Toxicology in Sweden

Author:
Lars Wiklund,
RegSafe – Regulatory Safety Sciences,
Sweden

Mail: lars.wiklund@regsafe.se
Web: http://www.regsafe.se

Note July 2010:
A version of this article was published in Information Resources in Toxicology, 4th Edition, Lars Wiklund, Elsevier 2009, and on The World Library of Toxicology (WLT), Chemical Safety, and Environmental Health, when launched on September 7, 2009.
WLT: http://www.toxipedia.org/display/wlt/Welcome

In Sweden, toxicology, ecotoxicology, health- and environmental risk assessment are disciplines at various universities and colleges and also at research institutions connected to central authorities and in clinics for environmental and occupational medicine. Toxicology in Sweden is concentrated in the Stockholm-Uppsala area. The main center for education and training in toxicology and health risk assessment is the Institute of Environmental Medicine (IMM), Karolinska Institutet (KI), Stockholm, while Uppsala University offers Sweden's most extensive education within ecotoxicology.

Historical notes in Swedish toxicology (1)

1663: The earliest regulations regarding the handling of poisons were announced via the medical legislation. In 1663 the "Kungl. Maj:t" (Swedish Government) issued a charter for *Collegium mediocorum*, resulting in the public recognition of certain physicians in Stockholm.

1707: Johan Linder, MD (1678-1724), later raised to the nobility Lindestolpe, published the first Swedish monograph in toxicology: *De Venesis* ("About poisons").

Carl Wilhelm Scheele **(1742-1786)**, a chemist and a pharmacist was the discoverer of many chemical substances, most notably said to discovering oxygen and chlorine. Like many other chemists of his time, Scheele often worked under difficult and even dangerous conditions. Also, he had a habit of tasting chemicals that he found. It appears that this, together with frequent exposure to poisonous chemicals, was the cause of his premature death at the age of 43. At the end of his life he showed symptoms resemble mercury poisoning.

1773: Carl Peter Thunberg, a student and successor of Carl von Linné (1707 - 1778), sends a letter from his journey to Japan to the Swedish academy of sciences, describing poisoning with white lead, accidentally contaminating food.

1810: Karolinska Institutet (KI) was founded. A letter from King Karl XIII to the *Collegium Medicum* authorized the immediate establishment of a ”college for the corps of field surgeons”. The name *Medico Chirurgiska Institutet* was established in 1811 and *Carolinska* was added in 1822. In 1813 Jöns Jacob Berzelius (1779-1848) became one of KI’s first professors and laid the foundation of the Institute’s scientific orientation. In 1895, Alfred Nobel (1833-1896) appointed Karolinska Institutet to award the annual Nobel Prize in Physiology or Medicine. Today, Karolinska Institutet is a leading medical university celebrating its bicentenary.

1845: NJ Berlin (1812-1891), the last student of Jöns Jacob Berzelius, published a book with the title: “Anvisning till de allmännaste gifters upptäckande på kemisk väg - För Läkare och Apotekare” (Instructions for the chemical detection of the most general poisons – For physicians and pharmacists).

1850: On behalf of “Kungl. Maj:t” (Swedish Government), the “Sundhetskollegium” (something like: “the Health teaching-staff”) give a proposal for a poison regulation (“giftlagstiftning”).

1872: “Kungl. Maj:t” (Swedish Government) decides that a position for forensic chemistry should be established, followed by changes in regulations for investigations of poisons at post-mortem examination of corpse. The first holder of this position was Nils Peter Hamberg (1815-1902). The position was later gradually developed to “Statens rättskemiska laboratorium” (Swedish National Laboratory of Forensic Chemistry).

1876: Ordinance regarding care and the selling of arsenic and other poisonous substances and products is published in “Svensk författningssamling” (Swedish Code of Statutes).

1889: The Riksdag (Swedish Parliament) approve a law on occupational risks. The first labor inspectors are appointed.

1900-1919: Possible arsenic poisoning from paints and wallpaper in houses. Development of new analytical methods indicating arsenic in blood, urine and spinal fluid, and the presence of organic arsenic.

1906: In the “Giftstadga” (regulation on poisons) the poisons are divided in two classes: poisons of first degree and poisons of second degree.

1930: Erik MP Widmark (1889-1945) publishes a method for the quantification of alcohol in blood. His research on the absorption, distribution, and elimination of ethanol in the body was very influential on forensic alcohol analysis and toxicology, and paved the way for innovative traffic safety legislation that stipulated punishable limits of alcohol in the blood of a person driving a car.

1930-1939: Carl Gustav Santesson (1862-1939), professor in pharmacology at Karolinska Institutet, is studying the mechanisms of action of arrow poisons and hallucinogenic natural products.

1939-1941: "Statens institute för folkhälsa" (Swedish Institute for Public Health) was established. Important findings regarding metal toxicity was published. The institute was closed in 1971.

1943: A new "Giftstadga" (Poison Control Act) was launched.

1958: Karl Borg, at the National Veterinary Institute (Statens Veterinärmedicinska Anstalt, SVA) demonstrates high levels of methyl mercury from pesticide treated seeds in seed eating birds.

Toxicology becomes organized

Toxicology in Sweden received an organized form in the 1960:s. In 1963 the Poison Board (Giftnämnden) was established, and was later replaced with the Products Control Board (Produktkontrollnämnden), that became the Swedish Chemicals Agency (KemI) in 1986. In 1964 the medical research council established a research group in toxicology, which was later reorganized to the department of toxicology at Karolinska Institutet. The European Society of Toxicology (EST) had its annual conference in Stockholm in 1965: "Experimental studies and clinical experience. The assessment of risk".

The scientific community in Sweden has for long time provided important contributions for improved awareness of chemical risks and environmental protection. Swedish scientists, for instance, focused attention on the health hazards from organic mercury compounds used in agriculture several years before the Minimata poisonings in Japan brought those problems to the attention of the rest of the world. In 1966, PCBs were identified for the first time in wild animals in the Baltic, and later also in humans, by the scientist Sören Jensen, Stockholm University. In 1971 the first legal step to restrict PCB use in Sweden was taken (the Act on PCB), and legislation and bans were soon followed in many other countries. The Swedish Ordinance on PCB was revised in 1989 and a final time limit for the use of existing PCB was set to January 1st 1995.

Other Swedish milestones include the establishment of the Swedish Society of Toxicology (SFT) in 1969, although not formally formed until year 1977/78. Prof. Bo Holmstedt was the first president of SFT (1978-1979) and later elected as its first honorary member. The Swedish Society of Toxicology attracts individuals from many areas of toxicology, and the number of members in SFT is currently approximately 400.

Karolinska Institutet began special education in toxicology in 1973. In 1976 this education was expanded to a Master program in toxicology, at that time the first cohesive toxicology educational programme in Europe. Among the initiators of this unique toxicology programme ("Toxikologutbildningen") were Prof Bo Holmstedt, Prof Sten Orrenius, Ass. Prof Torbjörn Malmfors and Dr Anders Bergendorff, all later elected as honorary members of SFT.

Bo Holmstedt (1918-2001) was a prominent toxicologist both nationally and internationally, well-known in the toxicology community for his outstanding research, engagement in education, contributions to toxicological organizations and role as a leading authority in toxicological evaluation. He became Sweden's first professor in toxicology in 1964, and in 1974 he was elected to the Swedish Royal Academy of Sciences. He held several international leading positions, most prestigious President of the International Union of Toxicology, IUTOX (1983-1986).

Sten Orrenius has been on the staff of Karolinska Institutet in various positions since 1967 (professor of forensic medicine, professor of toxicology and director of the Institute of Environmental Medicine (IMM)). He was also Dean of the medical school 1980–1987, and member of the Karolinska Institutet Nobel Assembly 1971-2002. He holds honorary memberships in several international societies, and is also a member of the Royal Swedish Academy of Sciences. Sten Orrenius was president of SFT 1979-1981.

Torbjörn Malmfors, Malmfors Consulting AB, received his PhD at Karolinska Institutet in 1965. Torbjörn Malmfors has been instrumental in many international and national toxicological educational activities with a particularly focus on risk assessment. A major educational initiative he started in 1985 is the Risk Assessment Summer School (RASS), a program of the IUTOX, with Torbjörn Malmfors as the course director. Other successful educational initiatives include BTox, a toxicology education programme in Estonia, Latvia and Lithuania, and STox in Slovenia. Torbjörn Malmfors has been active in various toxicological societies, e.g. President of SFT (1983-1986), Secretary General of the Federation of European Societies of Toxicology (FEST), and Treasurer of IUTOX.

Anders Bergendorff has from the start of the masters training programme in toxicology at Karolinska Institutet in 1976 up to his retirement 2003, served as the Director of Studies, and he has been the prominent person for this united and broad education in toxicology. During all the years Anders Bergendorff has successfully managed the programme, and also introduced renewals and developments in order to maintain and improve the high quality. Anders Bergendorff was the secretary of SFT 1983-1988.

The contributions and commitment to the educational activities from all these initiators of the first toxicology programme at KI have been exceedingly important for promoting the competence, knowledge and development of toxicology in Sweden.

In 1986 the Swedish Chemicals Agency was formed and in 1993 the Eurotox conference: “Use of mechanistic information in risk assessment” was held in Uppsala.

Today the science of toxicology and ecotoxicology as well as health- and environmental risk/safety assessments are natural parts of the Swedish society, e.g. at universities, governmental and non-governmental organizations, industries etc. In 1999 and 2005 the Swedish Parliament adopted 16 national environmental quality objectives. The environmental quality objectives create a transparent and stable framework for environmental programmes and initiatives, and serve to guide such efforts at various levels in society. “A non-toxic environment”, one of these objectives aims to reduce health and environmental risks associated with the manufacture and use of chemical substances. The Swedish Chemicals Agency is the responsible agency for this objective.

The need for continuing education courses in toxicology was early recognized, and especially in the field of risk assessment. In the early 2000, IMM, KI started to develop a programme of several one-week courses in various aspects of risk assessment within the KI postgraduate program “Environmental Factors and Health” and in collaboration with the EU-funded programs CASCADE and RA-COURSES. The programme provides a comprehensive training covering all aspects needed for future scientists and professionals in European health risk assessment. The courses are given by experienced risk assessors and course coordinators from KI and at partner universities to European postgraduate students as well as to senior scientists and professionals from authorities and industry from 2004 and onwards. Since 2009

the European Union-funded project TRISK, where KI/IMM contributes as one of the leading partners, aims at developing a model for a University based training program in risk assessment that can lead to accreditation as risk assessor at the European level. This training model is planned to be integrated into regular KI training programs at master and postgraduate levels.

1) Parts of the historical notes cited from:

- Holmstedt B, Malmofrs T, Svensk Förening för Toxikologi, 1969-1994, Historiska återblickar, Stockholm, Maj 1994.

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