.

'He demanded a rigorous verification of traditional knowledge and new research on an experimental basis, mainly animal experiments,' says Steinke. 'He separated doubtful from verified facts and established a solid basis on which the future generations were able to create modern physiology.'

Using vivisection of large series of animals, Haller precisely mapped the responses of different parts of the body to stimulation. He showed that only muscle fibers could contract upon irritation (a property he called 'irritability') and that they were responsible for movement. He distinguished muscles from parts furnished with nerves, which he saw as having 'sensibility', being capable of transmitting sensual impressions.

When Haller stood up to read his findings to Göttingen's Royal Society in 1752 what he was proposing was nothing less than a complete revision of prevailing beliefs on sickness, health and the body.

Steinke says: 'It showed that the body was not – as hitherto thought – a passive machine guided by the soul but an active organism reacting to stimulations.'

However, Haller's findings – and the gruesome methods by which he had achieved them – were not met with universal approval. For 20 years controversy raged, fuelled by a potent combination of revulsion at experiments on live animals, differing theoretical positions and contradictory results thrown up by wide variations in practical technique. It was not until the middle of the 19th century that Haller's ideas found general acceptance.

Shortly after his 1752 reading, Haller left Göttingen, where he had been productive but never really happy, to return to Bern. Back in his home town, he turned his attentions to politics. He was given the important task of overseeing the nearby salt mine and generally took on the role of the respected civic figure, becoming a regular feature of the city's municipal committees and public bodies, while continuing his scientific research and writings.

During his life, Haller produced an avalanche of texts, thousands of which survive to this day. Haller's habit of putting down his daily thoughts in writing have given historians an insight into his mind that would otherwise have been impossible to come by.

His writings, and those of his contemporaries, have allowed historians to coalesce around the opinion that he probably would not have made a great dinner guest. While some of his contemporaries found him entertaining, he could be rude and sharply critical. As Otto Sonntag noted in his 1974 *Isis* review, Haller's incessant labors caused him to tend towards righteousness. Sonntag wrote: 'Contemporary accounts portray an unbending seriousness that led him to frown on play and idle amusements, to renounce the self-indulgence of tobacco and wine at an early age, and to scorn all luxuries other than books.'

The motivations driving Haller to produce work on an almost industrial scale are still subject to some debate. Sonntag dwells on Haller's Calvinist religious beliefs and Swiss-German background, asserting that the desire to better know God by unraveling the mysteries of His creation was the prime motivator for many scientists in the German-speaking world.

While acknowledging Haller's religious motivations, Steinke also emphasizes more worldly characteristics that are familiar traits of successful scientists to this day: driving ambition, unrelenting curiosity and the conviction that the advance of knowledge is unstoppable.

- Haller was not just a brilliant scientist, he was also brilliant for business. Find out how he kick-started the Swiss tourist industry at www.karger.com/gazette.

Further Reading

Frixione E: Albrecht von Haller (1708–1777). J Neurol 2006;253:265–266.

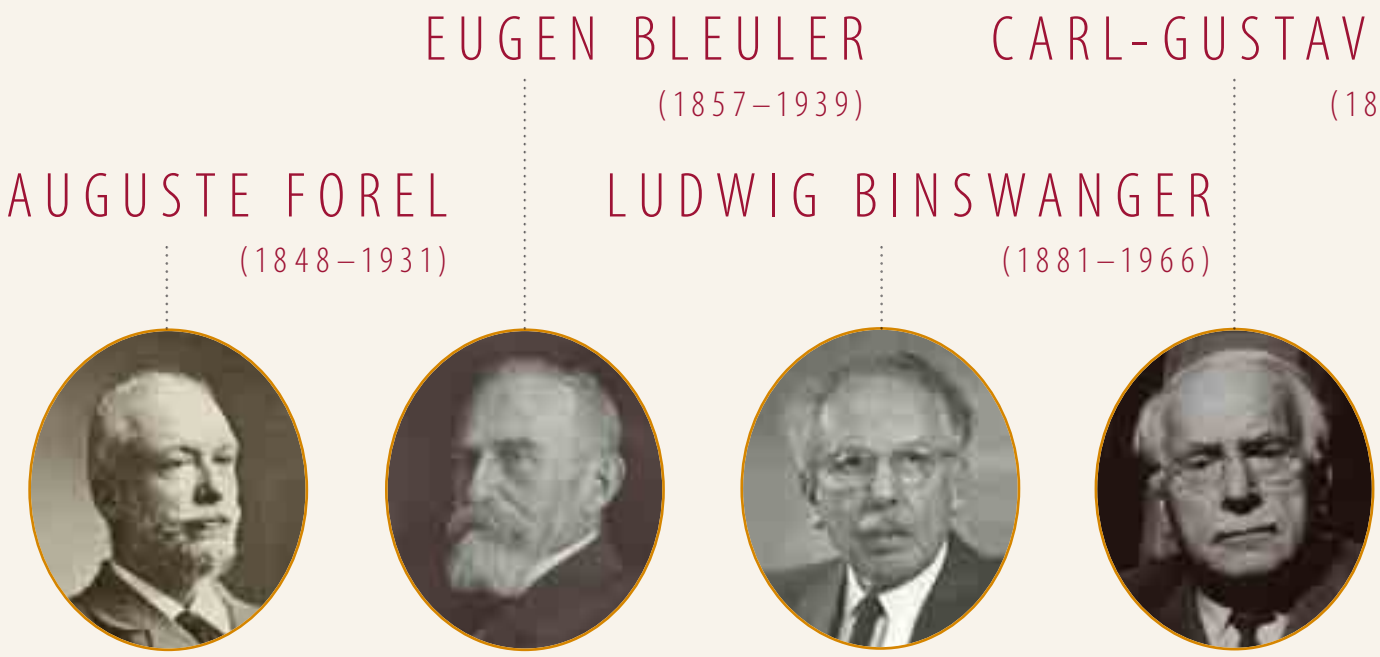
Sonntag O: The motivations of the scientist: the self-image of Albrecht von Haller. Isis 1974; 65:336–351.

The Haller Foundation: Haller 300 biography. www.haller300.ch

David Paterson is an editor of the Karger Gazette

Matters of the Mind

The last decades of the 19th century saw a flourishing of Swiss psychiatry on the world stage . This outpouring of ideas would last until the 1940s, and its influence is still felt today.



E. HEIM

It is truly extraordinary that in the last third of the 19th century and the first half of the 20th century, scientists from such a small country as Switzerland – which only made up a tenth of the German-speaking world – influenced developments in psychiatry so profoundly.

There were two main reasons for this imbalance. First, a fertile scientific environment: medicine in German-speaking countries was making great advances and renowned worldwide. In 19th century Europe, positivism was the leading school of thought in medicine. In psychiatry, this meant mental disorders were seen as a result of neuropathological processes. Proponents of this belief included Westphal, Meynert and Wernicke.[1] The German neurologist Wilhelm Griesinger (1817–1886) is also grouped together with this trio of scientists, albeit somewhat unfairly. He was the first to posit a connection between psychiatric processes and altered brain structures. He was, however, far ahead of his time in that he believed in multi-dimensional psychiatry, in which symptoms not attributable to organic disease (and thus considered to have a psychological origin) were considered of etiological importance. As professor of internal medicine in Zürich, he made psychiatry an independent discipline with a specially designed hospital the university clinic Burghölzli which would become the setting for many key events that followed.

The second factor that positively influenced the development of Swiss psychiatry was the country's new political order. In 1815, a sovereign state with a modern constitution (1848) was formed. With the accompanying liberal thinking and feelings of social responsibility, the idea of open and humane treatment of psychiatric patients found fertile ground. In addition to research and teaching, psychiatry at the university level made the treatment of patients at university facilities mandatory (in contrast to the situation in Germany). This fusion of academic theory and clinical practice allowed psychiatrists to make detailed observations of the course of an illness and the effects of treatment.

> Forel was committed to informing the public about the dangers of alcoholism

This rich environment went on to produce some of the most extraordinary thinkers ever seen in the field of psychiatry. The talents and vision of the key players described below brought about revolutionary changes that are still felt by psychiatrists today.

From Anatomy to Psychiatry

Auguste Forel (1848–1931) was a true polymath – he made a name for himself in neuroanatomy, psychiatry and the reform movement. After his early retirement, he turned his attention to his childhood hobby of studying ants, a field in which he would achieve an international reputation.

Like many psychiatrists of the 19th century, he began his career in the neuropathological laboratory,[1] specifically in anatomical research of the brain. Forel dedicated himself to these studies under the supervision of Bernard von Gudden, who would later become the first director of Burghölzli. Thanks to their collaborative invention, the microtome, they were able to dissect most regions of the brain. Forel did extensive research on the organization of the tegmentum with its complex fibrillary and nuclear structures: he was the first to describe the zona incerta and the so-called H fields that still bear his name (campus Foreli).[2] Moreover, his anatomical descriptions of neurons have led him to be considered as a co-founder of neuron theory – the topic of his professorial thesis.

At the age of only 30, Forel became director of Burghölzli and was instrumental in helping it achieve international acclaim. Correlating his knowledge of the brain with psychiatric processes and recognizing the importance of meaningful work for mental health, he created holistic treatments for his patients, including occupational and milieu therapy.

His work with the mentally ill also led him to become an effective social reformer. Confronted with alcohol-addicted patients every day, he decided to abstain from drinking although he had never been a teetotaler before. He was committed to informing the public about the dangers of alcoholism and, in 1880, he opened a special clinic for alcohol dependency (today called the Forel Clinic). A few years later he was active in establishing a Swiss chapter of the International Order of Good Templars, which aimed to support the prevention of alcoholism.

This period coincided with his writings on eugenics, which from today's perspective would seem racist, but were in fact suggesting a way to halt the spread of genetic defects (especially addiction-related ones). As a free thinker and socialist, Forel was very far from the views of later proponents of racial hygiene in the Nazi era, but was often quoted out of context by them. Although Forel succumbed to many falsehoods in questions pertaining to race,

Painting by a patient who was sexually abused in her childhood and adolescence, depicting the paralyzing clasp of her depression. The picture is part of a series of 48 paintings created during her psychotherapy in an attempt to work through her sexual trauma and published in the book *Trauma and Art* (Authors: Rut, G. Benedetti and G. Waser; Karger, 2004).

these should in no way be equated with racism. Throughout his life, he remained critically and steadfastly opposed to discrimination and prejudice, including antisemitism.

Forel worked just as passionately on social topics. His widely acclaimed book *Die sexuelle Frage* (The Sexual Question) published in 1904 was translated into several languages. With this, he contributed in a more pragmatic way to the public perception of sexual problems than Freud's early writings did. He supported the sexual equality of men and women, the decriminalization of concubinage and unrestricted use of contraceptives. Through the secularization of law, he wanted a 'reasonable' regulation of the sexual question, and in doing so became a leading pioneer of sexology. In the late Victorian Age his views naturally resulted in fierce protests and resistance, especially from religious leaders, but Forel would not give up. It was only after many years of fighting and as a consequence of a stroke that he became milder and more tolerant; in 1920 he even joined the Bahá'í faith as he was impressed by its reconciliatory beliefs.

Forel also devoted a significant part of his research efforts to consolidating and publicizing hypnosis, authoring the first textbook on the subject. His book *Der Hypnotismus oder die Suggestion und die Psychotherapie* (Hypnotism or Suggestion and Psychotherapy) was printed in several editions and was widely circulated. His student and later successor Eugen Bleuler contributed an article to the second edition, entitled 'Two Hypnotized Hypnotists', in which he described in a humorous but scientific manner how he and Forel hypnotized each other. Additionally, Forel founded the *Internationale Gesellschaft für Medizinpsychologie und Psychotherapie* (International Society for Medical Psychology and Psychotherapy), which was one of the first organizations in the field.

As with most brilliant minds, Forel gives the impression that he must have lived more than one life. At barely 50 years of age, he stepped down as director of Burghölzli to dedicate himself to ant research (see box on page 8).[3]

Two of Forel's students became prominent specialists in psychiatry: Adolf Meyer and Eugen Bleuler. **Adolf Meyer** (1866–1950) is not usually associated with his Swiss heritage, as he emigrated to the USA after his training. He worked at several psychiatric institutes before he became a professor at Johns Hopkins University from 1913 to 1937. Familiar with psychoanalysis, he developed his own psychodynamic theory of personality, which he termed 'psychobiology', which was closer to the neopsychoanalysis of Sullivan, Horney and others. He became famous in the USA for being a pioneer of medical and psychiatric didactics, which were still held in high regard after World War II.[4]

The Divided Mind

Being the founder of the 'Zürich School', **Eugen Bleuler** (1857–1939) assumes a special place in the history of psychiatry. He saw disease in an integrative way – giving equal consideration to findings from the natural sciences and the new methods of psychoanalysis. Bleuler shared his teacher Forel's conviction that alcoholism was a social evil, one that he too had to combat. This may also have been the reason why he held on to Forel's misguided views about eugenics.[1]

Bleuler was not even 30 years of age when he became the director of the mental hospital in Rheinau in 1886, where he devoted his life exclusively to his patients. He spent his days with them, made observations and kept countless notes on their behavior. This allowed him a completely different level of access to their suffering than was typical. In 1898, after he succeeded Forel at Burghölzli, he further developed his observations and introduced the concept of 'schizophrenia' (lit. 'split mind') to depict the inner conflict and the division of the consciousness. His interpretation was based on the psychological concept of 'association' (here referring to the links between psychological functions); 'dissociation' on the other hand is seen as segregation within the thought process. His use of terms such as autism and ambivalence also found acceptance in the clinical world.[5]

Bleuler was successful in combining psychoanalysis with psychopathology – a feat accomplished by neither Kraepelin nor Freud. From psychoanalysis, he gained a dynamic understanding of how disorders correlate with life history. Bleuler's enthusiasm for and openness to psychoanalysis sustained its development. In 1904, he was the first university teacher to begin correspondence with Freud and take him seriously. He was also the first person outside Vienna to embrace psychoanalysis and, while keeping a critical distance, encouraged his colleagues and students to explore it. When Bleuler, however, recognized a certain orthodoxy in the psychoanalytic movement, he decided to leave the international association, nevertheless he remained a proponent of the discipline in public, which Freud greatly appreciated.[6] Partly because of this view, Bleuler attempted to have medical psychology implemented into the medicine curriculum in order to better train students in the doctor-patient relationship.[4]

His ideas about 'depth psychology', a term coined by him to take into account the role of the unconscious, referred not only to the mentally ill but also to human behavior in general. His students, especially Jung and Binswanger (see below), developed this approach further according to their own ways of thinking.

Becoming Oneself

Carl Gustav Jung (1875–1961) was the most famous student of the Bleuler School.

Impressed with Jung's talent, profound education and scientific interest, Bleuler brought him into contact with Freud in 1907. After their first encounter Jung became so fascinated with Freud and his teachings that he began to neglect his clinical duties in favor of his research. Thus, Bleuler asked him to resign from the clinic in 1908. After doing so, Jung became more active in psychoanalytical research. The analytical psychology he developed had almost as large an international audience as Freud's psychoanalysis. He adopted the term 'complex' to refer to an unconscious set of feelings and beliefs, and had his own ideas about the unconscious, to which he later added the term 'collective unconscious'. His education in the humanities enabled him to view psychological processes in a new light. He saw symbols found in artwork, fairytales, mythology and dreams as the key to understanding the unconscious. He coined new terms like 'archetypes', 'anima/animus' and 'shadow'. Spirituality as found in mythology, Gnosticism and religion was an important source of self-discovery for him: *Werde der Du bist* ('become who you are') summarized his ideas of individuation. Becoming oneself was for Jung not only a therapeutic goal, but a personal one, achieved only after dealing with internal and external conflicts.[4] Freud's teachings had a major impact on Jung in the short time that they worked closely together. They shared the idea of an unconscious, to which access is provided through dreams, and felt that childhood development has a great impact on the adult psyche. They held each other in such high regard that Freud nominated Jung to be the first president of the new International Psychoanalytical Association. Freud asked Jung to accompany him on speaking tours in the USA, appointed him as an editor and saw him – his most important non-Jewish student – as his future successor and protector of the psychoanalytical movement.

> Jung became so fascinated with Freud that he began to neglect his clinical duties in favor of research

Nevertheless, the importance Freud placed on childhood sexuality, the omnipresence of the Oedipus complex and the idea of a libido that was purely sexually orientated were themes Jung could no longer support. He parted ways from Freud in 1913, setting off many lasting conflicts in their field. It was very hard for Freud to overcome his deep disappointment, as he had hoped Jung's international contacts would bring him out of his intellectual isolation. Jung, on the other hand, fell into a deep inner crisis after the loss of Freud's spiritual-fatherly support.[7] However, Jung stepped back from his professional activities and developed his own theories further. He embarked on a journey to discover inner truth that was unique in the history of science. He immersed himself in an incessant stream of inner fantasies and images, which would later help form his theories. His process of finding inner truth lasted for more than a decade and was recorded by Jung in a book, *Liber Novus*.[8] This mysterious 'red book' (the leather cover was red) slowly became known among Jung devotees, but his heirs withheld it from the public. It was not until 2007 that Jung's grandson agreed to have the book published. It turned out that the book was not a collection of autobiographical notes, but rather numerous symbolic sketches and texts, which were only of limited interest to the wider public.

In his papers and books, Jung comes across as sensitive and introverted. There was, however, another side to him, a 'homo politicus', which was very active in the organization and expansion of psychotherapy in its early days – a talent which had been utilized by Freud. While in later life Jung insisted he was not interested in starting any 'schools', in the mid-1920s he was very much involved in the congress movement, serving as vice-president of the *Allgemeine Ärztliche Gesellschaft für Psychotherapie* (General Medical Society for Psychotherapy). When one of the co-founders, Ernst Kretschmer, resigned in protest against the restrictions placed upon them by the National Socialists, he encouraged Jung (as a representative of a neutral country) to found another society, the *Internationale Allgemeine Ärztliche Gesellschaft für Psychotherapie*, which Jung agreed to do in order to protect persecuted Jewish colleagues. Despite this, he simultaneously began to cooperate with the institute of Matthias Göring (a relative of a senior Nazi). Additionally, it was found that some of his writings contained racist views. So, although he tried to maintain contacts for scientific discourse on an international level, his political views posed problems for him in the 1930s as well as in the post-war era.[4,7] In 1985, the American historian Geoffrey Cocks came to the conclusion that although Jung showed a naïve enthusiasm for the National Socialists, he was never active in supporting them in their political goals.

Prominent Figures

Three other prominent Swiss psychiatrists who also completed at least part of their training at Burghölzli should be mentioned: Ludwig Binswanger, Hermann Rorschach and Medard Boss.

Of Ants and Men: Did a Small World Give Forel His Big Ideas?

Auguste Forel was a leading neuroanatomist and psychiatrist, but humans were not his only study subjects. He was fascinated by ants and may even have seen parallels between their tiny but complex worlds and our own societies.

From the age of 11, Forel was enthralled by these creatures, devoting all his summer vacations to their study. In 1874, at the age of 25, he published his monumental monograph *Les Fourmis de la Suisse* (The Ants of Switzerland), which earned him several awards and even lavish praise from the great Charles Darwin, who wrote to Forel: 'I have now read the whole of your admirable book and seldom in my life have I been more interested by any book.'

Over his lifetime Forel would amass a collection in which more than 6,000 species were represented. He described 3,500 new ant species and, based on his profound knowledge of their anatomy, proposed a new taxonomy. His magnum opus, however, was a beautifully illustrated five-volume treatise on the social world of ants, printed between 1921 and 1923, and which is still considered a major contribution to the field. Right up to his death in 1931 at the age of 83, Forel remained active as a private scholar in his fields of interest – ant research and the promotion of social welfare.

Some modern-day researchers discern links between Forel's studies on the highly structured behaviors of ants and his thoughts on the human world. André Parent, professor at the department of psychiatry and neuroscience at the University of Laval (Canada), notes that Forel made insightful observations on the neural control of sensory and instinctive behaviors common to both humans and insects. Parent speculates that: 'Detailed studies of animal societies that are so rigidly organized as ants must have played a role, at least unconsciously, in shaping his opinions about birth controls, education, sexuality, etc.'

Charlotte Sleigh, senior lecturer in the history of science at the University of Kent (England) and author of the 2004 book *Ant*, is more forthright, believing that Forel's psychiatry and myrmecology were completely interwoven. She says: 'He took ants as a model for what humans could achieve: social harmony, eugenic reproduction, the lot.'

Sleigh suggests that Forel's most important theory was that the human learning process echoes the evolutionary path taken by ants, which over thousands of generations had acquired useful behaviors that were laid down as habits or instincts. 'This showed how humans too – notably alcoholics – could be re-educated out of their harmful behaviors and into new, socially useful habits,' she says, but adds: 'Do I personally think this is valid? Not at all.'

Forel appears to have admired the orderly nature of ant societies, an admiration that could have found expression in his ardent pacifism and internationalism. More disturbingly, Forel may have drawn on the highly structured world of the ant to determine a 'naturalized' system of ethics, which he then applied to humans. 'A dangerous thing,' Sleigh says, 'where nature's supposed *is* dictates a human *ought*.' Sleigh sees a link between Forel's thinking and later evolutionary psychologists who would use 'natural' behaviors in our ancestors to explain human behaviors today.

In 1978, the Swiss National Bank honored the memory of Forel on its 1,000 franc banknote. Its design reflected Forel's passion for myrmecology, with the reverse side given over to an image of three ants and a cross-section of an anthill. In the wake of renewed debate over Forel's ideas on eugenics, the note was withdrawn from circulation in 2000. *(pl)*

Rorschach® Test. © Verlag Hans Huber, Hogrefe AG, Bern.

What Do You See? The symmetrical forms of the Rorschach test, developed in the 1920s by Swiss psychologist Hermann Rorschach, are the most iconic images in psychology. The tester scores a subject's responses to 10 ambiguous shapes in order to develop a profile of their personality. The results are thought to reflect the subject's attitudes, interpersonal skills, grasp on reality and ability to structure situations. It is still widely used today as one of the major projective tests (even in court cases). Its psychometric reliability, however, is debated. The image shown here is from Rorschach's experimental phase and does not form part of the test.

Hermann Rorschach (1884–1922), who died from a surgical complication at the age of only 38, was seen as the promising star of Swiss psychiatry. Under Bleuler's supervision, he wrote a dissertation about the processes of perception. However, it was his ink blot test (see image) – perhaps the psychological test that is most well-known to non-professionals – that would go on to make him a household name.

Ludwig Binswanger (1881–1966) was born into a family of psychiatrists, his grandfather was the founder of Bellevue, a well-known psychiatric clinic on Lake Constance. After his initial training at Burghölzli, Binswanger became the director of Bellevue for almost half a century. This institute had a reputation for the close communal life its patients, doctors and members of the Binswanger family shared, and Binswanger's networking made it Europe's center of intellectual thought. Prominent figures from both science and the arts were regular guests.

Binswanger was the first to combine psychotherapy with existential analysis in an attempt to give psychopathology a new epistemological foundation. In 1941, influenced by the existential philosophy of Heidegger's Sein und Zeit (Being and Time), he created the term *Daseinsanalyse* for his approach. He saw it not so much as a therapeutic method, but as another scientific way of understanding people who live in their 'own' world, connected to others important to them and with whom they form a 'common' world. Regardless of whether a person is sick or healthy, one's unique 'existence' should be respected (see box). In his publications Binswanger applied his theories mainly to schizophrenic and manic-depressive psychoses. Binswanger always kept an attitude of critical distance concerning psychoanalysis. Nevertheless, he maintained a lifelong and good relationship with Freud, who respected Binswanger's philosophical stance, even though Freud pointed out that he saw his own roots firmly planted in the natural sciences.[9]

After World War II, there was a split between Binswanger and his students. Those who followed **Medard Boss** (1902–1990) sought out ways to treat patients which were more therapeutic in approach and less epistemological. With support from Heidegger, the 'Zürich School of *Daseinsanalyse*' grew and developed. This school of thought is still taught today and views its approach as a synthesis of Freudian psychoanalysis, Jung's analytical psychology and existential philosophical findings.

Boss, however, also deserves to be mentioned in another light. As a result of the political turmoil and war of the 1930s and 1940s, professional discourse naturally suffered as scientists were unable to meet each other. A few far-sighted colleagues began to re-establish contacts and organized conferences after the war, which among other things tried to grapple with its psychological effects. As Switzerland was spared from this war, it played a crucial role. Boss was instrumental in these efforts and sought to establish an organization to succeed the *Internationale Allgemeine Ärztliche Gesellschaft für Psychotherapie*. This led to the foundation of the important umbrella organization for European national psychotherapy organizations – and later others from all over the world – known as the International Federation for (Medical) Psychotherapy (IFP), which is still active today.[4,7]

> Binswanger applied his theories mainly to schizophrenic and manic-depressive psychoses

After the Pioneers

As mentioned above, it seems somewhat surprising that such a small country like Switzerland could contribute so much to a medical area in such a short time period. Perhaps it is also surprising that no comparable developments have been made since World War II. This needs to be viewed in the light of specific post-war socio-cultural conditions, but could also reflect a general trend.

Three socio-cultural trends became evident after World War II. Europeans were suffering from personal losses, trauma and material scarcities, and for many people the restrictions of living as part of a collective had become unbearable. The rapid growth of existentialism, which called for a self-reliant individual, had a major effect on psychiatric practice – boosting support for psychotherapy in general, and existential analysis and psychoanalysis in particular.

Developments in the USA and England were influenced heavily by emigrants from Europe – many of whom were Jewish – trained in psychoanalysis. They dominated the field, taking over the academic world step by step until hardly any key position in psychiatry or psychotherapy was filled by someone who was not a psychoanalyst. It was not until the 1960s that the tide turned in favor of the community mental health movement and other newer developments. The third development was political in nature. The socialist countries of eastern Europe decided Pavlovian behaviorism should be the dominant approach.

A final yet crucial trend – not only seen in Swiss psychiatry or medicine, but through the whole of science – is that the course of scientific research is no longer determined by outstanding individuals, but rather by teams or even academic centers. The time of the individual pioneer seems to be over – a development which is not necessarily a disadvantage for science. Nevertheless, this should not stop us looking back at the trailblazers within our disciplines, such as the ones described in this article, and draw inspiration from their lives and many achievements.

References

1 Schott H, Tölle R: Geschichte der Psychiatrie. Munich, CH Beck, 2006.
2 Forel A: Untersuchungen über die Haubenregion und ihre oberen Verknüpfungen im Gehirne des Menschen und einiger Säugethiere, mit Beiträgen zu den Methoden der Gehirnuntersuchung. Arch Psychiatr Nervenkr 1877;7:393–495.
3 Forel A: Le monde sociale des fourmis du globe comparé à celui de l'homme (5 volumes). Geneva, Kundig, 1921–1923.
4 Heim E: Die Welt der Psychotherapie. Stuttgart, Klett-Cotta, 2009.
5 Scharfetter: Eugen Bleuler 1857–1939: Studie seiner Psychopathologie, Psychologie und Schizophrenielehre. Dietikon, Juris, 2001.
6 Bleuler E: Die Psychoanalyse Freuds. Verteidigung und kritische Bemerkungen. Jahrbuch für psychoanalytische und psychopathologische Forschungen, II. Leipzig, Deuticke, 1911.
7 Heim E: Development of psychotherapy. Psychother Psychosom 2010;79(suppl 1):1–90.
8 Jung CG: The Red Book: Liber Novus. New York, WW Norton, 2009.
9 Binswanger L: Erinnerungen an Sigmund Freud. Bern, Franke, 1955.

Translated from German by Alan Tootle.

Edgar Heim
University of Bern

Prof Heim was co-chair of the Department of Psychiatry at the University of Bern from 1977 to 1994 and President of the International Federation for Psychotherapy from 1988 to 1998.

The Case of Ellen West: Triumph or Tragedy?

Anorexia nervosa is still one of the most prominent eating disorders, but the therapeutic approach has definitely changed over the last hundred years: Whereas Binswanger still based his treatment on a strictly psychodynamic ground, it nowadays calls for a more comprehensive approach, including cognitive-behiavoral techniques. It is nevertheless interesting to look almost 10 decades back at a different therapeutic culture.

In 1923, psychiatrist Ludwig Binswanger discharged Ellen West, a deeply troubled anorexic patient, from his sanitarium. He was fully aware that she was at high risk for suicide, which she duly committed shortly after. Twenty years later Binswanger published her case to support his *Daseinsanalyse* – and he described her death as a successful treatment outcome.

Binswanger's fusion of psychotherapy and existential analysis demanded an individual's 'existence' be respected. For him, diagnostic labels were less important than understanding a patient's existence and experiences from their own perspective.

This approach was made famous by the case of West, who used writing and poetry to vividly describe her inner turmoil.

When she came under Binswanger's care she weighed only 92 lbs (41 kg). Previous therapy had failed and she had twice tried to commit suicide. She seemed unable to relate to herself as a real person, writing in one of her diaries: 'I am isolated. I sit in a glass ball. I see people through a glass wall. I scream but they do not hear me.'

Despite becoming physically healthier, the suicide attempts continued. Eventually, she and her husband were given the choice of a closed ward and expected deterioration of her condition, or release. They chose release.

She immediately felt better, ate happily, spoke to her husband, and wrote letters to friends. Then she took a lethal dose of poison.

Though West's fate was tragic, Binswanger did not see it as a failure. As David Lester commented in the *Psychoanalytic Review*, Binswanger believed that 'only in her decision for death did she find herself and choose herself. The festival of death was the festival of the birth of her existence.'

Questions will always remain about whether West could have avoided suicide had she been treated differently, and today opinion is divided over whether Binswanger's approach created a reasonable outcome for the patient, or was a case of psychic homicide. *(pl)*

Healing Mind, Body and Soul

ITA WEGMAN
(1876–1943)

In 1921 Ita Wegman founded a clinic in Switzerland based on a revolutionary approach to medicine – healing the soul as well as the body.

P. LAVENDER

When Ita Wegman died in 1943, the huge collection of correspondence she left bore testimony to the esteem in which she was held by European medical professionals.

An enormously driven woman, in her 67 years, Wegman forged not just a career in medicine – itself unusual for a woman in her time – but founded a new medical doctrine combining patient care with a life philosophy. As the inspiration behind anthroposophical medicine, she was an influential figure in what we now call complementary medicine.

'Many letters she received were extremely reverential – almost worshipping her,' says Gunhild Pörksen of the Ita Wegman Institute in Switzerland, which preserves her archive. 'Her replies were always friendly and positive, but never encouraged this devotion at all.'

Anthroposophical medicine is an integrative form of medicine developed by Ita Wegman and the philosopher Rudolf Steiner. It is based on Steiner's spiritual philosophy 'anthroposophy', and is 'integrative' as practitioners are first qualified in traditional medicine. Anthroposophy posits the existence of a spiritual world, which followers attempt to experience through self-development. This has since expanded into the more practical and everyday realms of education, agriculture and medicine.

Practitioners of anthroposophical medicine view disease as a result of a biological, psychological or spiritual imbalance. Therapies designed to create a healthier self-image and emotions and are not just 'nice to have', but are essential for a complete cure.

Lukas Schöb, a senior doctor at the Ita Wegman Clinic in Arlesheim, Switzerland, sees anthroposophical medicine as stimulating the self-healing mechanisms of the body-mind complex in three ways:

– On an intellectual level, the patient must understand the causes of their health and not just their illness – stopping the downward spiral that results from viewing themselves simply as an ill person.

– The patient needs to identify more with positive feelings while releasing suppressed negative emotions. Schöb explains: 'We've found music, art and dance therapies to be particularly effective. Cases of extreme pain have sometimes disappeared after a large emotional release.'

– On a physical level, given in addition to conventional medical treatment, specific anthroposophical medicines created using natural medicinal ingredients are used – the most well-known of these being mistletoe for cancer. These substances are also utilized in therapies such as rhythmical massage (created by Ita Wegman) and compresses. A healthy diet also plays an essential role.

According to this approach, the patient is therefore not simply a passive recipient of medicine, but an active participant in the whole healing process.

Ita Wegman before 1900

Early in Wegman's life there were no indications of her future path. Born in 1876, she was the daughter of a well-off Dutch family living on Java, an island of the then Dutch East Indies. Upon moving to Europe, she soon became taken with the life reform movement, a mixture of groups critical of industrialization and advocating a return to nature. Through this, she met Rudolf Steiner, whose ideas led to the development of the Waldorf schools, and who remained her life-long teacher.

> 'Disease is a result of a biological, psychological or spiritual imbalance'

Steiner strongly encouraged her to carry anthroposophy into the field of medicine. At the relatively late age of 30 she began to study medicine in Zürich, one of the few European universities to then admit women. She set up a practice shortly after and in 1917 started preparing mistletoe-based medicines for cancer patients (currently known as Iscador). In 1921, she opened her clinic in Arlesheim, with enough room for 12 patients and a small laboratory to prepare medicines, many of which are still in use. Today, the Ita Wegman Clinic has grown to accommodate 63 patients, with many outpatients, and the laboratory has become Weleda, an international producer of natural medicines with 1,800 employees.

At the Arlesheim clinic, practitioners followed the philosophy of Steiner, seeking physical, mental and spiritual development for themselves and their patients, with medicine being a way to achieve this. Anne-Marie Gass, matron at the clinic, explains: 'Humans are not just physical beings, but spiritual beings. Ita Wegman wanted medicine that would treat both aspects, to help patients develop further along their life paths.'

Although Steiner was not a doctor, Wegman trusted his medical intuition, and he often helped patients and offered some suggestions for suitable medicinal substances. According to Gunhild Pörksen from the Ita Wegman Archive, the respect was mutual: 'Steiner was very impressed with this passionate and strong-willed lady who was able to take his ideas on medicine and convert them into reality – she got things done.' She also picked up on his passion for working with disabled children – particularly those with mental disabilities – at a time when such patients were often subjected to severe medical treatments, if any. In 1922, she founded the Sonnenhof Children's Home, which is still in existence.

After Steiner died in 1925, Wegman continued to develop his ideas and worked hard to spread them across the whole of Europe. As a result, there are currently 28 anthroposophical medicine centers with 140 outpatient clinics worldwide, giving weight to Wegman's words: 'Despite difficult times, it is absolutely necessary to keep moving forward and developing.'

Who Calls the Tune? The Future of Anthroposophical Medicine

In some countries, such as Switzerland, where it was founded, anthroposophical medicine is generally well accepted and is paid for by general health insurance. However, it is subject to the major criticisms leveled at complementary and alternative medicine. Marcia Angell, ex-editor-in-chief of *The New England Journal of Medicine*, wrote in 1998, 'There cannot be two kinds of medicine – conventional and alternative. There is only medicine that has been adequately tested and medicine that has not.'

Lukas Schöb, a senior doctor at the Ita Wegman Clinic, acknowledges this problem, but sees it as indicative of a far deeper concern. 'We're still experiencing the results of debates in the Middle Ages centered around the problem of universals – how to define reality,' he says. 'We chose but never proved a world view which we have continued to hold ever since. There are other methods to infer what is real or not other than our current one – we've simply forgotten'. This, he believes, has created a mindset that over-relies upon double-blind placebo studies to the exclusion of other types of research. The view has been echoed by some mainstream scientists, such as Smith and Pell in 2003, who wrote a wry article in the *BMJ* pointing out that the efficacy of parachutes has never been proven using double-blind placebo studies.

With insurers and governments tightening their purse strings, there is increasing pressure on medical practitioners to produce effective and replicable results. However, due to its highly individualized treatments, anthroposophical medicine does not easily lend itself to double-blind placebo studies. Even when such studies are possible on a specific aspect of treatment, clear-cut answers do not always follow. For instance, despite many studies on the effectiveness of mistletoe in cancer, the National Cancer Institute reports that results in humans remain uncertain.

In the scramble to gain mainstream acceptance, proponents of anthroposophical medicine, such as Helmut Kiene, have created a new methodology – cognition-based medicine. This places more emphasis on case studies, cross-over designs and cohort studies, and includes physician judgment and intuition as a variable rather than considering it as a confounder. Whether this will satisfy the critics remains to be seen.

Schöb is realistic about the immediate future, saying, 'It will definitely become more difficult for anthroposophical medicine practitioners. However, as this pressure increases it will cause a backlash – people intuitively know this treatment works and they want it. They understand that if we continue on our current path, there is a real danger that we will lose the very essence of medicine.'

Music therapy at the Ita Wegman Clinic

Further Reading

Kiene H: Komplementäre Methodenlehre der klinischen Forschung. Cognition-Based Medicine. Berlin, Springer, 2001.

Smith GCS, Pell JP: Hazardous journey: parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials. BMJ 2003;327:1459–1461.

Paul Lavender is an editor of the Karger Gazette

A NEW WAY OF LIVING

MAXIMILIAN BIRCHER-BENNER
(1867–1939)

At the dawn of the 20th century, Maximilian Bircher-Benner opened a sanatorium in Zürich to heal the sick through healthy eating. His ideas would influence nutrition for decades and give rise to an icon of Switzerland – muesli.

E. WOLFF

Maximilian Bircher-Benner counts among the best-known and most influential Swiss physicians of the 20th century. But how did he influence medicine? Discovering a disease? Inventing a new and effective therapy? No, his influence was quite different. His most visible impact was beyond medicine: it was on menu cards, shop shelves and breakfast buffets all over the world, where his Bircher-müesli, müesli, müsli, muesli, museli (or however it is differently spelled around the globe) changed dietary habits of millions and millions. Next to cheese and mountains, muesli (which means 'little mush') counts among the best-known things attributed to Switzerland.

Today, a 'muesli' is commonly understood to be a mixture of basic ingredients like cereals, milk or yoghurt and some fruit – dried or fresh. It is typical modern food. It is convenient, for a quick breakfast or snack, made from ready-made cereal mixtures bought in the supermarket. It is also a very modern dish since it can be made for individual interests and tastes: for sportspeople, for children, for organic food devotees or gourmets. Muesli remains popular today largely because it tastes like a healthy option.

Bircher-Benner was neither a chef nor a marketing consultant for a food manufacturer. In the beginning, muesli was quite different – its recipe, its image, its purpose, its consumers, and even its name. Bircher-Benner named his creation *Apfeldiätspeise* (apple dietary dish). Its most crucial ingredients were Bircher-Benner's dietary ideas.

At the end of the 19th century he studied medicine at the University of Zürich. After the first years of his medical practice, Bircher-Benner converted to naturopathy and temperance and focused more and more on the importance of nutrition for a healthy life. However, he was definitely not a pioneer in this respect. It was a time when naturopathic ideas were gaining popularity, in parallel with and as a reaction to developments in such fields as bacteriology, surgery and laboratory research. Vegetarianism was the antithesis of the prevailing Justus von Liebig theory of protein (which practically meant: meat) as being crucial for healthy nutrition. Bircher-Benner radicalized vegetarian ideas to the propagation of uncooked food: the more both healthy and ill people would eat raw food the more their state of health would be stabilized. He was not the first to do this but he became the most famous of what in German is called a *Rohkostapostel* (an apostle of raw food) – with all the ironic undertones of this term.

> Patients were trained to conduct a strict regime, constantly practicing self-control

Fresh Thinking

Raw food is not everybody's favourite. Bircher-Benner's aim was to create a raw dish that both contained the most important foods and was attractive to eat – even for the toothless. So muesli's most important ingredient was absolutely fresh grated apple. In the 1940s, when muesli had developed to be a Swiss national dish, one of Bircher-Benner's sons, Ralph, complained about restaurants still serving in the evening muesli that had been made in the morning.

The grated apple had to be mixed with some oat flakes and sweetened condensed milk, a very popular Swiss diary product of that time and still available today. Finally, lemon juice and chopped nuts were added. The original muesli would not have won a food beauty contest, but even to a sceptical muesli-eater the taste would have been respectable.

Today, a typical dietician would argue for the health value of the original muesli on the grounds of its vitamins, low calories and cholesterol and high fiber content. Not so Bircher-Benner. Among his arguments one was prominent: in his eyes, raw food contained a high level of energy taken from solar light. This energy was lost by cooking or having been digested by animals. This is why, for Bircher-Benner, meat was of especially minor value: in his eyes it had lost its energy twice – once when the animal digested the plant and once when the animal's meat was being cooked.

When Bircher-Benner presented his ideas to his non-sectarian Zürich colleagues, he more or less lost his reputation as a serious academic. It was not until the late 1920s and 1930s that he achieved broad popularity and became an authority in nutrition and healthy living in unconventional medicine circles of the time.

For Bircher-Benner, muesli was not a convenient breakfast dish or something swallowed for a hurried lunch between appointments. It was part of a strictly fixed health regime and a structured daily schedule. Muesli was meant to be served as a starter for every menu. Breakfast, lunch and dinner were part of a tight timetable of healthy living. According to Bircher-Benner's regime, which was called *Ordnungstherapie* (order therapy), one had to get up at 6 am and take a stroll before breakfast. One should stay out in fresh air working or strolling as much as possible during the day and avoid indulgences like coffee, alcohol or tobacco. At 9 pm one should go to bed and turn down the light at 9.30 – at the latest.

A regime like that had to be exercised and internalized. For this purpose Bircher-Benner founded a sanatorium in which the patients were under supervision more or less the whole day. In 1904 he moved his facility to a new building on the famous Zürichberg, on a paradise-like piece of land with a marvellous view over Lake Zürich to the Swiss Alps. Soon patients flooded his Sanatorium Lebendige Kraft (Vital Force Sanatorium), hoping to get rid of their neurasthenia, obesity, constipation or depression.

The Lebendige Kraft became one of the most renowned places for healthy living in early 20th century Europe, and a growing number of celebrities and wealthy people stayed there. Guests included art celebrities like Yehudi Menuhin and politicians like Sir Stafford Cripps, Habib Bourgiba and Golda Meir. Thomas Mann, German literate and later Nobel Prize laureate, took his cure at the sanatorium in 1909 and in a letter he named it a *'Hygienisches Zuchthaus'* (which could be translated as 'health jail'). However, patients subjected themselves to the therapy regime completely voluntarily.

Bircher-Benner's sanatorium did not stand alone, it was a part of an early multimedia popular health movement. This consisted of an idea, a simple message (raw food) that could be identified with a popular person (Bircher-Benner) and a symbolic practice (eating muesli). It had a concrete center (the sanatorium) and was publicized through various media: a popular monthly journal *(Der Wendepunkt)*, brochures that sold over 100,000 copies, self-help books and exhibits. Health campaigns in later decades – Jane Fonda's workout, for example – were in principle based on a similar concept.

Years before the rise of the Lebendige Kraft in Zürich, in the United States a sanatorium with a similar reputation could be found. The American Seventh-Day Adventist physician John Harvey Kellogg (1852–1943) had much in common with Bircher-Benner – except the idea of raw food, as can be seen by the cornflakes developed by him and his brother. Kellogg's sanatorium in Battle Creek, Michigan, was also meant to internalize what its founder saw as a healthy life: vegetarian diet, asceticism, exercise – and enemas to clean the bowels. T.C. Boyle immortalized Kellogg's ascetic sanatorium in his novel *The Road to Wellville*.

An apple a day: Workers at Bircher-Benner's sanatorium prepare original-recipe muesli, which was mainly mushed apple.

Original muesli recipe

- 1 tbsp. of rolled oats, left to soak in 3 tbsp. of cold water for 12 hours
- 1 tbsp. of sweetened condensed milk
- 1 tbsp. of lemon juice
- 1 large or 2 small apples, freshly grated with the skin
- 1 tbsp. of ground hazelnuts or almonds

Article continues on next page

What the Lebendige Kraft and Kellogg's sanatorium have in common is that they both were places where patients were trained to conduct a strict regime, constantly practicing self-control and focusing on the health of their body and mind. This phenomenon is still seen in today's wellness practices, where it is commonly described as 'healthism'. As today, Bircher-Benner's numerous patients were practicing healthism without any compulsion from outside but nevertheless influenced by the presence of a higher authority, personified in Dr. Senior, as Bircher-Benner was called inside the Lebendige Kraft. The French sociologist and philosopher Michel Foucault described this phenomenon as 'governmentality', and saw it as a crucial factor in making modern societies work.

Medicine in the Media Age

To conclude: in which way did the Swiss physician Maximilian Bircher-Benner have an influence on medicine? It was not his somehow weird theory of nutritional energy from solar light, which had never been broadly accepted. Even if he promoted an ideal dietary plan that has some similarities to the ones of today, there is no direct line between the two, since he promoted raw food for partly different reasons. His nutritional eponym in the German-speaking world – Birchermüesli – is less and less known, while muesli's recipe and image have substantially moved away from the original form. However, Bircher-Benner, like John Harvey Kellogg and others, had a remarkable influence on medicine in a broader sense. His ideas of *Ordnungstherapie*, with its strict health regime, his internationally renowned sanatorium to practice this regime and a multifaced set of mass media to promote it established an early and well-known platform of modern popular health practices, for better or for worse. Remember this the next time you bite into an apple instead of a steak.

This article is based on research funded by the Swiss National Science Foundation.

Further Reading

Melzer J, Melchart D, Saller R: „Entwicklung der Ordnungstherapie durch Bircher-Benner in der Naturheilkunde im 20. Jahrhundert". Forschende Komplementärmedizin und Klassische Naturheilkunde 2004;11:293–303.

Meyer-Renschhausen E, Wirz A: Dietetics, health reform and social order. Vegetarianism as a moral physiology: the example of Maximilian Bircher-Benner (1867–1939). Medical History 1999;43:323–341.

Wirz A: Die Moral auf dem Teller dargestellt an Leben und Werk von Max Bircher-Benner und John Harvey Kellog. Zürich, Chronos, 1993.

Wolff E (ed): Lebendige Kraft. Max Bircher-Benner und sein Sanatorium im historischen Kontext. Baden, hier + jetzt, 2010.

Wolff E: Moderne Diätetik als präventive Selbsttechnologie: Zum Verhältnis von heteronomer und autonomer Selbstdisziplinierung zwischen Lebensreformbewegung und heutigem Gesundheitsboom; in Lengwiler E, Madarasz J (eds): Das präventive Selbst. Eine Kulturgeschichte moderner Gesundheitspolitik. Bielefeld, Transcript, 2010, pp 169–201.

Eberhard Wolff
University of Zürich

Dr Wolff is a medical historian and cultural anthropologist at the universities of Zürich and Basel.

The

Up to the 1870s operative surgery hardly existed and was, in most places, a dirty and brutal business. Infections were rife and septic bleeding common. But in Bern a Swiss surgeon was developing a careful, precise technique that would revolutionize operations forever.

U. TRÖHLER

In 1909, the eminent Swiss surgeon Theodor Kocher delivered his lecture as that year's Nobel laureate in Medicine or Physiology. In his oration, he discussed the rapid progress made in previous years, saying: 'In the great majority of so-called internal diseases a surgical treatment crowned with the most splendid curative successes has been made possible. Within less than half a century, it has become possible to expose all organs of the body – brain and heart not excluded – without danger, and to carry out the necessary surgical interventions on them.'

> Kocher aimed not just to remove diseased parts, but to preserve and restore function

Indeed, when Kocher had made his career choice in the middle of the 19th century, surgery was undergoing a radical and exciting period of change. In 1846 and 1847 inhalation anesthesia with ether and chloroform, respectively, had started their triumphal march around the world. A decade later, Rudolf Virchow proposed the doctrine of the cellular origin of diseases, providing the theoretical basis for interventions in all bodily cavities, and in 1867 Joseph Lister first published on his antiseptic techniques. Surgery was developing from a craft into a science and would, in the following decades, become one of the most active and successful fields of medicine (lacking such tools as hormones, antibiotics and vitamins, internal medical treatments of the time were restricted to diet, bed rest and herbal remedies).

Early Years

Theodor Kocher, the second of six children of an engineer father and a deeply religious mother, was born in Bern on August 25, 1841. He studied medicine in Bern and Zürich, where he was also taught by the surgeon Theodor Billroth. After his university studies, Kocher broadened his horizons by visiting leading surgical clinics throughout Europe. He visited Berlin and London, and – being fluent in German, French and English – was able to meet with such important figures as Rudolph Virchow, the pathologist, and Thomas Spencer Wells. The latter he had witnessed performing Switzerland's first ovarectomy (oophorectomy) in Zürich. Kocher ended his tour in Paris where he was not impressed by the dirty surgery he saw.

Upon his return to his hometown, he became resident in the department of surgery at the University of Bern. In 1872, at just 31 years of age, he was appointed Chair of Surgery. Deeply rooted in his native Bern, in later life he would turn down opportunities of chairmanships in major cities of German-speaking Europe, including Prague, Vienna and Berlin.

Kocher's meticulous nature and zeal for perfectionism were perfectly suited to the challenge of improving surgery. For one, despite the basic advances mentioned, hospital infections and septic bleeding were still commonplace. Unlike most surgeons of the time, who saw speed as a sign of operative finesse, Kocher developed a slow, methodical technique where precision was key. He saw painstaking hemostasis as of critical importance. Kocher rejected the then common technique of mass ligation of the arteries and developed 'Kocher clamps' for use as hemostats. From the mid-1880s, based on animal experiments by the Bern physiologist Hugo Kronecker, Kocher combated 'shock' during surgery by administering warm 'physiological' saline intravenously. These are just two points of Kocher's system of 'safe' surgery, described in five increasingly voluminous German editions of a textbook on surgical operations (1892–1907), which was eventually translated into six languages.

Kocher's surgery, like that of most of his contemporaries, was initially based on pathological anatomy and aimed to simply remove diseased tissue. However, in his later period, he began to foster 'physiological' surgery, aiming not just to remove the diseased parts but, when doing so, attempting to preserve or to restore bodily functions.

In these buoying decades Kocher was able to contribute significantly to domains which have long since become specialties (see table). In addition to his work in general surgery, he also made advances in asepsis, anesthesia, endocrinology, neurology and neurosurgery. He invented instruments, a high-pressure sterilization device, a mask for inhalation anesthesia, and, above all, many specific operative procedures that are still called by today's surgeons by his name.

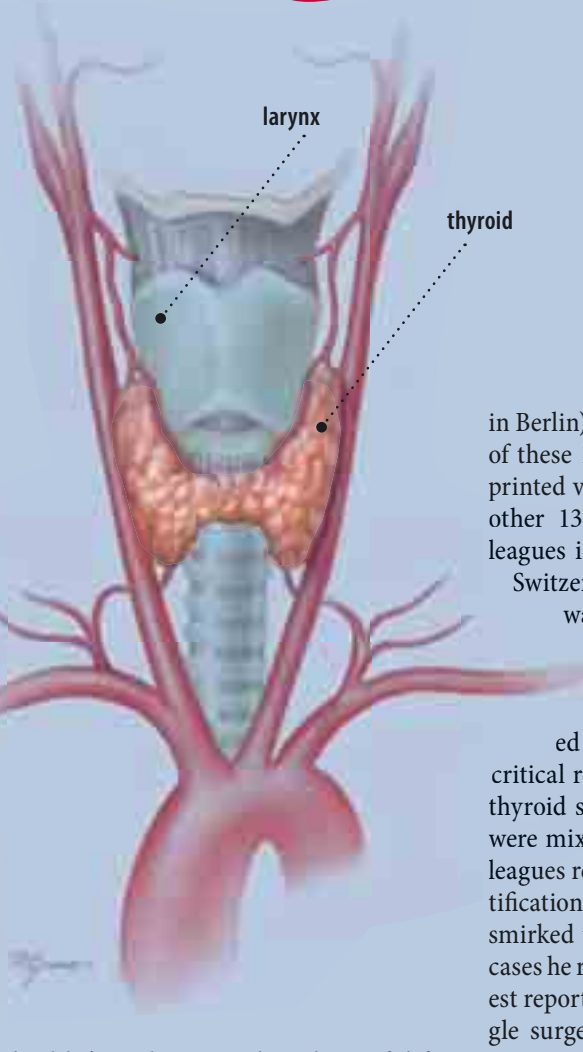
Kocher's innovations and masterly technique turned his clinic in Bern into a world-renowned center of excellence. In themselves his advances in surgical methods would have been enough to earn him name recognition from every student of surgery the world over, but Kocher will forever primarily be linked with his insights into a critical gland that, during his time, was so enigmatic that physiologists generally thought it had no function at all – the thyroid.

The Thyroid

From the 1830s onwards, surgeons and physiologists in many countries removed the thyroid gland from various species of animal to see what happened. The results were ambiguous: since neither antisepsis nor the existence of the parathyroid glands were known, it was not possible to know

THEODOR KOCHER
(1841–1917)

Subtle Knife



whether the post-operative observations reflected infection or an organic failure.

As physiologists had been unable to determine a function for the thyroid, surgeons of the time assumed it had none, and so some removed the gland in its entirety.

Thyroidectomy was an important intervention for Kocher working in Bern, for there was a particularly high incidence of endemic goiter (a swelling of the thyroid gland caused by iodine deficiency). After performing his first thyroidectomy in 1872, Kocher would perform the surgery over 7,000 times in his career. Increasingly he followed the prevailing wisdom of the time and completely ablated the gland, until he made an unexpected and personally terrifying discovery which would change this opinion forever.

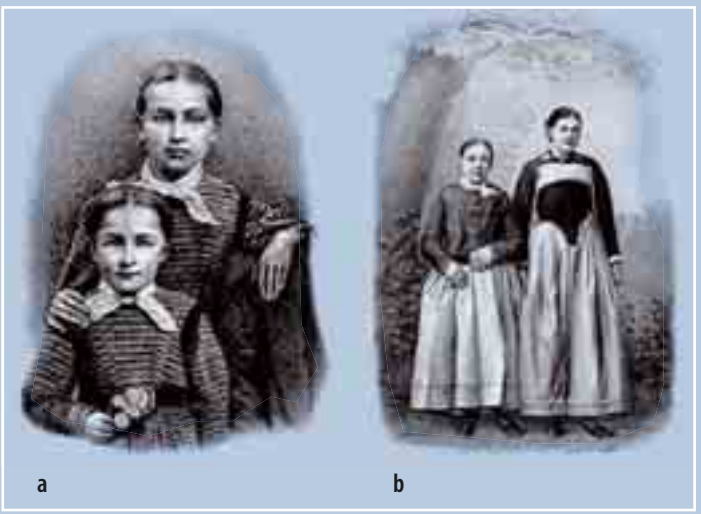
In 1874 Kocher had performed a complete thyroidectomy on a young girl. When he saw her again, early in 1883, he realized that she had undergone a 'complete and substantial change' and become cretinoid (a condition of severe stunting of physical and mental development). In 1883, during a lecture to the German Society of Surgery in Berlin, Kocher explained – using the unsentimental language of the time – the difference between this girl and her younger sister, with whom she had previously often been confused: 'Whilst the younger sister has now grown up to a blossoming young woman of very pretty looks, the sister operated on has remained small and exhibits the ugly looks of a semi-idiot.'

After this discovery, Kocher immediately wrote to 77 of the 102 goiter patients he had operated on since 1872. Not all answered or came to see him, but he was able to notice a difference between 28 patients in whom he had carried out a partial removal of the gland, and the 24 in whom the gland had been completely ablated. While the partial removal group were in good health 'very happy with and grateful for the success of the operation,' only two of the complete removal group showed an improvement.

In the girl who first caused Kocher alarm, he noted slow physical and mental decay following the total removal of the gland, puffiness of the face, hands and body, decreased growth in height and noticeable pallor caused by anemia. He designated the concurrence of these and other physical signs as a new disease specific to the removal of the gland. He concluded that its relation to 'idiotism and cretinism' was unmistakable, and so named the condition 'cachexia strumipriva' (decay resulting from the lack of goiter).

In his lecture to the German Society of Surgery, Kocher speculated at length about the possible functions of the thyroid (his discussion ran to 15 pages in the printed version of his speech). In conclusion he said that the thyroid's task was 'to paralyse the influences which produce stupidity.' In support of his hypothesis he used examples from the complete list of all 102 cases on whom he had operated between May 1872 (when he had taken over as head of the Bern surgical clinic) and March 29, 1883 (five days before his lecture in Berlin). A list summarizing the features of these 102 patients was included in the printed version of his lecture, as were another 134 cases collected from 15 colleagues in German and French-speaking Switzerland and southern Germany. It was an early example of a complete surgical audit, which included frank reporting of mishaps.

Although Kocher had initiated this masterly lecture with a long, critical review of operative techniques in thyroid surgery, the reactions to his talk were mixed. While one or two of his colleagues realized its main point – the identification of a new disease entity – others smirked that the large number of thyroid cases he reported (his was by then the largest reported series operated on by any single surgeon) reflected solely his lust for operating, and so dismissed his ideas. Most participants at the congress were unreceptive to the new information, thinking that Kocher's cachexia strumipriva was nothing really new. For them, the early stages of cretinism were characterized by an increase of thyroid volume. So-called cachexia strumipriva, they believed, was simply a late stage of cretinism which had developed despite the removal of the thyroid. Such a view meant that there was no

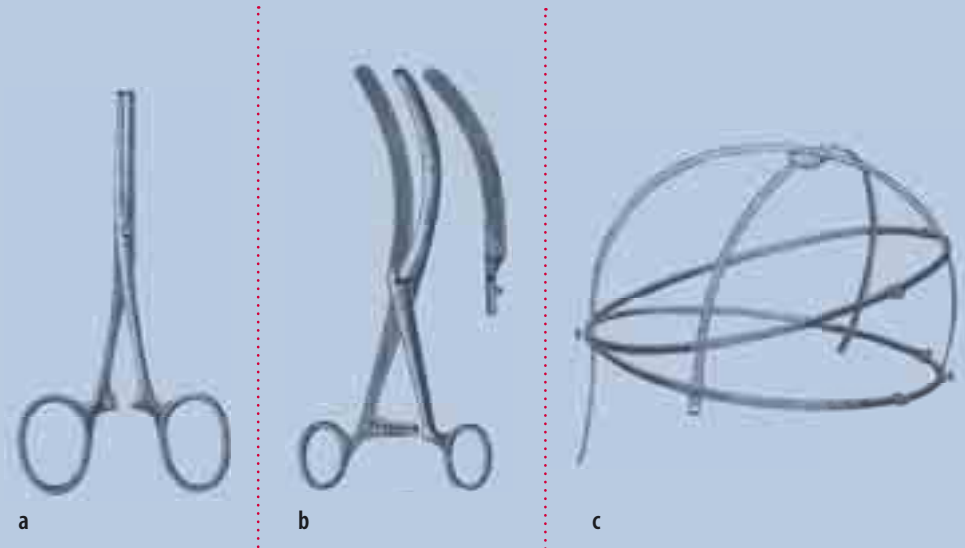


Terrifying discovery: In 1883 Kocher realized that complete thyroidectomy could cause cretinism. In lectures he used this photo of two sisters, previously alike, to illustrate the 'complete and substantial change' after surgery on the older sister (on the right in **a** and left in **b**).

Kocher's innovations impacted on many fields of surgery

Trauma	Introduced 'reduction technique' for shoulder dislocation, based on an exact anatomical and functional study of the shoulder joint.
Surgical instruments	Developed numerous surgical instruments. In addition to his clamp for stopping minor bleeding, he also devised a craniometer, artery and bowel clamps, probes, kidney-holding forceps, scissors, chisels and files. Yet many contemporary surgeons attached their names to their own similar 'inventions'.
Anesthesia	As did other surgeons, Kocher devised sequential chloroform-ether narcosis and designed better masks for delivery of the gases. He introduced pre-operative preparation of patients who were to receive anesthesia to avoid aspiration of gastric content.
Goiter	Described effects of total and partial thyroidectomy. Was able to 'measure' and explain increased, decreased and normal functioning of the thyroid.
Methodology	Prioritized hygiene, counseled against washing hands in stagnant water. Investigated effects of various techniques for sterilization. Kept meticulous surgical records that quantified success and failure.

Further discussion of many of the above innovations can be found in Ake André-Sandberg and Gaby Mai's 2001 article for *Digestive Surgery*, 'Theodor Kocher (1841–1917) – A Surgical Maestro' (vol. 18, pp 311–316).
It is available at www.karger.com/dsu.



a b c

Instruments of a maestro: Surgical tools designed by Kocher.
a The Kocher clamp, an arterial forceps with serrated blades and interlocking teeth at the tips for controlling bleeding or holding tissues. **b** Bowel clamp. **c** Craniometer. Illustrations reproduced from a catalog from M. Schaerer AG in Bern (1907), which produced the instruments according to Kocher's drawings

specific function of the gland that would have been abolished once the gland had been removed.

Kocher insisted that the thyroid had specific functions, and tried – in vain – to isolate the 'active principle' using chemical techniques. However, he did not at this time conceptualize the gland as having a remote function, instead explaining it mechanistically by its local action.

So convinced was Kocher that the thyroid had important functions, that from 1883 onwards he began implanting human thyroid tissue in thyroidectomy patients in an attempt to replace the loss of the postulated functions. In so doing, he became the pioneer of organ transplantation.

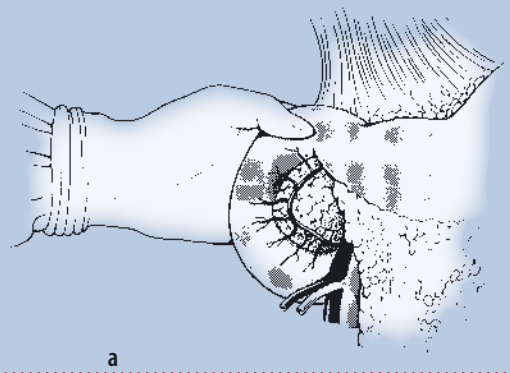
Kocher continued to refine his operating technique on the thyroid (and on thyroid transplantation) throughout his life and eventually achieved a complication and mortality rate for thyroidectomy of just 0.5%, which was astonishingly low at the time – and still is today.

Kocher went too far with one of his claims during his Berlin lecture, however. He claimed that 'for the first time – as far as is known to us – a relation of dependence between the thyroid gland and cretinism has been demonstrated with certainty'. This was an overstatement. Well known clinical and anatomical observations – not least in cretins – had led to such thoughts during previous decades, particularly in Great Britain, yet proof had been lacking.

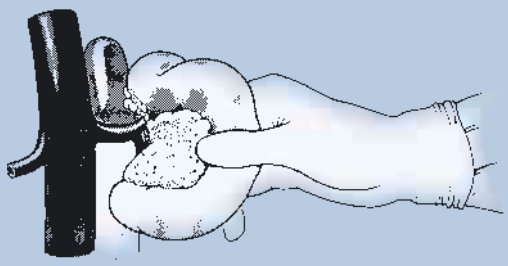
> 'Surgery was developing from craft to science, and would soon be the most successful branch of medicine'

Kocher also failed to acknowledge his contemporary and colleague in Geneva, Jaques-Louis Reverdin. Aware of the British literature, Reverdin had coined the term 'myxoedeme opératoire' in one of a series of articles in the *Revue Médicale de la Suisse Romande*, beginning 11 days after Kocher's lecture in Berlin. The context of the publication of Kocher's and Reverdin's findings led to a priority contest between the two Swiss surgeons.

Both Reverdin and Kocher contributed to the discovery that lack of thyroid gland causes severe physical and mental damage, and in so doing laid the basis for what we now call endocrinology. That said, Kocher's prompt and detailed description of his investigation of a possible adverse effect of his therapeutic intervention is a real milestone. The paper is a classic example both of surgical audit and of the investigation of unanticipated effects of a treatment which had been deemed to be safe.



a



b

Kocher's maneuver: The term 'Kocher's maneuver' is used in surgery today to describe how the head of the pancreas may be mobilized and assessed during an operation. Kocher discovered that there is a layer between the back of the duodenum and pancreatic head and the retroperitoneum which contains no important blood vessels. After separating the peritoneum along the duodenum's lateral edges, it is possible to dissect forward to the aorta and feel and inspect the pancreas head.
a Palpation of the pancreas head back side during dissection using the maneuver.
b The head of the pancreas fully mobilized after the maneuver, uncovering the vena cava inferior and the left kidney vein, and freeing the aorta's right side.

Reproduced from Aké Andrén-Sandberg and Gaby Mai's 2001 article for *Digestive Surgery*, 'Theodor Kocher (1841–1917) – A Surgical Maestro' (vol. 18, pp 311–316). Available at www.karger.com/dsu

Recognition and Influence

Kocher's painstaking surgical technique impressed his peers and, during his lifetime, he was regarded as one of the world's foremost surgeons. In 1909 he received the imprimatur of professional excellence when he was given the Nobel Prize in Physiology or Medicine, the first surgeon to ever receive the award. The Nobel committee bestowed the award on him for his work on the 'physiology, pathology and surgery of the thyroid gland'.

By the dawn of the 20th century, Kocher was known also in the United States and the UK as an innovative surgeon. His clinic's reputation attracted visits from such personalities as William Halsted, young Harvey Cushing, George Crile and Lord Berkeley Moynihan.

Today, Kocher's memory endures through some surgical innovations that still bear his name, such as the Kocher clamp and the Kocher maneuver. In addition, he is more publicly recognized in his hometown of Bern, where he survives visibly in two busts, and a street as well as park are named after him.

In 1967, fifty years after his death, the Swiss post office issued a commemorative stamp from which Kocher gazes out with the stern but intelligent eyes of a great surgical innovator.

The Man

Kocher was a great surgeon, entirely and exclusively devoted to his work and his patients. He was a serious man of great composure and an exacting, unemotional nature. He held that, 'life has taught me that if one man dies from overexertion, 999 perish from doing nothing.' This was – in a good sense, not a tyrannical one – a feature of his relations with his collaborators.

He was probably more admired and respected than loved, but this was anyhow no question. He asserted priority for his advances and the superiority of his methods up to the end of his life.

The *British Medical Journal* wrote in 1911: 'While not slow to recognize the many surgical workers in all lands [Kocher] does not hesitate to claim for himself, in the sure knowledge of his own experience and attainments, the right to express his own opinions with no uncertain voice.' [BMJ 1911, ii, 1477]. This is understandable in a man whose sole interest was surgery.

Though professionally pretentious, he was personally unassuming – his fees were considered modest by a patient from the highest ranks of the aristocracy. This had to do, perhaps, with his religious beliefs. He and his wife belonged to the pietist association of the Moravian Brothers. His religion helped him to relativize his successes and to overcome the inevitable mishaps, which affected him very deeply. It was also the motivation for him to donate the Nobel Prize money for a research institute, the future Theodor Kocher Institute of Bern University, which carries forward his spirit of research to this day (see box).

Further Reading

Boschung U (ed): Theodor Kocher 1841–1917. Bern, Huber, 1991.

Kocher T: Ueber Kropfexstirpation und ihre Folgen. Archiv für Klinische Chirurgie 1883a;29:254–337.

Kocher T: Contribution to the discussion on "Exstirpation des Kropfes", Verhandlungen der Deutschen Gesellschaft für Chirurgie 1883b;12:37–38.

Kocher T: Über Krankheitserscheinungen bei Schilddrüsenerkrankungen geringen Grades; in Les Prix Nobel en 1909. Stockholm, pp 1-59.

Reverdin J-L: Note sur vingt-deux opérations de goitre, avec 3 pl. photographiques. Revue Médicale de la Suisse Romande 1883;3: 169–198, 233–278, 309–364.

Tröhler U: Der Nobelpreisträger Theodor Kocher. Basel, Birkhäuser, 1984.

Tröhler U: Kocher, Emil Theodor; in Bynum WF, Bynum H: Dictionary of Medical Biography. London, Greenwood, 2007, vol 3, pp 746–747.

Tröhler U: Towards endocrinology: Theodor Kocher's 1883 account of the unexpected effects of total ablation of the thyroid. The James Lind Library, 2010. Available at: www.jameslindlibrary.org

An extended reading list is available online at www.karger.com/gazette

Ulrich Tröhler
University of Bern

Prof Tröhler was founding president of the European Association for the History of Medicine and Health. He has written extensively on the history of regulation of animal and human experimentation, surgery and obstetrics. He is co-editor of the James Lind Library (www.jameslindlibrary.org).

Theodor Kocher Institute

A Noble Prizewinner

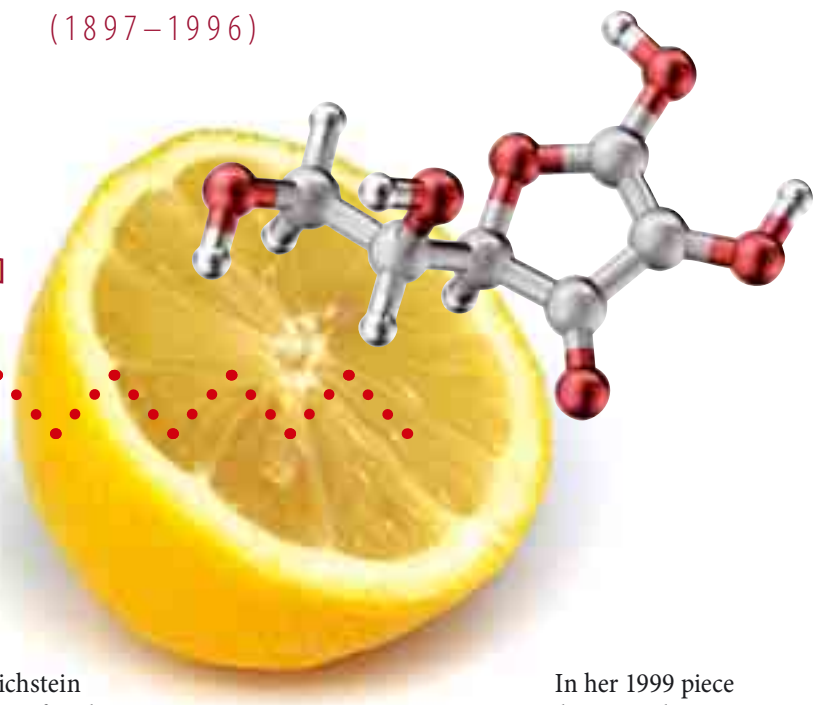
Kocher's greatest legacy will always be the countless lives that would have been lost or blighted on the operating table were it not for his methods. But he did not just leave the world novel surgical techniques and tools, he also enshrined in bricks and mortar his pioneering spirit. Using the money he received from his Nobel Prize, Kocher provided an endowment to finance and build a research institute at the University of Bern that still bears his name.

Today, the Theodor Kocher Institute focuses on immunity and inflammation, as well as vascular biology and the blood-brain barrier. It boasts advanced live cell imaging equipment, including in vitro time lapse videomicroscopy and two-photon microscopy, and forms part of the university's Microscopy Imaging Center. The institute is also a significant teaching facility for students of medicine and the life sciences.

For more information on the Theodor Kocher Institute go to www.tki.unibe.ch

TADEUS REICHSTEIN
(1897–1996)

The Fruits of Labor



The industrial production of vitamin C was a crucial step in the fight against malnutrition. But it was only possible because of the demise of a humble fruit fly.

D. PATERSON

In 1934 a preparation of vitamin C called Redoxon was launched onto the market by Hoffmann-La Roche, a Swiss pharmaceutical company. Redoxon was ground breaking for being the first industrially synthesized vitamin C to be sold to the public. Its production was based on a revolutionary process developed by Tadeus Reichstein, a Polish-born chemist working at the Swiss Federal Institute of Technology in Zürich.

Vitamin C – also known as ascorbic acid – is an essential nutrient, being an antioxidant and also critical to the production of collagen, the main protein in connective tissues. Most animals and plants are able to synthesize vitamin C from glucose but, in a curious evolutionary twist, humans lost one of the enzymes necessary for this process and so must obtain the vitamin from their diet. The shortcomings of this evolutionary strategy only really became apparent when humans set out on long sea voyages with no access to fresh foods, and found that they rather frequently died of scurvy.

> ‘In an evolutionary twist, humans lost one of the enzymes needed to produce vitamin C’

Although the curative effects of fresh fruits and vegetables were known as early as the 16th century, it was not until 1932 that the ‘antiscorbutic factor’ now called vitamin C was isolated and linked to scurvy in laboratories headed by Albert Szent-Györgyi and Charles Glen King.

Once news of the discovery broke, a number of research groups began looking at ways to synthesize vitamin C on a large scale. Among those interested was Tadeus Reichstein. The tricky step in making vitamin C from glucose was converting sorbitol, a reduction product of glucose, to L-sorbose, a sugar. Reichstein knew that so-called sorbose bacteria could carry out this transformation, but he could not get his hands on a culture that carried out the process efficiently. Drawing inspiration from a 19th century publication by Gabriel Bertrand, a French chemist, Reichstein set out to catch some wild bacteria using half-a-dozen glasses filled with an acidic mixture containing red wine, vinegar, yeast and sorbitol. After leaving these glasses outside for a few days, Reichstein returned to discover a *Drosophila* fly had drowned in this unpleasant brew. From one of its legs, long sorbose crystals were growing. Reichstein was able to isolate the *Drosophila*-borne bacteria and put them to work making sorbose. Soon after, his team had the remaining steps worked out and the first industrial process for creating vitamin C was born.

Although Reichstein received the patent for the production process – which still bears his name – his work was not recognized as widely as it could have been. In 1937, the Nobel committee awarded the Prize in Chemistry to Walter Haworth, a British competitor of Reichstein, partly in recognition of his work on vitamin C. Haworth’s team in Birmingham had been the first to make crystals of the levo form of ascorbic acid (the isomer that is found in nature) through a painstaking 11-step process. However, Reichstein’s method was more suitable for industrial production.

Photo: Gotthard Schuh © Fotostiftung Schweiz

In her 1999 piece on Reichstein in the *Biographical Memoirs of Fellows of the Royal Society*, Miriam Rothschild, a British entomologist and personal friend of Reichstein, was astonished that he did not receive greater recognition. She wrote: ‘Many people were surprised at the fact that Tadeus did not receive the Nobel Prize for the synthesis of vitamin C, or at least shared the honor with Szent-Györgyi and perhaps Oppenauer [one of Reichstein’s PhD students]. It was recognized that the work had laid the foundation stone for the modern bridge spanning organic chemistry and medicine.’

However, Reichstein was to receive recognition from the Nobel committee when, in 1950, it awarded him – together with Edward Kendall and Philip Hench – the Prize in Physiology or Medicine for his later work on the structure and functions of adrenal cortex hormones, chiefly the isolation of cortisone.

Further Reading

Rothschild M: Tadeus Reichstein. 20 July 1987–1 August 1996: Elected For.Mem.R.S. 1952. Biogr Mems Fell R Soc 1999;45:449–467.

Nobel Lectures, Physiology or Medicine 1942–1962. Amsterdam, Elsevier, 1964.

David Paterson is an editor of the Karger Gazette

Testing the Acid

ALBERT HOFMANN

(1906–2008)

D. PATERSON

In northwestern Switzerland, where the river Rhine turns right to begin the important business of separating France from Germany, sits the city of Basel. The peaked roofs and church spires of its old town center are an unlikely backdrop for the birth of one of the most controversial drugs of the 20th century, but just beyond the medieval cathedral and city hall stand the chimneys and office blocks of the city's globally important pharmaceutical industry. It was in a one of these buildings in 1938 that the chemist Albert Hofmann first synthesized a compound called lysergic acid diethylamide, a compound that would come to be known as LSD.

In the 1930s Hofmann was working for the pharmaceutical division of Sandoz (now part of Novartis), which was investigating the ingredients of traditional remedies to isolate and synthesize their active components. Hofmann was looking at the fungus ergot of rye *(Claviceps purpurea)*, which had been used to induce childbirth since the 16th century. Ergot's alkaloids, which were based around a lysergic acid core, were known to have physiological activity, so Hofmann began synthesizing lysergic acid derivatives. In 1938 he synthesized his 25th lysergic acid amine – in German called *Lysergsäure-diäthylamid-25*, or LSD-25. From its structure Hofmann thought it might have activity as a circulatory respiratory stimulant, but Sandoz's pharmacologists found nothing remarkable and so LSD-25 was quietly filed away.

But it was not forgotten. Hofmann had what he termed a 'peculiar presentiment' and, in 1943, on a hunch that LSD-25 could have secrets it did not yield on first inspection, he decided to take another look.

Bicycle Day

Hofmann returned to LSD-25 in the hope of finding some physiological property that could hint at a medicinal use for the drug. What he found was one of the most powerful psychoactive drugs ever created by man – and he found out firsthand. During his second synthesis of LSD-25, a small amount of it somehow came into contact with his skin, and Albert Hofmann became the first person in history to go on an acid trip. He quickly entered a dreamlike state, which he described as 'an uninterrupted stream of fantastic pictures, extraordinary shapes with intense, kaleidoscopic play of colors.'

After he had recovered his senses, Hofmann realized that LSD-25 had strange and powerful properties. Fascinated by his experience, three days later he began what he thought would be a controlled LSD experiment on himself. Unaware of the drug's extreme potency, Hofmann swallowed 0.25 mg of LSD, a huge overdose by today's standards, and sat down to record his experiences in his laboratory journal. This attempt at scientific rigor was wildly optimistic: Hofmann wrote only a few words before being overwhelmed by the effects of the drug. He became anxious, started experiencing paralysis and began seeing things. Hofmann's presumably alarmed lab assistant then had the unenviable task of getting his delirious boss home on a bicycle (wartime petrol rationing precluding the use of infinitely more practical forms of motorized transport).

> Hofmann never thought LSD would find popularity as a party drug

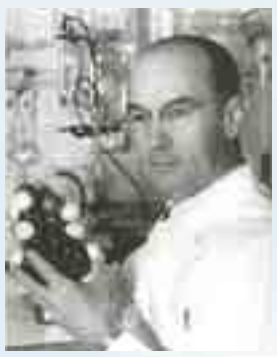
Once home, the turmoil in Hofmann's head intensified, and he experienced a succession of delusions that ranged from acute irrational fears to rather pleasant tableaus of colorful images. Remarkably, a doctor could find nothing physically amiss, except Hofmann's by then extremely dilated pupils. Even more incredibly, when Hofmann awoke the next morning, he felt fine and could remember everything.

Psychedelic Dream

Sandoz quickly realized that such a drug could have therapeutic potential in psychiatry and soon made LSD available to clinical researchers. From today's standpoint, in a world where governments speak of LSD in the same breath as heroin, it seems remarkable that it was first greeted by the mental health community as a potential therapy or useful research tool. Psychiatrists saw in it the potential to bring about a 'model psychosis' in healthy patients that could be used to study schizophrenia, while psychoanalysts became interested in its apparent ability to give insights into a person's unconscious.

Ergot on rye. © Novartis Company Archives

During the 1950s several hundred research articles on LSD appeared in the medical literature, most of them positive and reporting few ill effects. Some research groups even saw startlingly strong results in using LSD to treat alcoholism.



However, this period in the sun would not last long. Lacking today's strict controls on clinical trials, LSD soon found its way out of the research setting and into recreational use, first among artists and intellectuals – notably *Brave New World* author Aldous Huxley, a personal friend of Hofmann – and then on university campuses. By the 1960s a thriving black market in LSD had sprung up and newspapers began running lurid stories of mayhem wrought during uncontrolled LSD binges. By the middle of the decade Sandoz had ended production of the drug and, in 1966, the death-knell for legitimate LSD use was sounded when the USA, UK, Netherlands, France and Canada banned it.

When Hofmann discovered LSD's properties he had hoped it would find use as a therapy. He was also interested in its ability to induce a transcendental state and was open to the possibility of using it to gain new perspectives on the world. But Hofmann never thought LSD would become popular as a party drug and he frowned upon what he termed this 'profane application'. Speaking in 1993 at a symposium to mark the 50th anniversary of LSD, he said: 'What I never would have expected for the future of LSD was that it would ever find application as a pleasure drug on a large scale, considering the demonic, terrifying effects I had also experienced in my first self-experiment.'

Throughout his life Hofmann maintained an interest in the powerful effects of psychoactive drugs, particularly those used in ancient cultures. He became interested in the sacred drugs of pre-Columbian Mexico and found both the 'magic' mushroom *teonanacatl* and *ololiuqui*, the Aztec name for seeds from the morning glory plant family, contained compounds structurally similar to LSD.

Flashback to the Future

Although LSD has now been in the scientific wilderness for more than 40 years, Hofmann lived to see the first tentative signs of a government re-think before his death at the age of 102. Organizations such as the Multidisciplinary Association for Psychedelic Studies in the USA and the Beckley Foundation in the UK pressure governments to alter their outright bans on LSD and allow its use in medicinal research. In the last few years they have seen their first successes.

Amanda Feilding, Lady Neidpath, who is director of the Beckley Foundation, says: 'I visited Albert Hofmann when he was 99 and promised him that for his 100th birthday I would give him a present worthy of such an occasion: approval for the first scientific research on LSD using human subjects.'

The foundation did not quite make that date, but in 2007 it, together with the University of California Berkeley, received the go-ahead to start limited LSD research. The Beckley Foundation is currently supporting two studies, one in the USA looking at the effect of LSD on brain connectivity and creativity, and one in Switzerland looking at the use of LSD to ease anxiety among the terminally ill.

Among the aims of the foundation are the re-establishment of LSD as a tool for exploring consciousness and as a possible treatment for conditions such as cluster headaches. Lady Neidpath adds: 'Most medical practitioners still view LSD with suspicion, but there seems to be a stirring of interest in some quarters.'

Further Reading

Engel G, Herrling P (eds): Exploring the Frontiers: in Celebration of Albert Hofmann's 100th Birthday. Basel, Schwabe, 2006.

Hofmann A: LSD: My Problem Child. Santa Cruz, MAPS, 2005.

Pletscher A, Ladewig D (eds): 50 Years of LSD: Current Status and Perspectives of Hallucinogens. New York, Parthenon, 1994.

David Paterson is an editor of the Karger Gazette