

Special issue: *Pharmacology in The Netherlands*

Pharmacology in The Netherlands: past, present and future

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The physician Rudolf Buchheim (1820–1879), who was appointed Professor of Pharmacology in 1849 at the University of Dorpat (now Tartu in Estonia), is looked upon as the founder of experimental pharmacology [1]. He set up a pharmacology laboratory in his own home, resulting in the world's first institute of pharmacology (in 1860). Buchheim was succeeded by his pupil Oswald Schmiedeberg (1838–1921), who is often considered to be the founder of modern pharmacology [2]. In 1872, Schmiedeberg moved from Dorpat to Strasbourg. His pupil John Jacob Abel (1857–1938) became the first Professor of Pharmacology in the United States (Ann Arbor, 1890). Arthur Robertson Cushny (1866–1926), who had done research under Schmiedeberg, was appointed Professor in the first department of pharmacology in England (University College London) in 1905. Among the 200 or so pupils of Schmiedeberg, *circa* 40 became the head of a university department. These included Rudolf Gottlieb (1864–1924), Professor in Heidelberg, who taught pharmacology to the physician Rudolf Magnus.

On 2 May 1908, Queen Wilhelmina appointed Rudolf Magnus (1873–1927) to the post of Professor in the Medical Faculty of the State University of Utrecht for the speciality of pharmacognosy and pharmacodynamics [3] (Figure 1). This appointment thus actually created the first chair in pharmacology in the Netherlands. Magnus began his research in Utrecht in the Leeuwenbergh Building, a building that resembles a church and was built in 1567 as a nursing home for victims of bubonic plague. In that building he carried out his pioneering physiological research into the posture of animals, resulting in his classical monograph entitled 'Körperstellung' (Posture) [4]. His pharmacological research concerned the gastrointestinal tract, the cardiovascular system and the theory and practice of bioassay. Magnus died suddenly on 25 July 1927 during a holiday in Switzerland. In that year he was a serious candidate to be awarded with the Nobel Prize in Physiology or Medicine. The Rudolf Magnus Institute of Utrecht University is named after him.

Ernst Laqueur (1880–1947), a contemporary of Magnus, was appointed Professor of Pharmacology in Amsterdam in 1920 after doing research in Heidelberg and Groningen (Figure 2). His scientific career, a combination of pharma-

cology and endocrinology, was determined by his fascination for the action of insulin, obtained by extraction from animal pancreases. Whereas Magnus was a pure scientist, Laqueur was both a scientist and an organiser who maintained close contact with the pharmaceutical company (Zwanenberg)-Organon, of which he was one of the three founders.

Magnus and Laqueur initiated two fertile lines of pharmacological research in The Netherlands. The Magnus-line, including Everhardus Jacobus Ariëns, concentrates on drug–receptor interaction and pharmacokinetics, whereas the research of the Laqueur-line, including David de Wied, is at the interface of pharmacology and endocrinology. These lines are still recognizable in the contributions of Dutch research groups of pharmacology to this special issue of *Trends in Pharmacological Sciences* on the occasion of the celebration of 100 years of Pharmacology in The Netherlands.

Three contributions can be placed in the Laqueur-line. First, an article on type 2 diabetes, discussing new pharmacological interventions to preserve β -cell function by targeting β -cell mass [5]. Laqueur in fact initiated research on insulin and the pancreas [6]. Second, an overview of the current knowledge on neuronal circuits implicated in and pharmacological treatment opportunities for obesity [7]. This research started with the observation showing the involvement of melanocortin receptors in the energy balance, a type of research related to the field of neuropeptides and brain function initiated by De Wied in the Rudolf Magnus Institute [8]. Third, a review on the impulsivity: its neural basis, its significance for psychiatric disorders and its neuropharmacological manipulation [9]; research connected to that on experimental addiction was also started by De Wied's group [10].

Three other articles are more or less related to the Magnus-line. First, a paper describing the significance of mechanism-based PK-PD models for drug discovery and development [11]. This type of research was started with studies on the mathematical basis of pharmacokinetics by Jacques van Rossum (a colleague of Ariëns, known for his pioneering studies on drug–receptor interactions [12]) and further explored in the Leiden/Amsterdam Center for Drug Research [13]. The second article in this line also has its roots in Nijmegen but was further developed in the Cardiovascular Research Institute Maastricht [14]. It concerns

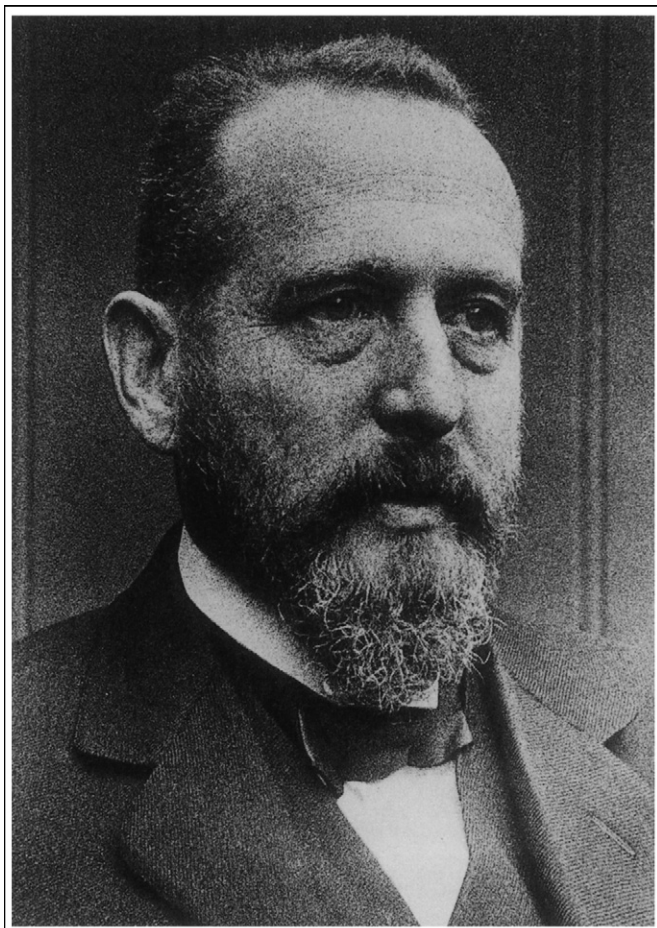


Figure 1. Rudolf Magnus (1873–1927). Taken with permission from O. Magnus [3].



Figure 2. Ernst Laqueur (1880–1947). Taken with permission from 'Pharmacology in The Netherlands', published on the occasion of the XIth International Congress of Pharmacology, 1990.

novel approaches for treating cardiac hypertrophy by targeting the Wnt/frizzled/GSK3 β pathway [15]. The third paper in the Magnus-line is dealing with a transporter molecule (MRP4) as a new therapeutic target, combining pharmacokinetic and pharmacodynamic aspects in drug development [16].

The remaining two articles in this issue are on immunopharmacology, an area with elements from both the Magnus- and Laqueur-line, and investigating drug targets for diseases in which immunological and inflammatory mediators play a significant role. One paper deals with immunoglobulin free light chains as a potential therapeutic target in the treatment of chronic inflammatory diseases [17]. The other concentrates on the potential use of the CXC chemokine receptors for the treatment of chronic respiratory diseases [18].

This issue provides a selection of research topics currently under investigation in The Netherlands in the area of basic pharmacology. No research on clinical pharmacology is included, although different research groups in The Netherlands are very active in this field. But this issue is dedicated to Rudolf Magnus, indeed a brilliant pharmacologist and physiologist at the time that pharmacology was recognised as a new field of science in medical faculties. Since then, pharmacological research and principles have spread to other domains of medicine and pharmaceutical sciences. Independent pharmacology

departments are becoming rare, but both preclinical and clinical pharmacological research is incorporated by important university research institutes and is increasingly being performed by scientists from various disciplines in interdisciplinary research groups. The principles of pharmacology have penetrated into practically all medical and pharmaceutical research. The pharmacotherapeutic applications of pharmacology are among the most important achievements of contemporary medicine.

Thus, the future should be bright. There are, however, serious concerns. First, pharmacology is less visible as a separate discipline, which has consequences for funding and further development of pharmacological principles. Second, the number of new chemical entities has been decreasing in recent years, and we lack efficacious medicines for important diseases. This medical need was summarised in the report 'Priority Medicines for Europe and the World' by the World Health Organization (<http://mednet3.who.int/prioritymeds/>). To stimulate the development of new medicines, initiatives for Public-Private Partnerships have been taken. In Europe, the 'Innovative Medicines Initiative' (http://imi.europa.eu/index_en.html) was launched, a partnership between the European Community and the pharmaceutical industry. In The Netherlands, the Top Pharma Institute (<http://www.tipharma.com/>) was established, funded by the Dutch government, academia and industry (ca. 300 new positions).

Forty-four projects were competitively selected in the domain of priority medicines, with a special emphasis on innovative pharmacological tools. Education and training is also part of the initiative. Hopefully, pharmacology and patients will benefit from this enterprise.

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