

to communicate scientific information to occupational professionals or other stakeholders, (iii) could lead to guidelines or regulations for occupational health, (iv) could lead to product development for the protection or promotion of the health of the workforce.

The evaluation group also met with representatives of various stakeholder groups and representatives of the research groups. The participants in these meetings were asked to consider a set of questions for the meetings (see the appendix). The Council secretariat received research material from approximately 60 research groups; this material was subsequently dispatched to the International Evaluation Group for its assessment in advance of its final meeting.

The International Evaluation Group met over a 5-day period to review all of the material submitted, interview stakeholders and researchers, and prepare a draft of the final report. In the subsequent month, this report

was completed by correspondence and presented in a seminar for the work environment research community. Thereafter the report was finalized and submitted to the Council for its consideration.

This supplement provides, for the first time, the history of Swedish work environment and occupational psychosocial research. The timing is appropriate as it is exactly 100 years since the Section for Occupational and Environmental Health of the Swedish Medical Society was inaugurated, and many of its members have been given due credit in the texts. The supplement also provides a summary on the context of the Swedish work environment, actors, and researchers and the final report of the International Evaluation Group (somewhat abbreviated). In addition, a commentary has been provided on the lessons learned from this evaluation and from a similar exercise concerning Swedish public health research that was completed 2 years earlier.

Broad overview of the history of Swedish occupational health research

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In this section, different aspects of Swedish occupational health research are presented, generally according to the following organization: (i) the underlying structure of Swedish research, development, and education (ie, institutes, university departments, and hospital clinics), (ii) major research areas, and (iii) the influential researchers associated with this work.

Research in a particular area is understood to have been initiated in a certain time period, after which continued success evolved over time. In this description, the full account for the different major research developments have been placed in the decade when each accelerated with subsequent follow-up to the present, in order to give continuity to the evolution of the area being described.

To select “influential” researchers in a certain area is, to say the least, a difficult task. This description does not aspire to completeness. Many other researchers have made important contributions, but completeness would have gone far beyond the aim, which was to give a short overview of the strengths and weaknesses of Swedish research in occupational health.

In addition, the potential number of original articles that can be quoted is enormous, which is why only the names of the research group leaders have been included, omitting graduate students and other researchers who appeared originally. The interested reader is thus urged to look for the original papers, in which case the name of the senior scientist can be used as an entrance into the database.

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The evolution of research on the psychosocial work environment is addressed in a separate section of this supplement.

Pre-1960s

Structure

"Generator gas clinics". During World War II, many drivers were chronically exposed to carbon monoxide from gas generators attached to vehicles and fueled by wood (gasoline was in short supply and a substitute was needed). As a consequence, many suffered from persistent damage to the central nervous system. In order to examine such cases on an individual basis, a "generator gas clinic" was founded in the Sabbatsberg Hospital in Stockholm in 1941.

In 1945, an occupational medicine clinic was established in the Karolinska Hospital in Solna, close to Stockholm, and an outpatient clinic for occupational diseases (for the city of Stockholm) was established in the Southern Hospital (Södersjukhuset) in Stockholm at the same time. These units can be considered the beginning of Swedish occupational medicine.

In 1958, the first unit outside Stockholm was established, a clinic of occupational medicine in the University Hospital in Lund. It was characterized by the integration of competence and resources in medicine and occupational hygiene, advanced in an international perspective with great impact, with respect to both the examination of patients and research. The Örebro Regional Hospital established its clinic a little later.

National Swedish Institute of Public Health. The National Swedish Institute of Public Health (Statens Institut för Folkhälsa) was founded in 1937. It had a department of occupational hygiene, which did research in occupational health.

University departments of hygiene. The National Swedish Institute of Public Health was located on the campus of the Karolinska Institute in Solna, and it had close connections with the Department of Hygiene of the Karolinska Institute. The other three universities (in Lund, Uppsala, and Göteborg) also had a department of hygiene. But none of these was, at that time, carrying out research in the area of occupational health. Instead, their main activities were in general bacteriology. However, later, these departments also took up research in the area of occupational health.

Research

Chronic poisoning by generator gas—an unsolved enigma. Acute exposure to high concentrations of carbon

monoxide can cause symptoms and signs of poisoning that can persist for a long period. Experimental studies established that even low-level exposure, for example, from generator gas-driven vehicles, caused effects that could be registered by sensitive tests (S Åke Lindgren). Whether low-level exposure during prolonged periods causes chronic toxic effects in the central nervous system with clinical symptoms of a neuropsychiatric nature is unresolved to this day.

Sweden—a very strong position in metal toxicology.

During the 1950s, exposure to toxic metals was common and sometimes very high in Swedish workplaces. Workers were exposed in the chloralkali industry to vapors of elemental mercury, in seed treatment to organic mercury compounds (mainly methyl mercury, later also methoxyethyl mercury), in the paper and pulp industry to phenyl mercury, in mines and metal smelters to lead and arsenic, in storage battery production to cadmium, in the hard-metal industry to cobalt and tungsten, and in welding to iron, manganese, nickel, and chromium.

In the 1950s and 1960s, Swedish research explored the risks of mercury in a systematic way using animal experiments, hygiene measurements, and clinical and epidemiologic studies on workers (Axel Ahlmark, Maths Berlin, Åke Swensson, Stig Tejning, Ulf Ulfvarsson, Harry Öhman). This knowledge became important when, in the late 1960s, it was discovered that seed-eating and prey birds, and later fish, had high concentrations of mercury due to emissions from the aforementioned activities. Swedish research took a leading position in handling health problems related to exposure to methyl mercury in fish (Staffan Skerfving). Successful research on elemental mercury and methyl mercury is still on-going (Lars Barregård, Gerd Sällsten).

Extensive preventive activities, including a change from mercury to alternative agents, led to a decrease in occupational exposure in the Swedish chloralkali industry. This development resulted in a major export of metallic mercury from Sweden to the world market. The change caused a decrease in mercury prices and probably an increase in exposure to mercury in other areas. At the international level, use was seen especially in connection with gold mining in South America, Africa, and Asia, where mercury was used for extraction and then burned off, leading to inhalation exposure. Swedish researchers have been involved in studies of such toxic effects. The activities also cause contamination of the general environment, leading to methyl mercury accumulation in fish, both locally and in the oceans.

Swedish research had a profound impact regarding other metals (eg, lead). The important discovery that lead inhibited heme synthesis was an initial side-observation in studies of inborn errors of heme metabolism in the 1950s and 1960s. Such disturbances were traced

to lead workers, first in mines (in Lapland) and later in battery workers (Birgitta Haeger-Aronsen). Animal experiments helped elucidate the problem. Extensive studies of the metabolism and effects of lead were later carried out in Sweden, in particular in Lund (Andrejs Schütz, Staffan Skerfving, Ingvar Bergdahl).

Cadmium was shown early to cause kidney damage in workers producing nickel and cadmium batteries (Lars Friberg). Swedish research on cadmium toxicity has been successful ever since (Magnus Piscator, Gunnar Nordberg, Tord Kjellström, Carl-Gustaf Elinder, Lars Järup, Marie Vahter). A method of great importance to determining the toxicity of lead and cadmium was the development of methods for quantifying lead in the skeleton and cadmium in the kidney by *in vivo* X-ray fluorescence (Lars Ahlgren, Sören Mattsson). Such methods now have extensive national and international use.

Swedish experimental and epidemiologic studies resulted in the prohibition of cadmium use in the Swedish work environment. This step has recently been challenged at the European Union (EU) level, as a potential barrier to trade. However, studies in susceptible strata in the general Swedish population, without particular exposure to cadmium, have indicated effects on the kidney and skeleton at exposures far below the occupational threshold limit, a finding that supports the relevance of the prohibition.

Sweden played a dominant role in metal toxicology even after metal exposure decreased in its metal industries. Research on mercury, lead, and cadmium are good examples of positive interaction between occupational and environmental medicine.

A special note should be made of the pioneer work done by Swedish researchers in the field of risk assessment during the 1960s and 1970s (Lars Friberg, Staffan Skerfving, Gunnar Nordberg). The assessments of metals were at the international forefront for a long time. The methods developed for risk assessment had great importance with respect to exposure limits, both at work and in the general environment.

"Rönnskär disease". One particular workplace had great importance in the early development of Swedish occupational medicine. In the smelter Rönnskärsverken in Skelleftehamn in northern Sweden, workers developed chronic obstructive bronchitis ("Rönnskär disease") (Torgny Sjöstrand, Karl-David Lundgren). High concentrations of sulfur dioxide and arsenic were found to be important with respect to the complicated mixture of exposures in the smelter. Epidemiologic studies of smelter workers in the 1970s showed an increased risk of lung cancer in association with this arsenic exposure (Olav Axelsson, Göran Pershagen, Stig Wall). These studies were the starting point for extensive research on arsenic metabolism (Marie Vahter).

Silicosis—an almost eradicated disease. In the 1950s, 1960s, and 1970s, Swedish researchers made contributions to the clinical description of pulmonary fibrosis induced by crystalline silicon dioxide (quartz, etc), which was a major problem in many workplaces (Åke Bruce, Axel Ahlmark, Carl-Johan Göthe, Gideon Gerhardsson). These contributions formed the basis for a major preventive campaign (Silikosprojektet), which systematically surveyed the risk in all quartz-exposing activities in Sweden. Although the campaign was successful, single cases of silicosis are still being diagnosed.

Noise—sufficient medical knowledge for prevention, but too little action. Hearing deficiency caused by noise in the workplace has been recognized as a problem since the time of Ramazzini. In Sweden, particular attention was paid to the problem in the 1940s, especially in the shipyards and the engineering industry. Swedish researchers made important contributions in the 1950s and 1960s, particularly with respect to the exposure–response relationships between noise and the temporary hearing threshold shift (Bengt Kylin). Another problem explored at the same time concerned measurements and risk assessments for impulse noise (P Voigt).

Much of the Swedish research on noise and hearing has been performed at the divisions of otology within the departments of otorhinolaryngology at the university hospitals. An important contribution was the development of a protocol for a systematic evaluation of hearing loss (Ingemar Klockhoff), which has later been widely adopted in other countries. Furthermore, the development of miniaturized equipment for the personal measurement of noise in the 1980s in combination with records on hearing losses, supplied useful "field" information for target interventions (Alf Ivarsson).

These studies were important for the early establishment of an occupational threshold limit of 85 dBA. This limit has later been adopted in many countries. However, preventive work has only been successful to a limited degree since there has not been full compliance with the action limit and since a considerable fraction of the workers develops hearing loss even at that level of noise. Furthermore, occupational noise can induce problems at levels far below those damaging the hearing [eg, fatigue (Anders Kjellberg, Ulf Landström)].

1960s

Structure

National Swedish Institute of Occupational Medicine. In 1966, the Department of Occupational Hygiene within the Institute of Public Health was merged with the Institute of Work Physiology and units of occupational

medicine and dermatology at the Karolinska Institute into the National Swedish Institute of Occupational Medicine (Arbetsmedicinska Institutet). This merger meant a considerable enhancement of the structure for research in the field of occupational health.

Clinic of occupational medicine. The Clinic of Occupational Medicine was started at the Regional Hospital in Örebro in the 1960s (Lennart Sundell), leading to better resources for the examination of patients but also for research aiming at prevention. The combination of medicine and occupational hygiene expertise in conjunction with an occupational hygiene laboratory was particularly important.

Research

Swedish occupational dermatology takes a unique world position. A successful Swedish line of research was initiated in the field of occupational dermatology in the 1960s. The combination of competence in medicine coupled with analytical chemistry and occupational hygiene was unusual and has only rarely occurred in other countries. It meant that associations between chemical risk factors and allergic contact eczema could be explored in detail. The development of the epicutaneous (patch) test method was also important as it made it possible to test people with a series of common allergens, as well as with suspected compounds from the workplace. Swedish occupational dermatology research had a profound impact (Sigfrid Fregert, Jan Wahlberg). An important achievement was the development of the guinea-pig maximization test, which enabled controlled testing of the sensitizing properties of chemicals.

Many work-related contact allergens have been identified throughout the years. In particular, the identification of a series of allergens in epoxy-resins systems should be mentioned (Sigfrid Fregert). It was the starting point for successful primary prevention efforts, emphasizing technical changes of the systems, along with changes in workplace practices, which have significantly reduced the risk.

Swedish research in occupational dermatology was also influential regarding other resins [eg, phenol formaldehyde (Magnus Bruce, Erik Zimerson)], which, in addition to the importance for individual patients, has supplied important basic information on the relationship between chemical structure and the potency of sensitization. The same is true for the systematic studies of colophony and terpenes and their derivatives (Ann-Thérèse Karlberg). Allergenic rubber chemicals have been studied, including their binding to peptides serving as full antigens (Christer Hansson)

Other important concerns of occupational dermatology during the 1970s to the 1990s were related to

sensitizing metals. Allergic eczema caused by chromium was earlier a very significant problem among construction workers due to the presence of chromates in cement. An important Swedish invention was the risk reduction shown by adding iron salt to cement (Sigfrid Fregert, Birgitta Gruvberger). The method was simple and relatively cheap and has thus achieved wide application in several parts of the world. Other protection methods were also studied (Anders Boman). Swedish research on the risk of sensitization to nickel [eg, in coins (Carola Lidén)] was important.

An additional achievement in the 1980s and 1990s was the description of contact allergy to preservatives, some of which were potent sensitizers (Bert Björkner). The epidemiologic description of hand eczemas and their determinants (occupational and others) in the general population has also been valuable (Birgitta Meding).

Improved assessment of skin exposure resulted from the development of biomarkers with which to quantify exposures (Per Brunmark, Gunnar Johansson, Bengt Åkesson) or from direct analysis of the skin (Ingrid Liljelind).

Chlorinated hydrocarbon and hexavalent chromium. The production of chlorinated hydrocarbons in Sweden called for special interest in these chemicals. Swedish studies led to an occupational threshold value for trichloroethylene that was set lower than that used in other countries (30 ppm) (Bengt Kylin). Studies of the thermal decomposition of chlorinated hydrocarbons caused wide interest (JA Dahlberg). Studies on dermal lesions caused by hexavalent chromium were of great practical importance.

1970s

Structure

In the early 1970s, Sweden experienced several large strikes that resulted in an increased focus on work conditions and work environment issues. This occurrence strengthened the interest of society in work environment problems and was followed by a series of significant changes.

Swedish Work Environment Fund. In 1972, the Swedish Work Environment Fund was created. Up to then, research funding in this area had been scarce, especially since the Medical Research Council felt limited responsibility for the area. The importance of the Fund cannot be overestimated. It supplied economic resources that enabled the establishment of fairly large research teams in many parts of Sweden, as well as networking

nationally and internationally. The Fund mainly supported projects of direct relevance to improve different work environments. To some extent, in particular in the early period, it also funded more basic research bearing on exposures in the workplace.

National Swedish Occupational Safety and Health Agency. The National Swedish Institute of Occupational Medicine was transformed into a department within the National Swedish Occupational Safety and Health Agency (itself established in 1949), which meant that research was brought into close connection with the labor inspectorate. This was an advantage for the practical relevance of research, but it also had a tendency to make research more superficial. Due to the increased political interest in work environment issues in the 1970s, the department staff more than doubled to 300 persons. Furthermore, initiatives were taken to start a Swedish and a Nordic criteria group for documenting the scientific basis for occupational exposure limits and methods for their exposure measurements. The groups still exist and have published more than 250 documents in Swedish and English (Johan Högberg, Gunnar Johansson, Jan-Olov Levin).

Clinics of occupational medicine. A center for occupational medicine was started in Göteborg with a clinic of occupational medicine and a network of other occupationally related activities. Furthermore, a clinic of occupational medicine was founded in Linköping; it was linked to the first university department and professorship in the discipline.

Research

Further development of occupational hygiene. Occupational health research expanded throughout the 1970s due to the increased resources, the introduction of and partnering with epidemiology, and the availability of new and sensitive analytical instruments [eg, gas chromatographs (GC), high-performance liquid chromatographs (HPLC), and atomic absorption spectrophotometers (AAS)]. New analytical methods with lower limits of detection made it possible to develop improved air-sampling methods. There resulted an explosion of investigations for a wide range of exposures, including welding and the use of organic solvents, pesticides [including phenoxy acid herbicides and DDT (dichlorodiphenyltrichloroethane)], polychlorinated biphenyls (PCB), asbestos, synthetic mineral fibers, jet fuel, cadmium and lead, metal smelting plants, and diesel exhaust in the mining industry. Occupational hygiene research was also directed at improving the assessment of dermal exposures (especially those caused by epoxy compounds), approaches to characterizing exposure to

molds, asphalt work, electromagnetic fields, vibration, polyester-resin lamination, and ventilation. Thus almost the whole spectrum of the occupational environment was illuminated from the perspective of exposure assessment and control.

Occupational epidemiology—a Swedish flagship. Sweden has had a unique potential for advanced register epidemiology; similar conditions are only present in the other Nordic countries. The basis for this potential is the combination of reliable population registries (with a unique “personal registration number” for every Swedish citizen), coupled with well-functioning registries of deaths (since 1958), tumors, births, malformations, and diagnoses for in-patients from hospitals.

These basic preconditions began to be widely used in a creative way by Swedish occupational epidemiologists at the beginning of the 1970s. The most valuable research has derived from combinations of epidemiologic methods with advanced records of exposure to work environment agents that look at intensity and duration.

Swedish researchers played an international role in the development of epidemiologic methods (Olav Axelsson, Anders Ahlbom). In particular, the possibilities and limitations of the case–referent design were explored. In addition, multivariate modeling was developed. Theoretical aspects of confounding, effect modification, and other co-variation were explored, for example, the demonstration of the limited importance of confounding from smoking habits with respect to the risk for lung cancer in occupational groups (Olav Axelsson). Later, methodological efforts to enhance the application of exposure assessment in epidemiologic studies have been a major contribution to occupational health research, to which Swedish researchers have contributed significantly.

A wealth of occupational epidemiology studies on cancer and causes of death has been carried out by Swedish research groups. A few examples of interesting projects follow.

One of the first occupational cohort studies in Sweden concerned workers exposed to trichloroethylene in degreasing metal in the metal manufacturing industry (Olav Axelsson). A large register measuring metabolite trichloroacetic acid (TCA) in urine from exposed workers was used. There were findings of increased risks of several types of tumors. Later, in the 1990s, similar studies were made in cohorts of dry cleaners. The risks were confirmed in animal experiments elsewhere.

It has long been known that workers in uranium mining and processing experience an increased risk of lung cancer. In the 1970s, scattered observations indicated the possibility of an increased risk of lung cancer in Swedish nonuranium miners. A cohort study of Swedish zinc miners showed a 10-fold increase in the risk of

lung cancer (Olav Axelson). The cause turned out to be inhalation exposure to radon daughters formed through the decomposition of uranium in the ore. The observation induced a series of still on-going investigations in the iron mines of northern Sweden (Christer Edling, Bengt Järvholm). A twofold increase in the risk of lung cancer was also found in the mines. These observations have not only contributed to preventive work to reduce the exposure, but also to a wider understanding of exposure-response relationships for alpha radiation. The risk in iron mines is higher than can be explained by the levels of radon daughters, and it is probably due to an interaction with silica in the mine dust, which has been shown independently to induce lung cancer (Peter Westerholm).

The radon studies in mines subsequently led to the problems of radon in private homes. A series of studies showed that homes with significant radon levels caused about 500 cases of lung cancer each year in Sweden, mostly among smokers (Olav Axelson, Christer Edling, Göran Pershagen). Slowly, actions have been taken to eliminate the problem. The radon story again illustrates the often fruitful interaction between occupational and environmental medicine.

Many other Swedish accomplishments in occupational epidemiology are noteworthy. For example, the high risk of liver cancer for those exposed to vinyl chloride was verified among workers in a polyvinyl chloride plant after the risk had been reported in experimentally exposed animals (Anders Englund). Research also contributed to the growing evidence that certain rubber chemicals are carcinogenic. In addition, 200 years after Sir Percival Pott's report that chimney sweepers had an increased risk of cancer due to exposure to soot, a Swedish study showed increased risks of several types of cancer (Christer Hogstedt). Cancer risks were also shown for glass workers (Gun Wingren).

Pesticides—cancer in relation to herbicides. Sweden is a country with a more limited need for pesticides than many other countries. However, Swedish researchers have contributed to the knowledge on insecticide exposures in the forestry industry (Birgitta Kolmodin-Hedman) and have reported tumors (case-referent studies of lymphomas and sarcomas) associated with herbicides (in particular phenoxyacetic acids) in forestry and agricultural work (Olav Axelson). The latter has attracted intense international attention. There has also been fairly extensive pesticide research in cooperation with researchers in Central America. (See the later discussion.)

Asbestos—a major problem that was finally penetrated and eliminated. In the beginning of the 1970s, single cases of pulmonary fibrosis induced by asbestos

(asbestosis) were not unusual in the daily life of Swedish occupational medicine, in spite of the fact that the risk had first been reported in the beginning of the 1900s and in Sweden in the 1930s. There were regulations for health examinations of asbestos-exposed workers, but they had not been very effective from a preventive point of view.

In the 1970s, there was a dramatic change in the concept of acceptable risk, including the risks associated with asbestos. The clinics of occupational medicine performed large surveys in several asbestos-cement factories and other industries that used asbestos for insulation purposes, primarily shipyards and railway-coach factories. A significant fraction of the workers were found to have radiographic changes in the lung and pleura (pleural plaques). Many were also shown to have decreased lung function in spirometry, and some had symptoms and signs indicating respiratory failure, which sometimes caused death. Many workers received workers' compensation, including a large group who had X-ray evidence of pleural plaques, in spite of no diagnosed effect on their physical health status.

The great attention focused on asbestos in Sweden led to almost total prohibition of its use. This early leadership led to several other nations following the Swedish example, even though asbestos is, today, still used in too many countries. Despite this very early action in Sweden, the on-going use of asbestos in the developing world is partly assisted by equipment exported from closed Swedish industries; this situation indicates a need for increased international cooperation to eliminate exposures in all countries.

A series of epidemiologic studies was made on the association between asbestos exposure and cancer risk (Maria Albin, Kristina Jakobsson, Carl-Göran Olson, Hans Welinder). The risk among heavily exposed workers was approximately doubled for bronchial cancer, with a particularly increased risk among smokers. There was also a high risk of pleural cancer (mesothelioma), but, because this is an uncommon tumor, the number of cases was much smaller.

Extensive efforts were made to estimate the intensity of the asbestos exposure, and two important facts became evident. First, while risk was earlier mainly detected for blue asbestos (crocidolite), a clear increase in the risk among workers mainly exposed to white asbestos (chrysotile) was also found. Second, the exposure associated with risk was lower than earlier reported. Recent data indicate cancer risk at extremely low exposure levels (Per Gustavsson). These results attracted great international interest and were instrumental in changing the view of the risk, including new occupational exposure limits.

Mesothelioma may develop after low-intensity exposure, and there may be an extremely long latency

time between exposure and the onset of disease. This is probably the reason why the rate of mesotheliomas is still high in Sweden (Bengt Järvholm), despite the fact that exposures—in principle—disappeared decades ago. However, asbestos exposures still occur in the destruction and renovation of old buildings.

Organic solvents—another risk that was explored and solved. It has long been known that organic solvents may cause acute intoxication, with accompanying symptoms of the central nervous system. In the 1970s, painters and styrene-exposed boatbuilders with chronic neurasthenic symptoms began to be seen in Swedish occupational medicine clinics.

This occurrence was the beginning of one of Sweden's research areas in which Swedish contributions were the most prominent. In a series of investigations of cohorts of painters and other groups (carpet layers, printers, etc) with high exposure to organic solvents (white spirit, toluene, styrene, jet fuel, etc), increased frequencies of symptoms and neuropsychological deviations were found and supported by case-control studies (Kerstin Ekberg, Christer Hogstedt, Palle Ørbæk, Bengt Knave, Arne Wennberg, Göran Struwe, Ingvar Lundberg, Olav Axelsson).

The great concern for the exposure to organic solvents and other volatile compounds in the 1970s called for the development and establishment of new sampling methods. Up until 1970, available methods had been midget impinger (bubbler) sampling and sampling in various kinds of airtight ampules. After 1970, solid sorbent sampling was developed in combination with new, sensitive gas chromatographic methods (Kurt Andersson, Jan-Olov Levin). A spectrum of solid sorbents was tested for various pollutants (Bo Jönsson). A further development was the introduction of simple and practical methods for passive sampling (Jan-Olov Levin, Anna-Lena Sunesson).

Even rather low-level exposure to organic solvents caused toxicity. The results caused initial skepticism in other parts of the world, where it was believed that the disorders were due to inherent nonoccupational factors or to confounding agents (eg, alcohol). For quite some time, Swedish researchers stood rather alone (together with a few other Scandinavian or Nordic groups). The problem was even known as the "Scandinavian disease". Accordingly, there was some initial hesitation to compensate injured workers. However, studies performed later in other countries confirmed the presence of the effects. The new knowledge led to an intense campaign to reduce exposures to organic solvents in the work environment, including the lowering of occupational exposure limits and the development of appropriate inorganic substitutes. These activities were remarkably successful, and nowadays cases of organic solvent

encephalopathy are rarely seen in Swedish occupational medicine clinics.

Activities around the "solvent syndrome" also included testing for the early effects of chemicals on the central nervous system, in which Swedish psychologists played important roles (Kerstin Ekberg, Francesco Gamberale, Monica Hane, Anders Iregren, Björn Karlson, Kai Österberg). Neuropsychological test batteries were developed, now widely used throughout the world. The interest in organic solvents also caused a general focus on the neurotoxic effects of other agents (eg, lead and mercury).

Parallel to the studies of toxicity among solvent-exposed workers, extensive Swedish research was carried out on the metabolism of organic solvents. The uptake, distribution, and elimination of a long series of compounds were explored in human volunteers in exposure chambers (Irma Åstrand, Gunnar Johansson). Through these activities, a profound understanding was obtained regarding the relationship between chemical structure or physical properties and the metabolism of solvents. In particular, the accumulation in, and release from, fat tissue was understood.

A tangent to the studies of chronic toxic encephalopathy with respect to exposure to organic solvents was an interest in the dramatic reactions to exposure at extremely low intensities of chemicals when smelled, which is sometimes called multiple chemical sensitivity (Lena Hillert, Björn Karlson, Palle Ørbæk, Kai Österberg).

Research on cardiovascular disease. In addition to assessments of cancer risks, Swedish researchers have contributed to the understanding of relationships between occupational factors and cardiovascular disease. Swedish facilities for population-based epidemiology (hospital registries) have been useful. In particular, the WOLF (work, lipids, fibrinogen) and SHEEP (Stockholm Heart Epidemiology Program) studies should be mentioned. These efforts have focused primarily on physical workload (Christina Reuterwall), shift work (Anders Knutsson, Lars Alfredsson, Torbjörn Åkerstedt), and the psychosocial work environment factors (Anders Ahlbom, Töres Theorell), which will be described elsewhere. Excess risks of cardiovascular disease have also been found for several occupations [eg, dynamite workers and chimney sweeps (Christer Hogstedt)].

Research on occupational accidents. The Work Environment Fund and its predecessor had put considerable resources into creating a center for research on occupational accidents at the Royal Institute of Technology (Kungliga Tekniska Högskolan) in Stockholm. Although the center produced interesting studies, when the funding ended, it was not supported by the Institute and

the research team split up. There was another group concerned with studying occupational accidents within the Swedish National Institute of Occupational Health, but this research area has remained surprisingly small in Sweden. On the other hand, Sweden has an effective prevention record and has reduced fatal accidents from around 400 per year in the 1950s to about 50 annually today.

1980s

Structure

Swedish National Institute of Occupational Health. In 1987, the research department within the National Swedish Occupational Safety and Health Agency was reorganized into the Swedish National Institute of Occupational Health (Arbetsmiljöinstitutet). The headquarters of the Institute were located in Solna close to Stockholm, and a large detachment in Umeå was included.

As a result of continued interest in the work environment and health in the 1980s, the Institute obtained increased resources, reaching a total staff number of about 400 and a yearly budget of about 300 million Swedish crowns per year. The institute covered all aspects of the work environment, including the chemical, physical, physiological, biological, psychosocial, and organizational; only radiation was excluded. The Institute had a close association with the clinics of occupational medicine and dermatology at the Karolinska Hospital.

More clinics of occupational medicine and occupational dermatology. In the late 1970s and 1980s, more departments of occupational medicine and occupational dermatology were founded at the university and regional hospitals. In the end, every hospital region in Sweden had such units. The units varied in size, some having a staff of up to 50 persons and others having only a few. In addition, there were large differences in the structure. In some cases (Lund and Örebro), the units had laboratories with advanced competence in analytical chemistry and occupational hygiene, while, in others, staff consisted of physicians, nurses, and secretaries only. The strongest units are unique from the international perspective.

An important development, which started in 1980 and was gradually introduced in all of Sweden, was the assignment of clinic responsibilities to all people in the hospital regions (for instance, the southern Swedish hospitals cover 1.5 million inhabitants). The clinics had support from all of the county councils in the region, in relation to their population. Most of the counties maintained that the clinics not only held the responsibility for examining individual patients, but also for "science-like" activities in order to gather knowledge, as a basis for prevention.

These developments also meant that clinic personnel had the responsibility and possibility to visit workplaces to investigate patient disorders and promote preventive activities. This situation was of the utmost importance for creative research on the association between exposures and disease, which became the hallmark of much of the successful work environment research, a fairly unusual aspect of Swedish research. Such field work was, and is, not possible in most countries. This evolving system resulted from the combination of union interest in work environment issues and the willingness of employers to cooperate in addressing these issues. Examples would be "the solvent story" (introduced in one of the previous sections), reported cancer clusters that became the starting point for important epidemiologic studies [eg, leukemia in workers exposed to ethylene oxide (Christer Hogstedt)], soft tissue sarcoma and phenoxy acid compounds (Olav Axelsson), rhino-conjunctivitis and asthma and organic acid anhydrides (Staffan Skerfving), ischemic heart disease among dynamite workers (Christer Hogstedt), and eczema among rubber workers (Sigfrid Fregert).

University departments of occupational and environmental medicine. In the 1980s and 1990s, all of the Swedish universities (Lund, Göteborg, Karolinska Institute in Stockholm, Uppsala, and Umeå, in addition to Linköping) formed university departments of occupational medicine, which were combined with the clinics of occupational medicine in the university hospitals. Each university appointed at least one professor of occupational medicine, who was also the senior consultant and head of the clinical unit. This situation meant a definite strengthening of the structure for research (and education).

In the 1980s and 1990s, several of the departments of hygiene at the Swedish universities were too weak to be sustained as separate units. Accordingly, they were fused with the departments of occupational medicine to form departments of occupational and environmental medicine. Such a fusion was constructive since the departments had similar work areas, competencies, and resources and resulted in stronger organizations. In addition, it facilitated interaction in the training of students. At the same time, corresponding clinics of occupational and environmental medicine were established in close association. This development has not yet occurred everywhere, but will probably take place soon.

Occupational and environmental dermatology. A similar development occurred in some of the clinics of occupational dermatology at the university hospitals (Lund, Malmö, and the Karolinska Hospital). Most of the units changed their name to occupational and environmental dermatology, but, in several cases, occupational dermatology remained within the clinics of dermatology.

Research

Markers of damage to genetic material and susceptibility.

Theories that an important component in the development of cancer would be damage to genetic material existed from the beginning of the 20th century. Considering the long latency between exposure and the onset of a tumor, there was much interest in finding ways to detect such DNA (deoxyribonucleic acid) damage in humans in connection with exposure, long before the cancer caused symptoms and signs.

In the 1960s, reports revealed that patients who had X-ray therapy developed microscopic aberrations in chromosomes in peripheral blood lymphocytes. This finding offered the possibility also to study chemicals with suspected genotoxic effects. An early discovery was chromosome aberrations detected in fishermen exposed to methyl mercury through fish (Staffan Skerfving). From 1980 on, several groups of workers were studied, and Swedish researchers played important roles in this work. Lead and ethylene oxide (in the sterilization of medical equipment) were found to cause chromosome breaks (Benkt Högstedt). For styrene, such effects were even used as a criterion for the occupational exposure limit. Studies of chromosome aberrations were time-consuming; hence, alternatives were explored, for example, micronuclei and sister chromatid exchanges in peripheral lymphocytes.

Early on, there was some doubt whether chromosome aberrations really indicated risk of later cancer. Most of the agents that caused chromosome aberrations were carcinogens, but some chemicals that caused aberrations did not seem to induce cancer. Furthermore, it was not obvious that changes in lymphocytes, cells only rarely involved in cancer, were relevant (though easy to sample). However, in a large Swedish project, which was gradually widened to include Nordic and EU partners, it was shown that those who had a record of a high frequency of chromosome aberrations ran a higher risk of later cancer than those with a low rate of aberrations (Lars Hagmar, Benkt Högstedt, Felix Mitelman, Ulf Strömberg, Christina Reuterwall, Staffan Skerfving, Håkan Tinnerberg). Hence the work and conclusions in the earlier studies seemed justified.

Microscopic changes in the chromosomes are a blunt index of genotoxicity. Through the explosive development of molecular biology, a series of other methods became available and was applied to problems in occupational medicine. Swedish research has constantly been in the forefront of this work. Methods to measure point mutations in single genes [eg, the GPR1 gene] were used (Bo Lambert). An important forward step taken in the 1990s was the development of the postlabeling method to assess the binding of chemicals to DNA. This method allowed the use of adducts in peripheral lymphocytes as

an index of exposure to genotoxic agents and mutagen damage (Kari Hemminki). These methods have been applied in assessments of risk from exposure to polycyclic aromatic hydrocarbons (PAH) (eg, in aluminum smelters), as well as for other exposures.

The developments in molecular biology also enabled the characterization of some of the background of variations in sensitivity between persons with similar exposure. An intense search for individual susceptibility factors started. In particular, polymorphisms in genes (*N*-acetyl transferases, cytochrome P450s, glutathione transferases, etc) involved in the metabolism of chemicals have been investigated. Several Swedish groups have been deeply engaged in this work. For example, workers exposed to several groups of chemicals [eg, PAH and isocyanates] were examined (Agneta Rannug). In addition, according to recent studies, it seems that selected genetic traits are involved in the metabolism of mercury and lead (Karin Broberg).

This research area is promising but extremely complicated; meaningful engagement requires a combination of a wide range of competencies and resources (eg, in molecular biology, biostatistics and bioinformatics, epidemiology, biomedicine, occupational hygiene, and analytical chemistry). In cases when such competencies have not been available in a single research environment, Swedish research scientists have developed or participated in networks in Sweden and internationally. In addition, the ability to make field investigations and the willingness of the Swedish workforce to participate in these studies have been important success factors.

Occupational musculoskeletal disease—still a major challenge for prevention. Musculoskeletal disorders are a major cause of suffering and a burden to worklife, the health system, and society. There is consensus that a large fraction of these disorders is caused by work environment factors, but much has long been unclear, in particular as regards the pathomechanisms and the relationship between physical and other risk factors. Swedish researchers are very active in these areas.

As to the pathomechanisms, a few contributions should be highlighted. The Cinderella hypothesis is one positing an uneven load on different motor units with recruitment of the same ones first in every contraction (Göran Hägg). This hypothesis has some experimental support but is, for methodological reasons, very difficult to test. In basic research, studies on nervous system function should be mentioned (Håkan Johansson). In addition, important contributions have been made to experimental measurements of pressures in vertebral discs and in tendons in connection with varying positions and movements (Alf Nachemsson, Tommy Hansson).

As in many occupational studies, one of the crucial elements in describing the relationship between exposure

and risk is the proper recording of exposure. In this field, Swedish researchers have, during the 1980s and 1990s, contributed widely to the study of musculoskeletal disorders. These efforts have included methods for recording exposure through the use of questionnaires (Istvan Balogh) and observations (Åsa Kilbom, Jörgen Winkel, Christina Wiktorin), the use of mechanical, electro-optical, and microelectronic equipment (Gert-Åke Hansson), and also developments in study design for the assessment of physical workload (Svend Erik Mathiassen). Swedish research groups have also contributed to the development of electromyographic (EMG) methods (Roland Kadefors, Roland Örtengren). However, except for the microelectronic devices, the methods have only been used to a limited extent in epidemiologic studies of musculoskeletal diseases.

Regarding the medical endpoint—musculoskeletal diseases—Swedish research groups have supplied important information on risks and risk determinants of arthrosis (Eva Vingård, Helen Sandmark), upper-limb disorders (Kerstin Ohlsson, Catarina Nordander, Staffan Skerfving, Ewa Wigaeus Tornqvist), and back pain (Eva Vingård). Several studies have been devoted to risks associated with computer work (Ewa Wigaeus Tornqvist, Mats Hagberg).

In addition, studies on rehabilitation and secondary prevention have been carried out with respect to musculoskeletal disorders (Kerstin Ekberg), but the success in terms of return to work has been limited. Primary prevention seems to be the only feasible way forward. However, primary prevention has not yet been impressively successful. Heavy lifting has certainly been reduced, but other types of physical workload seem to be unaffected, and it is doubtful whether the prevalence of musculoskeletal disorders has really decreased. This uncertainty may have several explanations, for example, first, a lack of sufficient scientific evidence for adequate actions, second, insufficient interaction between biomedical research and technological process design, and, third, an unwillingness in society to accept the high costs that efficient preventive actions sometimes would mean for the individual company. Hence this is a field that requires much more research.

Vibration from handheld tools—a sufficiently well-defined risk waiting for prevention. Hand-arm vibration may cause damage to blood vessels, nerves, and bones in hands. Swedish research has contributed to the understanding of the relationship between exposure and response. Methods for measurement have been developed and applied (Ronny Lundström, Lage Burström), and risk patterns at various intensities and durations of exposure and pathomechanisms have been defined (Lena Ekenvall, Mats Hagberg, Ulf Hjortsberg, Göran Lundborg, Thor Nilsson, Ingrid Åkesson).

There is now, as a result of Swedish and other research, a sufficient base of knowledge so that primary prevention can be undertaken against local vibration. However, established limits for occupational exposure do not protect a significant fraction of the workers, and the enforcement of these measures has therefore not been sufficiently effective.

Whole-body vibration has also been studied (Jan-Erik Hansson, Ronny Lundström), although its association with health problems is less well established.

1990s

Structure

Swedish National Institute for Working Life. In 1995, the Swedish National Institute of Occupational Health was merged with the Work Life Centre (Arbetslivscentrum), into the Swedish National Institute for Working Life [Arbetslivsinstitutet (NIWL)]. The focus of the research activities of the Work Life Centre had been in the field of work organization and the labor market. The new institute was instructed to focus more on these areas and on issues concerning the psychosocial work environment than on chemical and physical factors. In addition, the new institute was ordered to reduce its volume, which caused several years of turbulence, resulting in partial deviation from the focus from research.

Eventually, many of its research groups in the areas of chemical, physical, and ergonomic risk factors were relocated to universities in different parts of Sweden, altogether about half of the former resources for this kind of classical occupational health within the Institute. Although they received a “backpack” with basic funding for several years, they still had to build up infrastructures in new research environments, which temporarily reduced their scientific productivity. The dispersed group had a formal responsibility to supply advice in their respective fields of competence, but the new national institute had problems in adequately and rapidly handling emerging risks in chemical, physical and ergonomic areas [eg, when the problems of acryl amide appeared (see the later discussion)].

The structure of the present Swedish institute therefore differed from that of the other Nordic central institutes, which still have major competence and resources in the field of chemical, physical, and biological risk factors. Now, even the centralized research focus of the Institute has been terminated and it closed in mid-2007 due to a decision made by the new government that took office in 2006.

Swedish Council for Work Life Research. Simultaneously with the emergence of the Swedish National Institute

for Working Life, the Work Environment Fund was transformed into the Swedish Council for Work Life Research [Rådet för Arbetslivsforskning (RALF)]. There was also a reduction in the resources available for work environment research, but, at least initially, still reasonable funding for well-established and productive groups.

International cooperation and European Union funding.

In the late 1990s, many Swedish research groups in biomedicine started to seriously compete for resources within the European Union's framework programs 4, 5 and 6 for research and technical development. Research groups in the work and general environment fields have been successful (in relation to the size of the country and its research structure). The main reason is the strength of the groups, which makes them attractive to international research networks.

Hence a long series of concerted actions, strategic targeted research projects, integrated projects, and networks of excellence have been, or are, coordinated by Swedish researchers in the work environment area. In addition, many Swedish groups have been partners in projects coordinated from other parts of Europe.

EU project activities have widened the networks of the Swedish groups, and research has become more international. Within projects, many objectives have been tackled that would not have been possible to solve on a local or even national level, for example, studies on the relationship between chromosome aberrations and later cancer (Lars Hagmar), and investigations on the toxic effects of persistent organic pollutants (Helène Håkansson) and metals (Staffan Skerfving).

On the other hand, EU activities have major drawbacks. One problem has been the limited and rigidly formulated scopes of the European Union's research programs. In addition, the necessity to raise matching funds from national or local Swedish research-funding agencies can be an obstacle. Furthermore, the activities of many senior researchers within these collaborative projects have been refocused to administration, instead of to practical research. Thus it may be questioned whether the resources spent in EU projects are really in parity with the achieved results. At least there is a need for substantial national funding, which can support creative research not fitting into the narrow EU perspectives.

To address a different objective of international research collaboration, Swedish researchers have, from the 1990s on, been active in Central and South America and also in Africa and Asia. Senior Swedish scientists have been principal investigators or co-workers in studies on the effects of climate conditions (Ingvar Holmér), exposure to pesticides (Christer Hogstedt, Olav Axelson, Ingvar Lundberg) and toxic metals (Lars Gerhardsson, Kristina Jakobsson, Maria Albin), as well as tutors for

successful doctoral students (Catharina Wesseling, Jamieth Miranda, Aurora Aragon, Patricia Monge).

Research

Occupational asthma, rhinitis and alveolitis. It had long been known that farmers have a highly increased risk of asthma and rhinitis, caused by the inhalation of proteins and sensitization mediated by immunoglobulin (Ig) E. Swedish research in the 1990s showed that such problems were still very common. For cohorts of farmers (Marianne van Hage Hamsten) and millers or bakers (Jonas Brisman, Linnea Lillienberg), patterns of sensitization were defined, and methods of diagnosis were improved. Laboratory animal allergy has been a useful model for protein-induced sensitization (Per Malmberg, Anne Renström).

In some work environments, exposure to microbial agents may cause allergic alveolitis induced by a type-3 allergic response. Swedish researchers have been active in this area, for example, in the evaluation of respiratory disorders among farmers (Anna Rask Andersson) and wood trimmers (Lars Belin). In addition, the practically important and theoretically interesting acute respiratory disease, which is very prevalent among personnel in swine confinement buildings, has been fruitfully explored (Per Malmberg, Kjell Larsson). Through field and experimental studies with bronchial lavage, the nature of the inflammatory reaction has been described. The studies have attracted much interest internationally.

Basic research on the pathomechanisms (biochemical and immunologic events) of obstructive lung disease has been performed in Sweden (Christer Tagesson).

There has also been great interest in airway sensitization by low-molecular-weight organic chemicals. One of the most interesting families of compounds is the organic acid anhydrides, which are used in the production of polyester and epoxy resins. A long series of studies of these compounds was launched in the 1990s. Some of these compounds turned out to cause the development of specific IgE and IgG antibodies in up to one-third of workers, even when exposed to extremely low concentrations. This finding indicates that these compounds form one of the most sensitizing groups of compounds ever encountered.

This finding was of practical importance for the examination of exposed workers and the understanding of the exposure-response relationship, as a basis for occupational exposure limits and prevention (Jörn Nielsen, Hans Welinder). For example, practical methods for the biomonitoring of the compounds through the analysis of metabolites in urine and protein adducts in blood were developed and employed in the workplace (Bo Jönsson, Christian Lind). However, the research also resulted in a wealth of basic knowledge on the process

of sensitization. The quantitative structure–activity relationship for organic acid anhydride was explored, and such an undertaking had never been attempted before for a type-1 allergen (Hans Welinder). The formation of the full antigen through reaction with hapten proteins was shown, and the exact binding of the allergens to the protein was demonstrated (Monika Kristiansson). This is a unique basis for the understanding of allergenic epitopes and the process of antibody formation. In addition, it was possible to describe the kinetics of IgE and IgG antibodies after the end of exposure. Research following up the findings on organic acid anhydrides is still on-going in 2007.

Similar progress in the understanding of risks associated with exposure to heterocyclic and tertiary amines was made possible by improved chromatographic methods (Kurt Andersson, Jan-Olov Levin, Gunnar Skarping, Bengt Ståhlbom) and should also be mentioned (Lars Hagmar, Bengt Åkesson, Staffan Skerfving).

Respiratory disorders in workers exposed to isocyanates were described as early as the 1950s. Swedish researchers have made major contributions in this area. Precise and sensitive analytical methods for air monitoring were developed during the 1980s (Carsten Sangö) and 1990s (Gunnar Skarping), as were means for biomonitoring isocyanate metabolites and protein adducts as indices of exposure and risk (Gunnar Skarping, Margareta Littorin).

The development of these sampling methods was facilitated by increasingly advanced chromatographic methods (Marianne Dalene), to be combined with mass spectrometers. Special focus was given to the complex products formed when polyurethanes were heated (Dan Karlsson). New and sensitive methods have been used for intensive monitoring of exposure at workplaces (Carl-Johan Sennbro, Håkan Tinnerberg, Håkan Westberg). This is one of many examples of the extreme importance of the development of advanced analytical techniques for the possibility to assess risk.

One major remaining problem is the lack of reliable information on the relationship between exposure, as measured by adequate methods, and risk. The gathering of such information has only just started. In addition, the explanation for the intriguing variation in sensitivity between workers with similar exposures has not been solved. It seems likely that polymorphisms in genes for enzymes involved specifically in the metabolism of isocyanates and generally in the development of respiratory disease are important factors. Even after decades of research, the pathomechanisms behind isocyanate-induced disease is still largely unclear; classical, specific IgE and IgG antibodies are certainly not the answer. Swedish groups have been active in these areas from the 1990s on.

In addition to the allergically induced respiratory disorders, the work on bronchitis in association with

welding fumes and diesel exhaust (Ulf Ulfvarsson, Bengt Sjögren, Thomas Sandström) and construction dust (Bengt Järvholm) should be mentioned, as well as population-based surveys of asthma (Kjell Torén).

Advances in occupational hygiene. This period was characterized by improved analytical methods and an accessibility to advanced instruments, such as mass spectrometers. The development of sensitive methods for the biological monitoring of exposure is notable. This development included studies on exposure to cytostatic drugs and acrylamide. Advanced instruments facilitated the increasing use of protein adducts as biomarkers of exposure. New findings on the exposure to aromatic and aliphatic isocyanates in “hot” environments were reported (Gunnar Skarping). Methods for studies on skin adsorption and natural allergens were developed.

The biological monitoring of exposure has increasingly been introduced for a variety of chemicals. Among the metals, methods were developed especially for cadmium (Hans Welinder, Staffan Skerfving) and chromium (Gun Nise) in parallel with the continuous development of the methods for lead and mercury. With respect to biomarkers for organic compounds, the studies on amines, isocyanates, and organic acid anhydrides have already been discussed. The wood industry in Sweden is important, and thus the studies on metabolites of terpenes should be mentioned (Kåre Eriksson). Biological monitoring development for toluene is another good example (Gun Nise).

An interesting and important development has been the introduction of biomarkers with different “time windows” in relation to exposure. For cadmium, analysis in the blood, urine, and kidney reflects different compartments with biological half-times from hours to years. The determination of lead in bone is another example of a very long-lived biomarker (Lars Gerhardsson, Andrejs Schütz, Staffan Skerfving). Kidney cadmium and bone lead can be analyzed by in-vivo X-ray fluorescence techniques. Metabolites in the form of stable adducts to proteins like albumin and hemoglobin have been shown to indicate long-term exposure due to the long half-time of the protein adducts. Such albumin adducts have been found for toluene diisocyanate (Pernilla Lindh) and hexahydrophthalic anhydride (Monika Kristiansson), along with hemoglobin adducts for hexahydro- and methylhexahydrophthalic anhydride (Christian Lind, Bo Jönsson).

Methods for retrospective exposure assessment were developed over the years (Tom Bellander, Gun Nise, Nils Plato, Håkan Westberg.) and applied in many epidemiologic studies.

Sick building syndrome—still an intriguing problem. In the 1990s, Sweden became interested in the mucosal and

cutaneous symptoms of people who worked or lived in damp buildings. Swedish research contributed to methods for measuring possible causative agents, including fungi and their volatile metabolites (Göran Blomqvist, Kurt Andersson, Barbro Andersson, Jan-Olof Levin).

In addition, extensive Swedish studies were performed with the aim of linking microbiological and chemical [volatile organic compounds (VOC)] exposure factors to symptoms and objective findings among people dwelling in the buildings (Carl-Gustaf Bornehag, Birgitta Kolmodin-Hedman, Dan Norbäck, Bernt Stenberg, Jan Sundell, Gunilla Wieslander). However, in spite of all the efforts, most of the links between moisture and symptoms still remain unclear.

Visual display terminals and electromagnetic fields—illness, skin symptoms and cancer. The perception of light is very complex (Rickard Küller, Lennart Wetterberg). Exposure from visual display terminals (Carola Lidén, Ulf Bergkvist, Bengt Knave) and flickering light (Rickard Küller) have received special attention in Swedish research, and this research has led to the improved construction of visual display terminals.

During the late 1980s and the 1990s, a significant number of Swedes claimed that they developed nonspecific symptoms (fatigue, tiredness, headache, vertigo, nausea, etc) and cutaneous irritation of the face when exposed to electromagnetic fields from video display terminals or other electric equipment. The phenomena were investigated epidemiologically (Bengt Knave, Lena Hillert, Bengt Arnetz, Sture Lidén, Kjell Hansson-Mild) and by double-blind provocations in supposedly sensitive persons. It was not possible to link, in a conclusive manner, the exposure to the symptoms. Instead, it is likely that the symptoms were mainly due to psychological and ophthalmological stress in sensitive persons. However, this conclusion has never been accepted by some of the affected persons.

In addition, the question was raised of whether electromagnetic fields induce cancer (in particular, leukemia and brain and breast tumors). The possibilities offered by the Swedish registries were used to study the risk in occupations with high exposure to electromagnetic fields (welders, engine drivers) (Birgitta Floderus), but conclusive associations could never be established. The interaction between occupational and environmental research led to studies of leukemia in children living close to power lines (Anders Ahlbom, Maria Feychting).

2000–2005

Structure

The Council for Work Life Research was transformed into the Swedish Council for Working Life and Social

Science [Forskningsrådet för Arbetsliv och Socialvetenskap (FAS)] at the same time that some of the resources aimed at technical development were transferred to The Swedish Governmental Agency for Innovation Systems (VINNOVA).

Research

Occupation and reproduction—great possibilities for the future. That exposure to certain chemical agents (lead, mercury, etc) in the work environment may cause reproductive effects is not new. Sweden offers good possibilities to perform studies in this area because of its well-kept birth and malformation registries. In addition, the willingness of the Swedish population to participate in studies is a great advantage. These fortunate preconditions have not yet been fully utilized, but they offer great possibilities for the future.

A series of different kinds of reproductive effects have been published from the 1990s on. Examples are indications of prolonged time to pregnancy, decreased birthweight, and malformations in female medical personnel exposed to anesthetic gases (Gunnar Ahlberg Jr), although the effects remain to be firmly established. Studies have also been carried out among female laboratory staff, hairdressers, and fishermen's wives exposed to persistent organic pollutants, polychlorinated biphenyls, and the like (Lars Hagmar, Lars Rylander, Anna Axmon).

Studies of disturbances in male reproduction are far rarer. Indications of effects on sperm, including data on the FISH (fluorescence in situ hybridization) analysis for fishermen consuming high amounts of fish contaminated with persistent organic pollutants have been reported (Lars Hagmar, Anna Rignell-Hydbom, Aleksander Giwercman). Another example is formed from studies of time to pregnancy in association with paternal occupational exposure to phthalates (Gösta Axelsson).

Acrylamide—occupational exposure and ingestion via food. In the 1980s, advanced gas chromatography–mass spectrometry methods were developed to assess the concentration of hemoglobin adducts of alkylating agents, initially ethylene oxide (Lars Ehrenberg, Margareta Törnqvist). The methods proved valuable in the biomonitoring of workers, but also as tools for the assessment of cancer risks, by extrapolation from data on radiation risks to chemical carcinogens. Stable adducts for albumin have been demonstrated for toluene diisocyanate (Pernilla Lindh) and hexahydrophthalic anhydride (Monika Kristiansson).

An investigation of an outbreak in the late 1990s showed that Swedish tunnel builders (and cows) exposed to acrylamide developed signs of toxicity of the peripheral nervous system. This finding started a fruitful

sequence of studies in which determinations of the hemoglobin adducts of acrylamide were the key to describing the relationship between exposure and toxic effects (Lars Hagmar, Margareta Törnqvist). The outbreak was also used for detailed investigations into the metabolism of acrylamide. The results attracted much international interest, since the exposure was fairly widespread.

These methods and metabolic data became unexpectedly useful once the discovery (Margareta Törnqvist) that acryl amide can be formed in foods with the heating of carbohydrates. In this case, the issue was not nervous system disorders but the risk of cancer in large population exposures to low doses. Again, the acryl amide story illustrates the usefulness of the close interaction between occupational and environmental health, and it is also a good example of the advantages of interaction between analytical chemistry, occupational hygiene, toxicology, epidemiology, and clinical and environmental medicine.

The history as illustrated by doctoral dissertations

It has been possible to identify the names of the authors of all doctoral dissertations in occupational health defended at Swedish universities, including those concerning the psychosocial work environment, from 1940 on (table 1). We have classified the dissertations into the following four main categories: chemical (including biological), physical, ergonomic risks, and psychosocial medicine. Furthermore, subcategories of the main aspects of epidemiology, occupational hygiene, physical

risks, and ergonomics have been listed, although many dissertations combine several of the subcategories.

For the whole period, 148 of the 324 theses concerned chemical hazards, 85 dealt with ergonomic aspects (musculoskeletal), 46 focused on psychosocial factors, and 46 concerned physical risks (when accident research is included). About half of the dissertations had an epidemiologic character, while about 60 mainly concerned occupational hygiene methods. Another 43 theses covered physiology and ergonomic exposure methods. Many dissertations classified as epidemiologic had a strong component of exposure measurements, for natural reasons. The large number of epidemiologic dissertations supports our opinion that Sweden has had a leading role in occupational epidemiology in all categories of occupational health research.

During the first 30 years, fewer than 10 dissertations were published per decade. The number of dissertations increased to 20 during the 1970s and to more than 80 during the 1980s, with a further increase during the 1990s (118 theses), and almost 80 during the first half of the 2000s. The increasing number of doctoral dissertations in occupational health corresponds with the general development of Swedish academia; exceptional resources made available during the late 1970s and 1980s paid off in a dramatic increase in doctoral students.

Time trends show no striking differences concerning the number of dissertations per category, except an increase in psychosocial dissertations during the last 5-year period, and possibly a decrease in dissertations on chemical risks during the last 10-year period when compared with the period 1986–1995.

Table 1. Swedish doctoral dissertations in the work environment sciences, 1941–2005. [Chem = chemical and biological risks; Ergo = ergonomics; Ph = physical risks; epi = epidemiology or registers, clinical, intervention; oh = occupational hygiene, toxicology; derm = skin exposures or dermatitis; exposure = ergonomic exposures; rad = radiation and electromagnetic fields; Phys = physiology, biomechanics; psychosoc = psychosocial and rehabilitation; + Dev = developing country (included in decade columns)]

	1942–1950	1951–1960	1961–1970	1971–1980	1981–1985	1986–1990	1991–1995	1996–2000	2001–2005	+Dev
Chem _{epi}	4	2	4	6	11	16	19	12	11	2
Chem _{oh}	–	–	–	1	8	13	10	11	9	–
Chem _{derm}	–	–	1	–	1	4	2	1	2	–
Phys _{noise, epi}	–	1	–	1	1	–	–	2	3	–
Phys _{noise, oh}	–	–	–	–	–	–	1	–	–	–
Phys _{vibration, epi}	–	–	–	1	–	2	1	2	4	–
Ph _{vibration, oh}	–	–	–	–	–	–	2	1	–	–
Phys _{light, epi}	–	–	–	1	–	–	1	–	–	–
Phys _{light, oh}	–	–	–	–	–	–	2	–	–	–
Phys _{climate, epi}	–	–	–	–	–	1	–	–	4	2
Phys _{rad, epi}	–	–	–	–	–	1	–	–	1	–
Phys _{rad, oh}	–	–	–	–	–	–	–	–	1	–
Ergo _{epi}	–	1	–	1	4	3	13	7	13	–
Ergo _{exposure}	1	–	–	–	1	1	2	5	6	1
Ergo _{physiology}	2	4	3	5	3	2	6	–	2	–
Psychosoc	–	1	1	4	–	8	7	5	20	1
Accidents	–	–	–	–	–	2	4	2	3	1
Total	7	9	9	20	29	53	70	48	79	