JAN 15 1965

Conf-6412061

ANALYTICAL CHEMISTRY IN INDUSTRIAL HYGIENE*

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Industrial Hygiene has been defined by the American Industrial Hygiene Association as "that science and art devoted to the recognition, evaluation and control of those environmental factors or stresses arising in or from the work place which may cause sickness, impaired health and well being or significant discomfort and inefficiency among workers or among the citizens of the community." Possibly, the important role of the analytical chemist is not apparent from this definition but I hope it will be before I finish. I would like first to point out the contributions of the general field of chemistry in this profession. The major hazards which must be subjected to "recognition, evaluation and control" include chemical, physical and biological hazards. Hazardous chemicals in this sense include solvents, paints, adhesives, plastics, mineral dusts, metals as well as more specific compounds. In dealing with chemical hazards, in particular, much use is made of the concept of a threshold limit value. Since most substances enter the body through inhalation, this threshold limit value is the concentration of the chemical in the air to which nearly all workers may be exposed repeatedly without adverse effects. This concentration is not a fine line between hazard and safety but must be interpreted by trained personnel who understand its

* Work performed under the auspices of the U.S. Atomic Energy Commission.

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limitations and applications; however, it indicates immediately the need for a measurement of air concentrations. Note also that in the definition of industrial hygiene stress is placed on the need for recognizing hazardous materials. This is more than a matter of simply memorizing toxicological information. Instead, there must be some knowledge of bio-chemical processes as well as the chemical nature of compounds encountered in industry.

Many industrial hazards occur in conjunction with chemical processing operations. Here again the chemist's side of the industrial hygienist is called on because of his knowledge of such operations. He also is in a position to anticipate hazards that might arise under adverse operating conditions. One of the methods occasionally used for controlling the hazard from a chemical substance is the use of a substitute material. The use of toluene in place of benzene or methyl chloroform in place of carbon tetrachloride can both lessen a hazard and significantly reduce the costs of controlling the hazard in a very simple manner. Here, of course, the knowledge of the chemist is extremely important and it must be at a high level of sophistication. Snap judgments in this field can make the industrial hygienist appear ridiculous and can go a long way in destroying confidence in his ability.

In addition to these general fields of chemistry that must be employed, there are a considerable number of areas where the analytical chemist, in particular, gives unique and indispensable assistance. The recognition of many hazards requires the

analysis of raw materials, intermediates, and products of various industrial processes. The raw materials usually are trade name items and, while some information regarding their composition may be obtained from the supplier, it is frequently necessary to make a qualitative and some times a quantitative analysis of these materials. Solvents in particular, since they tend to be flammable and volatile, are of particular importance and may consist of a considerable variety of components. The analysis of these materials usually is quite difficult and complex.

Breakdown products of process materials often are the source of hazards and these too must be analyzed. Pyrolysis products of sand-conditioning materials in foundries may contain acrolein. Teflon decomposition products may contain hazardous fluorinated compounds; other plastic materials yield toxic and irritating substances; welding produces complex reactions; photochemical processes may produce ozone in the atmosphere. The analytical chemist must be prepared to cope with and analyze all of these materials.

As previously mentioned, the basic measurement of the industrial hygienist is the determination of an air concentration in order to determine exposures. Such measurements are made under operating conditions and are repeated following the installation of necessary control equipment, i.e., the final test of a control system is the analysis of atmospheric samples. The concentrations encountered are all relatively low and hence sensitive analytical methods must be employed. In order to get

additional information on individual exposure, it usually is desirable to supplement air sampling with the analysis of biological materials, usually urine, although blood, air, breath, or other materials also may be used under certain circumstances. These are particularly difficult analytical procedures because here extremely sensitive techniques must be used and the material to be analyzed usually contains large quantities of compounds which interfere with many analytical procedures. Extensive separation steps usually are required. To further round out information regarding exposures or the efficiency of control systems, it may be necessary to analyze soil, water or materials rubbed off the surfaces in the working area.

In order to carry out a realistic industrial hygiene program, all air sampling methods and equipment must be subjected to frequent calibration. This usually involves a comparison of the field sampling method with some highly precise laboratory technique, and again the analytical chemist plays the most important role. With the continued, rapid introduction of new chemicals into industry, along with new types of processing and fabricating techniques, there is a continual need for the development of new measuring instruments and analytical procedures in the field. In the last 15 years, many exotic materials which were formerly only laboratory curiosities have been introduced into industry and are handled on a large scale. The analytical chemist constantly is called upon to develop new sensitive measuring methods for these substances.

Finally, the basis on which the threshold limit value is established usually is some type of toxicological research. This involves the exposure of animals to the suspected toxic materials under controlled conditions, requiring the frequent analysis of both air and biological samples.

I would like to illustrate the importance of analytical chemistry in industrial hygiene by sketching briefly the history of two problems in the field. These two examples, while interesting, are by no means unique and one could very well take other examples in other areas. These two happen to be those of particular interest to me and those with which I am personally familiar. The first can be called the "beryllium problem."

When one looks back at the early work on beryllium, it can be seen that at least some of its toxic properties were investigated as far back as the early 1930's. Most of this work was done by German and Russian chemists and was largely unfamiliar to Americans. In Massachusetts about 1940, a number of plants began the manufacture of fluorescent lamps. The phosphors used contained silica, beryllium oxide, zinc silicate and other materials. These materials were heated together at various temperatures and the products ground to form the finely powdered phosphor deposited as a lining inside glass tubes. About 1943, several cases of a curious lung disease occurred among workers in this industry. At first the connection with the plant processes was not recognized since the cases were not numerous and they were

diagnosed as sarcoidosis, an uncommon but a fairly well defined disease. As more cases came to light, the coincidence of their occurrence among fluorescent lamp workers became apparent. Suspicion was turned on beryllium because the effect of most of the other constituents was well known while there was no toxicological information on beryllium. However, there appeared to be nothing in the existing chemical information about beryllium to suggest it as a likely cause of disease. The early analytical methods available for air sampling studies and for the analysis of biological material for beryllium were colorimetric methods and were relatively insensitive and nonspecific, requiring elaborate separation procedures; however, even they could have detected sufficiently small quantities had beryllium been no more toxic than lead. Early work at this period on improved analytical methods centered on the fluorimetric and the spectrographic methods. The sensitivity of morin as a fluorimetric reagent was noted but was passed over at first because of its lack of specificity and the difficulty of obtaining purified morin. It was not until 1950 that a satisfactory morin procedure was published. The spectrograph was used as early as 1944 to detect beryllium in lung ash but only relative results could be obtained. Steadman at Rochester, Cholak at Cincinnati and Barnes at Westinghouse all worked on the spectrographic process and a satisfactory method was published by Cholak and also by Steadman in 1948.

Meanwhile, toward the control of all dusts, efforts were being made in the industry and the beryllium content of phosphors was reduced and finally eliminated entirely in 1949. As a result, the exposures practically disappeared in this industry before a fully satisfactory analytical method was available and applied. Because of the latent period, which is a distinctive feature of berylliosis, cases continue to develop and still are appearing today from the neon sign industry. Many aspects of the epidemiology of the outbreak in the fluorescent lamp industry still are puzzling because of the lack of satisfactory data on exposures.

In the Cleveland area, beryllium cases also occurred largely from processes connected with the preparation of beryllium from the ore, beryl, and similar difficulties resulted. In 1947, a symposium was held at Saranac Lake at which all the existing knowledge on this subject was reviewed. At this meeting, Elkins pointed out that in the case of beryllium it was likely that much more sensitive analytical procedures were needed, if it is assumed that an atom of beryllium is equally as toxic as an atom of lead, since the atomic weight of beryllium is only 1/20th that of lead. In commenting on the results of this symposium, Sappington called attention to the fact that many of the gaps in knowledge at this period were the result of the deficiencies of the analytical procedures.

By this time, however, the data overwhelmingly indicted beryllium and its compounds, with the exception of beryl,

as the cause of this disease. The morin fluorimetric and the spectrographic methods are used today for the analysis of beryllium in air and biological materials. The high cost of the spectrograph has limited its usefulness, although it is the most successful method for the analysis of tissue samples. For air samples, morin is an excellent reagent and its sensitivity is now comparable to that of the spectrograph.

In 1950, the Atomic Energy Commission established the first set of permissible air concentrations which were to be used by its contractors. They established three levels: $2 \mu\text{g}/\text{M}^3$ as the average concentration for an eight hour day, $25 \mu\text{g}/\text{M}^3$ as a concentration which should not be exceeded even for short periods, and $0.01 \mu\text{g}/\text{M}^3$ as the permissible exposure level for the general public outside the plant. These levels are still used throughout the industry and the first of them was adopted by the American Conference of Governmental Industrial Hygienists as a threshold limit value in 1957. The short term exposure limit created a new analytical need for an instantaneous recording instrument. A workable recording spectrograph for this purpose was developed at Harwell in England, and has been further improved and is used in many places today. The National Spectrographic Laboratory in this country developed a similar instrument; however, there still are difficulties with these devices.

The very low value of the non-occupational limit further spurred the work on higher sensitivity methods. The morin

method is particularly good for air samples since there usually are few interfering substances present. Recently, it has been pointed out that our methods probably are more sensitive than necessary at the present time, but an increased specificity would be desirable to eliminate some of the elaborate separation steps. Russian workers recently have reported the development of reagents that appear promising from this standpoint.

The story of plutonium covers a period of time similar to that of beryllium. Plutonium as an element was produced or discovered in 1941. It is of some interest that one of the discoverers of this element is now a member of the faculty of Washington University here in St. Louis. Also, some of the earliest usable material was made in the Washington University cyclotron. Early investigations of its chemical properties were carried out in 1943, at the Metallurgical Laboratory of the University of Chicago, using extremely minute quantities of material. Obviously, analytical chemistry played a key role here. Large quantities began to be produced at the Clinton pile in Oak Ridge, and at the Hanford pile base on uranium produced by Mallinkrodt Chemical Company here. The Monsanto Chemical Company also played an important role in the early work in this field. Thus, the early history of plutonium has a very close association with this city.

In 1943, an analytical chemist at the Metallurgical Laboratory in Chicago read about the early cases of disease in the radium dial industry and was struck by the fact that plutonium, like radium, was an alpha emitter. He wondered

whether plutonium, like radium, also would deposit in bone tissue where radium had done such serious damage. Shortly after this, Dr. Joseph Hamilton of San Francisco visited Chicago and presented the results of some experiments he had done by injecting some plutonium salts in a few mice. He had demonstrated that plutonium was indeed a bone seeker. This evidence indicated that plutonium probably was similar to radium in its degree of toxicity. However, in the case of radium, no one ever handled more than a few grams, while it was anticipated that many pounds of plutonium would be processed.

The search began almost immediately for a method of detection of this material in air and biological materials. The air sample problem was comparatively simple since it could be detected by its alpha ray emission. High sensitivity counting techniques were needed and the natural decay products of radon and thoron in the atmosphere do interfere. However, by counting after the sample was collected and again after a lapse of some hours, the effect of natural decay products could be calculated and eliminated. Various air sampling methods were tried, leading to the general use of filter paper. This, in turn, produced the problem of interference by the filter paper with the counting process, but this proved to be no real obstacle.

The breath analyses which had been so useful in detecting the deposition of radium in the body could not be applied to plutonium since it did not produce a gaseous decay product,

hence there was a need for a method of analyzing urine for plutonium. Calculations based on the radium experience indicate that the permissible body burden for plutonium would be about 1 μ g. Animal data and later human data indicated that only 0.01 of 1% of an injected dose of soluble plutonium is excreted in the urine per day. This meant that for a man having a full body burden only about 10^{-10} grams of plutonium is excreted per day. This must be measured in a 1500 ml urine sample with all of its interfering substances. Work on this was started by Langham at Los Alamos and led to the development of a method involving extraction with cupferron. Later the method was improved using coprecipitation with bismuth phosphate and extraction with TTA. About 1949, the permissible limits for plutonium were lowered and led to a need for a more sensitive method to detect quantities of the order of a micromicro-gram or a pico-gram. Healy and Schwendiman at Hanford provided the method. With some further improvements in this method, we now routinely measure 5×10^{-13} grams of plutonium in a 24 hour urine sample. Some details of the method will be given shortly.

The analysis of urine was so important that this could have been a limitation on the production of the early nuclear weapons. It was found quite early that in order to obtain results at the low concentrations anticipated, it was necessary to collect samples under unusually careful conditions. After trying other methods, an 8-bed ward was finally built on the local hospital and operators were confined there for

24 hours during the sample collection period. Prior to this, the lack of such facilities brought a threat of the discontinuance of these analyses and this was followed by full support for the program from Laboratory management in order to prevent a shut down of operations. Every plutonium facility today considers itself dependent upon this analysis.

Description of Present Method

1. Phosphoric acid and ammonium hydroxide are added to the sample and the precipitate, which carries the plutonium, is allowed to settle over an extended period.
2. The precipitate is separated and dried with nitric acid, then redissolved in nitric acid and transferred to an ion exchange column (Dowex 1X-2 anion resin in chloride form).
3. The column is washed with 7.5N nitric acid followed by 3 ml of conc. HCl.
4. The column is eluted with 0.5N HCl; nitric acid is added to the eluted material and taken to dryness, dissolved in HCl, neutralized with 8N potassium hydroxide, oxydized with sodium hypochlorite and electroplated as plutonium hydroxide on a stainless steel disk using a platinum anode.
5. The plated disk can be counted directly in a low background alpha counter, or the activity determined by the nuclear track method, which we use routinely.

In this technique, the disk is placed in contact with an NTA photographic plate for seven days in a refrigerator in the dark. The film is developed, dried, and the number of alpha tracks counted under a microscope. The method is highly specific for plutonium.

Recent developments in low background alpha counting have made it possible to obtain results by electronic counting with about the same degree of sensitivity as the nuclear track method. In this technique, the plated disk is covered with a disk of mylar plastic that is coated with zinc sulfide phosphor, the phosphor being placed next to the plated sample. This assembly is placed in a scintillation counter where it can be counted with a background of about 0.01 counts per minute.

Many other analytical techniques are used in the industrial hygiene field. In recent years, air sampling for chemicals has been assisted considerably by the development and use of color indicating tubes. In these tubes a chemical which changes color on reaction with the contaminated material is deposited on some carrier material such as silica gel and placed in a glass tube. Air drawn through the tube causes a color change and the concentration is related either to the length of the changed portion of the chemical or to the depth of the color change.

Such a concentration measurement is necessarily approximate and subject to many limitations. They do serve to locate sources of possible exposure very quickly and accurately.

measurements can be made in these same places later by collecting samples for analysis in the laboratory.

Many chemicals can be detected and measured directly in the field by means of their chemical and physical properties. The mercury vapor detector, which is a comparatively old instrument, uses atomic absorption spectra for analysis, which is now considered a new technique. Other airborne substances can be detected directly by the depolarization of an electrode in the case of oxygen, the de-ionization of a gas stream in the case of hydrocarbons and other materials, a change of conductivity for sulfur dioxide, decomposition followed by a conductivity change for chlorinated hydrocarbons. Collected samples may be analyzed by the release of iodine in the case of ozone, infra red, ultraviolet and x-ray spectra, colorimetry with dithiazone and other indicators, gas chromatography, polarography, fluorescent spectrometry, neutron activation and radioautography.

For radioactive materials, no laboratory is complete today without a multi-channel gamma analyzer. Similar techniques also are used with alpha spectrometry and, to some extent, with beta and even neutron spectrometry. Over the last ten years, there has been a steady growth of whole body counters, both liquid scintillators and crystal scintillators, and even high pressure ionization chambers. These, of course, cannot be used for alpha or most beta emitters. Many analytical procedures for radioactive materials involve

chemical procedures which utilize the radioactivity and the final determination.

The importance of analytical chemistry in the industrial hygiene field may be gauged somewhat by the prominent part it occupies in the activities of the American Industrial Hygiene Association. One of the most active of the twenty technical committees of the Association is the Analytical Chemistry Committee. This Committee has just produced the first set of annotated abstracts on analytical methods for one hundred substances. These will be made available for sale shortly. The Biochemical Assays Committee, another technical committee, is working on methods for the analysis of urine, blood, and other biological materials. It also is investigating the significance of such analyses for measuring individual exposure. The Association is one of seven societies cooperating in the development of a manual of standard methods for air sampling.

I am delighted at this opportunity to bring these facts to the attention of this Society as it is a field where you can make a real contribution and also experience a considerable degree of personal satisfaction.

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