

FILE NAME: Monsanto (MON)

DATE: 1960 July

DOC#: MON008

DOCUMENT DESCRIPTION: Conference Proceedings - 13th
International Congress on Occupational Health

Proceedings

THIRTEENTH INTERNATIONAL

CONGRESS ON OCCUPATIONAL
HEALTH

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THIRTEENTH
CONGRESS ON

July 25-29, 1960

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Library of Congress Catalog Card Number: 58-32683

Public Health

GIFT



DESIGNED BY HARVEY SATENSTEIN

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In addition, many others visited points of interest to them either before or after the Congress.

When the debris had been cleared away and the hubbub had subsided by Saturday, July 30, the paid registrations figures for the Congress were as shown in the following tabulation.

NUMBER OF REGISTRANTS—BY COUNTRIES

Country	Total	Country	Total
Afghanistan	1	Japan	20
Algeria	1	Luxembourg	3
Argentina	19	Mexico	6
Australia	3	Morocco	1
Austria	8	Netherlands	16
Bahrein	1	Netherlands-Antilles	2
Belgium	2	Northern Rhodesia	1
Bolivia	1	Norway	13
Brazil	5	Pakistan	1
British Guiana	2	Peru	4
Canada	54	Philippines	5
Chile	4	Portugal	5
Colombia	9	Romania	1
Cuba	5	Spain	5
Czechoslovakia	1	Sweden	29
Denmark	4	Switzerland	6
Finland	62	Thailand	1
France	39	Trinidad	2
Germany	36	Union of South Africa	9
Greece	1	United Kingdom	94
India	5	United States	1040
Indonesia	1	Uruguay	2
Iran	2	U.S.S.R.	1
Ireland	1	Venezuela	7
Israel	2	Yugoslavia	4
Italy	21	Total	1568

One hundred and ten people paid and registered but were unable, for one reason or another, to attend. Thus the total actually present, exclusive of wives or guests, was 1458.

It is the impression of the Organizing Committee that the Congress was an overwhelming success. Certainly the number and quality of the scientific papers delivered was outstanding. Dr. Irving Tabershaw and his whole Program Committee deserve a special note of thanks for the hard work entailed in bringing such an excellent program to the Congress. It is the hope of the Organizing Committee that all those who attended, especially those from foreign lands, not only learned much from their attendance at the Congress but found our land and our people friendly and hospitable. We hope that new friendships were made, new understandings reached, and that the memories of the Thirteenth International Congress on Occupational Health will linger long. Speaking for all members of the Organizing Committee, it was a pleasure and privilege for us to plan the Congress and welcome all who attended.

ml of the buffer described in Appendix 1, and continue as in Appendix 1. Normally for blood specimens the final washing must be performed four times, instead of thrice as for urine specimens.

APPENDIX 3—COPROPORPHYRIN ESTIMATION

To 5 ml freshly voided urine in a stoppered test tube add 0.2 ml 3 per cent hydrogen peroxide solution, 1 ml glacial acetic acid and 3 ml ether. Shake gently, release pressure, and place in a lightproof box overnight. Observe the red fluorescence under ultraviolet light, and grade the specimen 0-++++ by degree of fluorescence.

APPENDIX 4—HEMOGLOBIN DETERMINATION

Take 0.05 ml blood, and make up to 9 mls volume with 0.4 per cent ammonium hydroxide. Measure absorption on a colorimeter, using a standard filter (EEL 404), and convert the reading to hemoglobin

percentage to the nearest even number from a prepared calibration graph.

APPENDIX 5—PUNCTATE BASOPHIL COUNTS

Make a thin blood smear on a slide of 0.8-1.0 mm thickness, fix for about one minute in methyl alcohol, allow to dry and stain for 30 seconds in Sellars stain (1 g methylene blue, 6 g sodium bicarbonate in 100 ml deionized water). Wash in tap water until the slide is a sea green color.

Using a dark ground condenser and an Ehrlich eyepiece set to a 6-mm square, count the punctate cells in ten consecutive fields. (Although in counting, the punctate cells are classified as large, medium, small, very fine, or polychrome, according to the size of the intracellular structure, this differentiation is for further reference on an individual case, and normally only the total count is given.) Close the eyepiece to a 2-mm square, and count the R.B.C. in this square. Repeat both counts five times on different parts of the slide, to give a punctate count of 50 large fields and an R.B.C. count of five small ones. Calculate punctate per 1000 R.B.C.

NONOCCUPATIONAL ASBESTOSIS

RAIMO KIVILUOTO

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Introduction

Pleural reaction is very often observed in asbestosis. In the advanced cases of this pneumoconiosis pleural fibrosis has been almost always found, and a clear correlation between pleural changes and the severity of the pulmonary fibrosis has been observed by several investigators. Observations on the occurrence of pleural calcification in asbestosis have also been made. Reports of pleural calcification as a roentgenologic sign or complication of asbestosis have especially been made by the German authors (1). In addition to advanced cases of asbestosis, special cases have been presented in which pleural calcification has been the chief finding (2). Except in asbestosis, pleural calcification has also been observed among workers exposed to talc and mica (3, 4) or to various dusts including a short exposure to asbestos (5).

The diagnosis of pneumoconiosis is primarily based on occupational exposure to dust. Only very few reports of pneumoconioses without occupational exposure may be found in the literature (6, 7, 8). In Northern Karelia, Finland, during few past years interest has been attracted by the high incidence of cases of pleural calcification showing a rather curious and characteristic roentgenologic picture, very similar to that observed in pneumoconioses. The cases have been mainly found among the residents of a certain area, and in these cases no previous history of adequate pulmonary or pleural disease could be elicited. The occupations of the patients showed no uniformity, and the main part of the patients had no clinical symptoms of pneumoconiosis. A study of the areal distribution of cases revealed that they were grouped round two anthophyllite-asbestos mines. Asbestos constituted the common external factor sought. Even from a solely roent-

genologic point of view, asbestos dust inhalation had been considered the most probable etiology.

Pleural calcification resulting from hemothorax, tuberculosis, or empyema usually occurs unilaterally and is situated on the visceral pleura. In most cases marked pleural thickening and displacement of the intrathoracic organs is observed. The calcification resulting from dust inhalation usually occurs bilaterally and is most often situated on the parietal pleura. In advanced cases calcium deposits are found in the lateral parts of the chest, basally and mediastinally. The calcium deposits take various forms—large confluent plaques, bizarre figures, or roundish spots.

The Roentgenologic and Clinical Picture of Cases Observed in Northern Karelia

In the advanced cases calcium deposits are found bilaterally in the central parts of the diaphragm; on chest walls, especially anterolaterally but also dorsally, and on the mediastinal surfaces. In the incipient cases the calcium deposit takes place either on the anterolateral chest wall, more often on the left, or in the central parts of the diaphragm, apparently more often on the right. Pericardial calcification is sometimes present.

The calcium deposits are located on the parietal pleura. In a series of 150 cases no interlobar calcium deposits were observed. The parietal location has been demonstrated by diagnostic pneumothorax examinations, and it has also been noted in some autopsied and surgical cases. Using a tangential roentgen beam, the parietal location of solitary plaques may be observed, these plaques having their bases toward the inner chest wall or toward the diaphragm. In advanced cases the lack of soft tissue mass between the calcium deposit

and inner chest wall due to the parietal location is apparent, and diagnostical pneumothorax examination is seldom needed.

The majority of cases of pleural calcification described above have been clinically symptomless. In a series of 150 cases the ordinary chest roentgen examination by P-A and lateral projections revealed pulmonary fibrosis, corresponding to the anteprietary or primary stage of pulmonary asbestosis in only about 14 per cent. Even the main part of these cases had no subjective respiratory symptoms.

The series mentioned above has been selected solely according to the roentgen diagnosis without reference to other factors. The concentration of the cases around two asbestos mines in Kuusjärvi and its neighboring communes has as yet been the only way to confirm the roentgen diagnosis. The majority of 25 cases living outside this area had previously lived there. According to these facts, any other etiology would be very difficult to credit. In very few cases a previous occupational exposure to asbestos dust has been observed, which lends slight support to the roentgen diagnosis. The diagnosis has as yet not been confirmed by other methods. In the sputum of 20 cases no asbestos bodies were found, and asbestos fiber in one case. Small amount of anthophyllite asbestos was found in the lung of an autopsied case and in the lung of a cow from the vicinity of the asbestos mine.

Discussion

The total number of cases of pleural calcification around the two asbestos mines amounts to over 800, as previously reported by the author. This number of cases was found in a mass survey of about 10,000 adult inhabitants and may include cases with previous occupational exposure to asbestos dust. In the history of the main part of cases examined at the Central Hospital of Northern Karelia the lack of occupational exposure has, however, been apparent. Some of the patients have not had any idea how the dust inhalation could have happened; the same cases have presumed that the dust rising on the roads might be responsible. In Northern Karelia the roads (highways) do not have pavement. Without mineralogic examinations it is, of course, impossible to decide whether these calcifications are resulting from inhalation of anthophyllite-asbestos dust originating from the asbestos mines or from surface deposits of other fibrous dusts, such as tremolite-asbestos, which is a very common mineral in Northern Karelia. The first alternative seems to be more probable.

In occupational pneumoconiosis some authors have called attention to the absence of pulmonary fibrosis besides the prominent appearance of the pleural calcification (2, 5); on the other hand, a clear correlation has been observed between the severity of pulmonary fibrosis and pleural calcification (9). In nonoccupational asbestosis it is apparent that extensive calcification may occur without any roentgenologically detectable pulmonary fibrosis. It seems possible that even very small amounts of asbestos fibers may cause pleural calcifications.

Anthophyllite is more stiff than serpentine asbestos. In animal tests brittle mineral fibers have not caused pulmonary fibrosis (10), but fibrosis has been observed in workers exposed to anthophyllite-asbestos dust (11, 12). Further studies are needed to reveal the part possibly played by asbestos as an etiologic factor in

pulmonary fibrosis among residents around the two asbestos mines.

Some investigators have pointed out the difficulty of attributing the calcification to inhalation damage in view of its parietal location, few, if any, changes being observed in the lung or the visceral pleura (2, 5). It seems possible that the asbestos fibers move with the lung and visceral pleura in relation to the parietal pleura, thus causing capillary hemorrhages on this only, as previously presented by the author. The hemorrhage coagulates and organizes, forming a collagenous plaque which slowly calcifies. This theory could explain the course of the process resulting from inhalation of small quantities of fibrous mineral dust.

The clinical significance of the pleural calcification seems to be slight, the majority of cases showing no clinical respiratory symptoms. Further investigations on this point are needed.

From roentgenologic point of view, this endemic pleural calcification is of some significance. The roentgen diagnosis is in typical cases easy but in some cases difficult. Early pleural changes on the anterolateral chest wall may simulate infiltrations, and large calcified plaques may cause difficulty in interpretation of pulmonary changes by hiding infiltrations. The high kilovoltage technique can hereby be especially recommended. In chest roentgen examinations of workers of asbestos mines in Northern Karelia and of Outokumpu Copper mines located in the same area attention must be paid to the fact that even extensive bilateral pleural calcification does not have to be a sign of severe pulmonary changes resulting from occupational dust exposure.

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A REVIEW OF RECENT DEVELOPMENTS IN OCCUPATIONAL PULMONARY DISEASES OTHER THAN SILICOSIS

LEO NORO, M.D.

Finland

At the Twelfth International Congress on Occupational Health held in Helsinki three years ago, the French Professor Marchand presented a review of the subject mentioned in the title, a large and comprehensive bibliography being attached to his presentation. The Organizing Committee has at this time asked me to present a review of the same subject from the last several years. It must at once be said that the compiling of such a bibliographic review has not been an easy task. More than ever before, research work has been focused on occupational pulmonary diseases. The problem has been discussed at national and international meetings, the last time being only two months ago in Milan. From the literature which has been at my disposal, I have found almost 316 articles from the recent years dealing with this subject, and yet I cannot have had access to all the articles from this field published in the world. I shall follow, with some exceptions, Marchand's classification.

There is reason to state at the onset that the constant industrializing is causing the air we breathe to become more and more polluted. Great masses of people, even the peoples of the so called less-developed countries, are changing their breathing air through their movement from agricultural to industrial centers. I am here thinking specifically about the huge industrialization process right now taking place in India and China. But man's breathing organs, and especially his lungs, do not come in contact with hazardous influences only in the working environment. The most common pollutant of our breathing air—tobacco smoke—is rapidly triumphing all over the world with the rising standard of living, in spite of the efforts we doctors take to warn mankind of its danger. The automobile industry is producing cars in a rapid tempo to pollute the air of the traffic roads. With the growing population centers, and their increased use of fuel for power and heating, more pollutants enter the air. Bacteria, viruses, sponges, and other small organisms have not disappeared either. Thus, the environment of man, with reference to lungs, is changing continuously. While the great enemy of the lungs, tuberculosis, is gradually disappearing, new diseases are arising, giving new importance to the air impurities. Chronic bronchitis, asthma, emphysema, and lung cancer are already much more important diseases than tuberculosis in countries with highly developed industry and a high living standard.

Man himself and the changing of his reaction to the environment also require attention. Allergies are one problem, for example. The danger of allergens affecting organisms through the respiratory and digestive organs and the skin is continuously increasing; new medicines, foods, cosmetics, etc., are common allergens. Allergic reactions are important when we consider the breathing organs and their obvious connection with the air impurities. Many of the chronic occupational diseases of the lungs occur only after a long exposure time. We are gradually, however, observing the signs of these diseases among those occupational groups which have been exposed for some length of time.

Our knowledge of many factors influencing the lungs is already fairly complete: I am thinking only of asbestosis; those many chemicals causing acute lung injuries, such as chlor or nitrous fumes; and the diseases caused by bacteria, sponges, or viruses. Often our knowledge is still very restricted, and the interpretations in many individual cases are difficult to make. This is true of allergic diseases and chronic bronchitis, lung cancer, emphysema, and fibrosis on the whole, and especially of the role of nonprofessional and professional environments in their occurrence. Yet we have, with special appreciation to Great Britain's excellent vital statistics, important evidence at our disposal of the relationship between occupation and certain pulmonary diseases, such as chronic bronchitis.

After this general survey, now let us study the details. Since silicosis will be discussed in another connection, I shall begin with asbestosis.

Asbestosis

The major part of our present knowledge concerning asbestosis is contained in the excellent German book that appeared some months ago, *Die Asbestose der Lungen* by Bohlig-Jacob-Muller. This book contains, in addition to 700 of their own cases, references to practically the entire world literature in this field (some 650 references). There is nothing basically new about the pathogenesis, clinic, prognosis, and prevention of this disease. Further information is, however, obtained about the frequency of clinical symptoms as well as roentgenologic and bronchographic observations from the authors' careful examination on their material of 700 cases. The relationship between asbestosis and lung cancer is still statistically indetermined. In spite of this, "asbestos cancer" exists, and the authors give their own specification to it.

Does asbestos dust have similar nonoccupational affect as, for example, beryllium? This is a problem that has been exposed through the observations of 126 nonoccupational pleural calcification cases (so-called neighborhood cases) that had been found in the population living around two open asbestos quarries, published by the Finnish Dr. Kiviluoto. According to this study, the details of which the author will present himself at this Congress, more than 800 pleural calcification cases were found in the minute x-ray investigation of farmers, workmen, and their wives, who never had any occupational exposure. Calcification was usually located in parietal pleura, as it is also most often in occupational asbestosis. In most instances it occurred bilaterally on the inner chest wall. Basal and mediastinal calcification was also often observed, a pulmonary fibrosis being found only on a few cases. The calcification was noticed to appear slowly. These roentgenologically noticeable changes gave insignificant clinical symptoms. These observations make it evident that measures must be taken to prevent the air pollution of the environments surrounding the factories and asbestos quarries. The results of Dr. Kiviluoto's work are motivation for similar investigations in other countries to certify these observations.

Other fibrotic lung diseases and "benign pneumoconiosis" caused by silicates, mixed or non-silica dusts (Glass wool, sericite, sillimanite, talc, anthracol, carborundum, cement, Fuller's earth, china and ball clays, graphite, gypsum, kaolin, limestone, marble, mica, Thomas (basic) slag, etc.)

I shall pass this group with a brief mention of talcosis and graphite lung, which are still objects of continuous research. With great enough exposure, undoubtedly, the dusts of this group have their effect in the occurrence of fibrosis. However, it is evident that with improved hygiene these types of pulmonary changes will become more and more rare.

Pneumopathies due to toxic chemicals and metals

GASES, FUMES AND VAPORS (Cl, NO₂, SO₂, borans, desmodur, hydrocarbons, oils, kerosene, etc.)

METALS (Aluminium, antimon, barium, beryllium, cadmium, chrom, cobalt, fluor, gold, iron, manganese, nickel, osmium, platinum, selenium, sulfur, tungsten, titanium, vanadium, wolfram, zirconium, etc.)

The amount of toxic chemicals and metals influencing the lungs is continuously growing. Vanadium, chrom, and beryllium have been subjects of research, especially in Sweden and in our host country, the U.S.A. The importance of vanadium is especially increasing. It is necessary, however, to bear in mind that with the expanding use of oil heating, the crude oil coming from various parts of the world contains vanadium in very different amounts. The role of the acid sulfur compounds in the ashes is also to be remembered. For a detailed study of beryllium, I would refer you to the proceedings of the conference held at the M.I.T. in 1958 (*A.M.A. Arch. Indust. Health*); a comprehensive list of references on beryllium is contained in a publication on these proceedings. We in Europe, to my knowledge, do not have the big problems with beryllium which seem to exist in the U.S.A.

It is impossible, in this short presentation, to name all the new chemicals with irritant effect on the lungs. We industrial physicians have special difficulties attempting to evaluate the aftereffects of acute irritants to the lungs (nitrous fumes, Cl, SO₂, etc.), especially with reference to etiologic differential diagnostics in chronic bronchitis and emphysema.

Pneumopathies due to organic dusts, allergens and pneumomycoses (Actinomycosis, aspergillosis, coccidioidomycosis, cork (suberosis), cotton (byssinosis), drugs, dyes, feathers, flour, grain, gum acacia, hair, hay (farmer's lung), histoplasmosis, jute, leather (cannabiosis), linen, moniliasis, nocardiosis, sporotrichosis, sugar cane (bagassosis), tobacco (tabaccosis), tropical woods, etc.)

The agricultural population has received increased attention during the last few years in the investigation of the relationship between work and health. "Farmer's lung" and other pulmonary diseases found in agriculture have proved surprisingly common upon closer investigations. Unfortunately, so far there have not been powers to investigate these conditions in the countries where the agricultural population works under the worst hygienic conditions. We have not enough knowledge about the pulmonary diseases of the workers in the old Asian rice mills, for example.

The effect mechanism of most organic dusts is still unclear, and we are also in a difficult field, where bacteriology and allergology will be of much help in

several cases. What factors effect in different conditions—acute, subacute, chronic; proteins, alcaloids, irritating mechanic factors, toxic, allergic, bacteria, the silica included—are questions that are still waiting to be answered. In addition, for example, the experience with byssinosis is still contradictory in different countries. The interesting research results of Dr. Schilling of England make one think that this disease has not yet disappeared as has been contemporary thought in my own country.

Infectious and parasital pneumopathies (Amebiasis, anchylostomosis, anthrax, bilharziosis, brucellosis, hydatidosis, leptospirosis, ornithosis, tuberculosis, tularaemia, etc.)

With the diseases of this group there are continuous difficulties in etiologic diagnostics: when is the infection to be considered due to work and when not? The question is very important, for example, with tuberculosis. Of course, the relationship between tuberculosis and pneumoconiosis is under constant study.

Lung cancer due to occupation (Arsen, asbestos, chromates, isopropyl alcohol manufacturing, nickel, radioactive substances, etc.)

The Secretary General of our Congress, Dr. Eckardt, handles the role of working conditions in the occurrence of cancer in his book *Industrial Carcinogenesis* most variedly and with good criticism. Yet it is to be suspected that in industry many other substances also have a cancerogenetic effect. Our knowledge in this field, however, is still very limited, and although experimental cancer research has gone far, we still lack in practice necessary facts. It is hoped that the well-endowed cancer organizations and research institutes will more than before concern themselves with the occupational aspects in the etiology of cancer.

The results from the investigation by U.S. Public Health Service concerning the hazards of radiations to miners are expected with great interest. Whether the cases of Schneeberg and Joachimstal will get successors in the very widespread uranium mining is a question that will presently be answered.

Pneumopathies caused by radiation

The influence of radiation as the cause of cancer has already been referred to above. Our knowledge about the other effects of radiation on the lungs are very small. In connection with therapy, large doses (1000-2000 r.) have been found to cause changes in the lungs in the form of pneumonitis and fibrosis. From East Germany there comes the report of a chronic pneumonia case of a chemist, which led to death; the cause of death being considered the breathing of radioactive dust over a period of 20 years.

Conclusion

To our present knowledge, we already have a foundation for the technical prevention of these diseases. We are as yet in a weaker position as to their medical prevention: we know too little about why one person gets them and one does not. This question requires much research.

We have already reached far in the roentgenologic diagnostics of the pulmonary diseases, and there we are making constant progress. We are also aware, however, of the difficulties therein as to several of the disease groups referred to above. Together with the roentgenologic examination we must develop other clinical

examination methods, especially the physiologic lung function diagnostics. In its most advanced form, we have to apply it not only in laboratories but, above all, in the field examinations to the examination of population groups exposed to different exposures.

Above all, we need also in this field keen international collaboration to solve our common problems and to exchange information so that each of us in his own country could apply in practice the knowledge we already possess to the betterment of our working population.

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TREATMENT OF PLUTONIUM DEPOSITION IN HUMANS WITH DTPA — EFFECTIVENESS OF LONG-TERM ADMINISTRATION AND ORAL ADMINISTRATION*

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The recommended maximum permissible amount of soluble plutonium (Pu 239) in the human body is 0.04 microcurie—0.6 μ g (1). Rigid control methods are necessary to limit body deposition to this extent. For instance, allowable concentrations in air are lower by a factor of millions than the comparable allowable concentrations of many of our most toxic chemicals. There will be increasing potential for exposure to such isotopes with the expanding use of such materials in industry, defence, and medicine. Hence it becomes most important to have the safest, best, and most convenient method possible for treating the individual who has accidentally acquired a deposition of Pu 239 which exceeds the maximum permissible limit.

Treatment, here, of five employees who had harbored small quantities of Pu 239 for some years indicated that intravenously administered diethylenetriaminepentaacetic acid (DTPA) was much the most effective agent discovered to date for increasing the urinary elimination of Pu 239 (2).

The present study was made to improve knowledge of the effectiveness of DTPA in eliminating Pu 239 via the urine when treatment is extended over a period of many months. It was also directed toward determining the effectiveness of DTPA in increasing elimination of Pu 239 via the urine and feces when administered orally.

Long-Term Administration of DTPA

An employee who had accidentally received a deposition of about .4 microcurie of Pu 239 some 30 months previously was treated with DTPA intravenously. Initially the daily urinary output of Pu 239 was about 665 disintegrations per minute per 24-hour specimen of urine (Table I). It was considered advisable to cautiously continue treatment over an extended period unless evidence of kidney irritation or other untoward effect appeared during the treatment. This

would serve the dual purpose of eliminating a fair amount of Pu 239 and indicating whether or not there was a change in effectiveness of this agent when used over an extended period.

TABLE I
EFFECTIVENESS OF INTRAVENOUSLY
ADMINISTERED DTPA IN INCREASING
URINARY EXCRETION OF PU 239 WHEN
GIVEN FOR MANY MONTHS

Week of Treatment	Dose—DTPA in Grams Per Week	Average Daily Urinary Excretion of Pu 239 Expressed as Disintegrations Per Minute	Effectiveness Expressed as % of Initial Effectiveness
1	2	665	100
2	1.6	610	92
No treatment for period of 5 weeks			
11-12	1.6	481	72
13-14	2	495	74
No treatment for period of 5 weeks			
26	2	15	—
27	2	496	74
33	2	436	66
46	2	246	37
50	2	190	29
50	2	125	19

Average daily elimination of Pu 239 for periods preceding and following the above treatment was 12 disintegrations per minute in 24 hours.

*The DTPA for this study was kindly supplied by Dr. Murray Weiner, Geigy Pharmaceuticals, P.O. Box 430, Yonkers, New York. R. H. Wilson was most helpful in coordinating sample collection and assisting in the interpretation of results. G. D. Brown and staff performed the bioassays of the many samples.

Except for minor changes as shown in Table I, the employee was given 1 g of DTPA intravenously, in the Manufacturing Area Medical Center, on Monday and 1 g on Thursday of each week for three successive weeks. Such periods of treatment were alternated with periods of three weeks of no treatment. This was con-

tlement above the loss of wages the longer he was off work.

This case illustrates how an individual deliberately perpetrates his disability on a subjective basis in order to increase the size of his monetary settlement.

CASF No. 3—A 37-year-old trainman was injured while standing too close to a slowly moving train when his arm was struck by a grab iron, causing him to spin around and strike his head against the side of a car. He received a 5-cm vertical laceration across the middle of his forehead. The man was stunned but remained on his feet. The laceration was repaired at the plant dispensary. X-rays of the skull were negative. There were no other injuries except for a slight contusion of the right upper arm. Neurologic examination was entirely negative and remained so thereafter. No treatment was indicated other than analgesic medication for pain. The patient did not work his next turn and was seen again the following day. The previous night he had a mild headache but was now asymptomatic. Examination was again negative. The patient was seen again four days after the accident. The sutures were removed, and adhesive bridges were applied. His only complaint was occasional frontal headache which was relieved by aspirin. He had not returned to work; and when questioned as to why, he gave some vague complaints of soreness in his right arm and upper back. Examination was again negative for objective findings. It seemed to the physician that the man believed he could and should be working but for some reason had not done so. He was formally approved for work and was so advised. The patient returned to work six days after the accident and worked for several hours but then reported off because of headache. He was seen again the following day, complaining of headache, dizziness, and soreness of the upper back and right arm. The laceration was healing well. Examination results were negative once again. He apparently did not intend to work; he was treated symptomatically and seen again one week later, at which time his condition was unchanged. Following this visit he was not seen again for another two weeks. It was then 24 days since the injury. The

patient had taken his vacation in the interim, for which he had received vacation pay. He offered no complaints, and the examination was again negative. The man finally returned to work 30 days after this injury and remained at work thereafter. He instituted litigation against the company, because he demanded compensation about seven times his actual loss of earnings, and the company refused to grant the claim.

Each time this patient was seen during the 30-day period it seemed that he really believed he could work and that he actually wanted to. He was physically able and was not considered as having post-traumatic neurosis. Why then did he not work? There appeared to be several reasons. While the patient was being treated in the dispensary shortly after the accident, a company representative remarked that it would be good if he did not miss work, since his work group had gone for an unusual length of time without a lost-time accident. This was interpreted by the patient and his fellow workers as company interest in avoiding lost time rather than the employee's welfare. Resentment was incited and led to deliberate lost time. The patient was also encouraged to miss work because he had a head injury which required suturing. Another factor which played a part was encouragement by certain parties to deliberately perpetrate unnecessary lost time for the purpose of establishing a claim against the company for income greater than his regular earnings.

This case illustrates how management action, work group standards for lost time, and litigation practices in work groups interfere with the medical management of the injured employee and create unnecessary disability leading to excessive monetary gain.

Summary

In summary, I have outlined certain socio-economic factors that have a negative influence on the disabled employee. The discussion has dealt with why and how such factors interfere with the individual's recovery from an occupational injury, with the thought that a clearer understanding must precede any effort to do anything about them.

BASIC PRINCIPLES FOR PRECAUTIONARY LABELING

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It is an honor and a privilege to speak to you, as a representative of the Manufacturing Chemists' Association, regarding one of its activities. The Manufacturing Chemists' Association is an incorporated national trade organization composed of more than 180 companies engaged in the manufacture and sale of chemicals. These companies account for more than 90 per cent of the chemical production capacity of the United States.

From its founding in 1872, the MCA has been concerned with the many problems accompanying the growth of the chemical industry. Prominent among these has been the promotion of safety, and the Association is proud of its contributions to the record of chemical manufacturers in this regard, which is among the best in all industry. This achievement is the

more notable in view of the inherent hazards in many of the industry's processes and products.

The Association's interest in safety goes far beyond that of its members' employees to include those transporting, handling, and using its products. The objectives are promoted in a number of ways, but I shall discuss at this time only that phase concerned with the labeling of chemicals to instruct those handling or using them how to do so safely.

In the early days of the industry both the chemicals distributed and the trades using them were limited in number and each had been long established. Customers were so accustomed to the use of the existing compounds that specific instructions seemed unnecessary, and such warning labels as were used on industrial chemicals were limited to the stronger

acids and alkalis, and extreme poisons. There were, of course, the 1927 Federal Caustic Poison Act and a number of state poison and pharmacy acts, but these were chiefly directed to the labeling of household packages. In most cases they were pointed toward the hazard of ingestion and relied solely on the word "POISON" to warn the user.

The expansion of the industry and the broadened use of its products brought recognition of the need for more comprehensive labeling. One of the early steps in this direction came in 1934 and covered the uniform precautionary labeling of six products or product groups under a series of voluntary agreements between the manufacturers of these products and the Surgeon General of the United States. These agreements served a very useful purpose until they were discontinued by the United States Public Health Service in 1952 because specific labels for these products which had, in the meantime, been developed under the Manufacturing Chemists' Association's program were considered more appropriate.

As chemical products, especially in the organic group, multiplied and grew more complex, the need for further steps became evident. This was emphasized by a survey conducted by the Association in 1936 which resulted in distribution to its member executives of a printed book titled "A Confidential Report on Adequate Labeling—Its Importance to the Chemical Manufacturer." This report persuaded many companies to embark upon their own warning label programs or to expand those already begun.

World War II greatly accelerated the growth of our industry. Not only did established companies expand their production of well-known chemicals, but they developed innumerable new ones. Many corporations from other segments of industry, as well as completely new concerns, began chemical manufacture. And—most important of all, from the point of view of precautionary labeling—thousands of individual companies, large and small, and millions of workers began to operate processes using chemicals entirely foreign to any of their previous experiences. The need for a comprehensive program of education in the safe handling of chemicals was obvious. Early in 1944 MCA considered the problem at a meeting of its member executives. It was decided that the best method to reach the man in the shop using chemical products was by means of instruction labels, and the formation of a "Labels and Precautionary Information Committee" was accordingly authorized.

The LAPI Committee, as it has since been popularly called, met for the first time on May 17, 1944. To insure a broad view of the problem, the members selected included those with chemical, medical, legal, research, administrative, and sales backgrounds. Since that date, this has been a continuing and active committee. The work of LAPI is well known to industry and administrators of health and safety programs through its publication "Warning Labels—A Guide For the Preparation of Warning Labels for Hazardous Chemicals." This manual, frequently referred to as the "LAPI Manual," is now in the review stage, with a Fifth Revision scheduled for publication this year.

It might be assumed that, having agreed upon the need for precautionary labeling, the writing of labels would be simple. All one need do, you would say, is to mark a hazardous product POISON and add the

do's and don'ts. Unfortunately, the problem is more involved than that.

What are the meanings of the terms used? Chemicals may be harmful in a variety of ways. A product which may threaten your life solely by ingestion should not be labeled the same as one that may kill by absorption through the skin. Of course, there is also the matter of degree. How shall we distinguish between the vapor or gas which asphyxiates and one which causes cyanosis? What really is a "poison"? There is the difficulty of language. Statements must be brief but accurate. They must be expressed in terms that ordinary workmen understand. Not only must the statements help avoid accidents, but if such occur, first aid should not be delayed while someone hunts an interpreter. In the case of trade-named chemicals or proprietary compounds, what is our responsibility to the doctor who may be asked to treat persons injured by them?

As a result of these and many similar questions, the following principles were adopted. These principles are set forth in detail in and comprise Part I of the LAPI Manual.

1. Each chemical product presents a distinct problem and must be treated individually in the light of its own characteristics. Conclusions regarding the hazards of a product cannot safely be drawn either from the properties of the materials from which it is formed or by analogies based upon chemical structure. Mixtures of two or more chemicals may have properties that vary in kind or degree from those of the individual components; any warning label for mixtures should be based on the properties of the finished product. Impurities may contribute hazardous properties and should not be overlooked.

2. All statements on warning labels should be brief, accurate, and expressed in simple, easily understood terms.

3. Precautionary labeling should be used only when and to the extent necessary. The language should be practical, not based upon the inherent properties of a product alone, but directed toward the avoidance of hazards resulting from such use, handling, and storage as may reasonably be anticipated. The use of warning labels for relatively harmless products or the use of unnecessary words will develop a disregard for labels and defeat their purpose as surely as will failure to give adequate notice of hazards.

4. On labels of different products uniformity in language to indicate the same hazards and same degrees of hazard is most desirable in order to gain greater understanding through standardization.

5. The following subject matter should be considered for inclusion on a warning label: (a) name of product; (b) signal word designating degree of hazard—DANGER!, WARNING!, or CAUTION! (c) Affirmative statement of hazards; (d) precautionary measures covering actions to be followed or avoided; (e) Instructions in case of contact or exposure where advisable. (NOTE: under some laws antidotes are required when the word "POISON" is used.) Instructions for the handling and storage of containers should also be considered for inclusion on the label. This is information relating to characteristics of the container as well as those of its contents.*

6. The inclusion of the word "POISON" and the skull and crossbones on a label should be limited to those cases where the product is a poison according

to a definite toxicity standard or where such use is prescribed by law. When used, this legend should be in addition to the other label warnings and should not take the place of the words DANGER!, WARNING!, and CAUTION!, which are designed to show the relative degree of hazard.†

7. A nondescriptive code designation or trade name should not be used as the only identification of a hazardous chemical. If the complete name is not shown, the label should clearly state the type of chemical—e.g., "Corrosive Acid", "Lead Compound".

8. Warning statements should be grouped together in a prominent location on the label and should be printed in easily legible type which is in contrast by typography, layout, or color with other printed matter on the label. The label should be affixed firmly to and in a conspicuous place on the container.

In accordance with the principles just stated the usual warning label includes: (a) a "signal" word—"DANGER!", "WARNING", or "CAUTION"—to give a general indication of the severity of hazard; (b) a statement of hazard or hazards—such as "Vapor Extremely Hazardous", "Causes Burns," or "Rapidly Absorbed Through Skin"; (c) precautionary measures—such as "Do not breathe vapor," "Keep away from heat and open flame," or "Avoid contact with skin and eyes"; and (d), where appropriate, instructions in case of accident, as "In case of contact immediately flush skin or eyes for 15 minutes; for eyes get medical attention."

Using these or similar statements, a typical label may read:

ANILINE
DANGER! HAZARDOUS LIQUID AND
VAPOR RAPIDLY ABSORBED THROUGH
SKIN

Do not get in eyes, on skin, on clothing.

Avoid breathing vapor.

Use only with adequate ventilation.

In case of contact, immediately remove all contaminated clothing, including shoes, and flush skin or eyes with plenty of water for at least 15 minutes; get medical attention. Wash clothing before re-use.

POISON

**Author's Note: The Manufacturing Chemists' Association has available at its office, 1825 Connecticut Avenue, N.W., Washington 9, D.C., at nominal cost, a series of individual Chemical Safety Data Sheets on the properties and essential information for safe handling and use of 79 chemicals, Manuals on Standards and Recommended Practices on the use and handling of specific containers, and an outline of recommended general precautions for handling and storage of certain classes of containers in the MCA LAPI Manual. These data will serve as excellent guides in the development of applicable phrases for container handling and storage statements.*

†*Author's Note: The word "POISON" has been used indiscriminately in the past, and its meaning has been ill defined. For labeling purposes the MCA Manual recognizes poisonings by three modes of entry—viz., ingestion, inhalation, and absorption through skin—but limits use of the word to those cases where the toxicity has been demonstrated, either by human experience or laboratory animals tests, to exceed certain defined limits.*

Parts II and III of the LAPI Manual contain several hundred illustrative labels such as the one shown. Those in Part II are for industrial chemicals. Examples included are generally for those products most important commercially, and, as a whole, they take in a broad range of hazards. The labels in Part III cover the majority of pesticides sold in large volume. This section was added following the passage of the Federal Insecticide, Fungicide, and Rodenticide Act in 1947. The latter requires adequate warning labels for this important group of chemicals, and the MCA labels have the informal approval of the United States Department of Agriculture and are consistent with its Interpretation 18, Revision 1.

How successful is the LAPI Program? As may be expected, the LAPI principles have the broad support of MCA members, who, as stated earlier, represent 90 per cent of the U.S. production of industrial chemicals. In fact, chemical manufacturers, both in and out of the Association, fully supported these principles. The very fact that such a program exists and is supported exerts a persuasive force upon the manufacturer who might otherwise neglect proper labeling. The latter knows that, should he be called to court because of claimed injury by one of his inadequately labeled products, the opposing counsel would surely cite the warning statement used on similar competitive products.

Within months after the organization of the LAPI Committee in 1944, its chairman was asked to serve as advisor to the State of California, which subsequently became the first of several states to regulate the precautionary labeling of hazardous chemicals. Besides California, the ensuing years have seen similar regulations or laws adopted by Connecticut, Oregon, Hawaii, Illinois, Texas, New Jersey, New York State and New York City. All have been based upon the MCA principles.

Reference has already been made to the Federal Insecticide, Fungicide, and Rodenticide Act, and to the fact that LAPI labels comply with the regulations issued pursuant to it.

At meetings of the International Labor Organization, held in Geneva, Switzerland, the MCA's precautionary labeling system was endorsed and much of its content adopted for ultimate use by ILO on a world-wide basis.

A committee of the International Association of Governmental Labor Officials, which consists of U.S. and Canadian state, provincial, and federal administrators, has developed a "Suggested Draft for Uniform Rules and Regulations relating to the Labeling for Use, Handling, and Storage of Containers Holding Substances Harmful to the Safety and Health of Employees." This draft adheres to LAPI principles and was the foundation for the current regulations in New Jersey and New York State and City.

In this highly regulated era—when all of us, and industry particularly, are subjected to many restrictive laws and regulations—it is to the credit of the chemical industry that its adequate labeling practices began as a voluntary program and that the labeling legislation of recent years has been in support of the industry's principles rather than controverting them.

Further evidence of the LAPI Committee's influence is the fact that definitions for "POISON" substantially identical with that of its manual were written into the regulations under the Federal Insecticide Act and have also been substituted in the

Interstate Commerce Commission Regulations for the former definition of "Class B. Poisons." Again, LAPI has been instrumental in obtaining the acceptance of the word "flammable" by ICC and other public agencies as less likely to be misunderstood than "inflammable." Its reputation has extended so far that in 1953 the Association of British Chemical Manufacturers, which is MCA's British counterpart, sent representatives to this country solely to study the LAPI program and subsequently adopted one paralleling it.

This program is receiving additional impetus from other trade associations, which have been most generous in their cooperation. As already indicated, the LAPI objective is principally aimed at industrial chemicals. While the principles are generally acceptable to all groups, their application may vary in detail for different segments. A committee of the Chemical Specialties Manufacturers Association has prepared a model law for the labeling of household products. Directions for use are usually an important addition to small household packages and may convey information for proper use which supplements the precautionary statements. Similarly, the American Petroleum Institute recently published a manual of precautionary labels for petroleum products as distinct from petrochemicals. Both associations support LAPI principles.

The common aim of all these groups is the adequate and uniform labeling of the hazardous substances which they produce. Uniformity is essential for the free flow of commerce and important in educating people to understand the significance of label warnings. The public must be led to recognize that chemical products may, on occasion, be hazardous and require care in handling, just as experience teaches us that care in handling is necessary with edged tools and with electrical and mechanical devices. Unlike the latter, which seldom carry warning labels, chemicals will always require some precautionary labeling, because their properties can seldom be determined by visual inspection.

In conclusion, I should like to emphasize that any precautionary labeling program based upon the principles set forth by the Manufacturing Chemist's Association could not be considered experimental. The concept on which such a program was based has been time-proven and accepted in similar programs internationally. With such a program you have not only taken out insurance on the future of your products, but you have provided a necessary adjunct in the fundamental obligation to warn of the health hazards involved in the use of either new or established products.

I thank you!

THE CARDIAC CASE IN WORKMEN'S COMPENSATION

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It is my great pleasure to be able to address this thirteenth International Congress on Occupational Health. It is significant that common problems know no national boundaries, and together we have sought remedies in different countries of the world for over 30 years. It is apparent that this is the only sound method by which we can solve these problems. It is of additional significance that we are thus able to set a good example of the way in which other matters may be disposed of.

This afternoon we are to consider the cardiac case in workmen's compensation. To merely dismiss it with the wave of the hand is unworthy of the talent and intention of this organization. A search into the causes and results in this area is necessary and important. There is a continuing and growing interest in the cardiovascular episodes during and in the course of employment. Recently great attention has been paid to the increasing number of these cases which have come before the workmen's compensation boards for evaluation and adjudication. In New York State for the years 1947 to 1957 the figures have risen from 167 compensated cases to 545. For the first six months of 1960 up to 150 cases were closed without award for many reasons (failure to prosecute, withdrawal of claim, and failure to make out a proper case after trial). The most frequent involvement has been the coronary arteries resulting in postocclusive angina, failure, pulse irregularities, and infarction.

It is not necessary at this time to review the various skills involved in the diagnostic procedures, nor is it necessary to review the need for proper history and record keeping. We can safely assume that the

trained physician is fully aware of the need for these. There remains, therefore, only the consideration of the relationship of the pathologic process to the work load and the proper rehabilitation of the patient. It is suggested that the exact mechanics involved in the closure of a coronary vessel and the resultant myocardial infarction are not fully understood. It must be further conceded that the sclerotic process begins fairly early in adult life and this, undoubtedly, plays a large part in the occurrence in industry.

It has been the philosophy that the working man is hired for his abilities along with all of his disabilities, whether manifest or hidden. It is therefore incumbent upon the physician to be the first to recognize this in industry. Others should be cognizant of this as well. It appears to me that no defenses can be set up on the thought that in a given case with any degree of sclerosis the clinical end result would have occurred in any event. We must recognize that this type of reasoning leads nowhere, since generalizations have little value in this area. It is best to be prepared to take an attitude which appears reasonable to ordinary analysis and be ready to review each case on its own merits. Recognition that we do not have a full explanation at this time should not preclude us from drawing a conclusion.

It is important to keep in mind that the legal process is the dominant factor when the cardiac case in industry is discussed. Too often the physician becomes involved in a case to a point beyond his medical sphere. At that point he attains the status of an advocate in the proceedings for which he is not trained, for which he is obviously ill prepared and

daily work without intervals (which are not considered in stating MAC either) performing physical work which requires average minute lung volume of 12:1 (or 10:1; lower volume could be considered only for entirely sedentary work). From this calculation it was evident that a workman absorbs 3.4 g (or 2.8 g) of trichlorethylene in eight hours, modifies it into 850 mg (700 mg) of trichloroacetic acid and into 1897 mg (1412 mg) of trichlorethanol.

It is difficult to say how great is the pharmacologic effect of daily administration of 3 g of trichlorethylene, due to the fact that it does not occur in such doses in medical practice. In the past years 1 ml was administered per case in cases of angina pectoris or neuralgia n. trigemini, four times a day maximum. Beforehand, however, we can suppose a hypnotic effect especially if we take into consideration that the intermediary product in the metabolism of trichlorethylene is chloralhydrate. The ascertained daily dose of trichlorethylene corresponds, according to the American MAC, to 4.3 g of chloralhydrate. It is well known that the current hypnotic dose is 1-2 g, and it is also known that chronic intoxication with chloral is not very rare and is similar to chronic intoxication with trichlorethylene.

It is also possible to see to the effect of trichlorethanol, which is the principal metabolite of trichlorethylene and, in our opinion, it is primarily responsible for the symptoms of intoxication. Owing to the fact that pharmacologic literature does not often mention this substance, we can compare it with tribromethanol. Narcosis is attained by this substance after a dose of 3.5-5.6 g in a man weighing 70 kg. In our case there forms 1.9 g of trichlorethanol daily.

I think that these considerations result in the fact that the American MAC is rather too high. If it was created from experiments with animals, it is necessary to declare that animals are not suitable in trichlor-

ethylene cases because they have great desaturations by lungs and have entirely different ways of metabolizing trichlorethylene.

The dose required by Swedish authors, 50 mg of trichloroacetic acid in urine, corresponds theoretically only to the Soviet MAC—that is, 9 ppm about 50.

From our previous experiments, where we considered only trichloroacetic acid in smaller percentage, 16 per cent was found that in lower concentrations of trichlorethylene in air (up to about 400 μ g per liter—that is, 75 ppm) the ratio of trichloroacetic acid in mg to trichlorethylene in μ g in 1 l of air is about 1:2. This ratio was decreasing with the increasing concentration of trichlorethylene. Several observations from practice bear witness to this fact. From our recent experiments results that the ratio is theoretically 1:1 (Souček-Vlachová, Bartoníček). I think that it is not possible to give more accurate directions for practice, due to the great difficulties occurring in practical work and thus we can conclude that this ratio lies within the mentioned values 1:1 or 1:2.

On the basis of literature data that a great part of working people have health disturbances after a long-time work at 50 mg or 100 mg of trichloroacetic acid in urine per liter we see that it would correspond with 100 to 200 μ g of trichlorethylene in air. This concentration in air corresponds with 100-200 μ g of trichlorethanol in urine.

For the purpose of solving the question of MAC values in the most important industrial poisons there ought to be available a great number of carefully made observations in practice. It is also necessary to investigate, in laboratory experiments, the absorption, metabolism, and elimination of these substances. For medical thinking it is acceptable to consider the actually absorbed dose. Experiments with animals are suitable only for the orientation of newly introduced chemical substances.

SCIENTIFIC BASIS FOR THE ESTABLISHMENT OF TOLERABLE LIMITS ADOPTED IN THE UNITED STATES FOR THE PRINCIPAL INDUSTRIAL TOXINS

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In the United States, hygienic standards (tolerable limits) for inhalation are developed for the purpose of providing guides to be used for controlling exposures to toxic materials in industry. These guides are dependent on the basic philosophy that for most such materials there are levels of exposure which can be tolerated without adverse effect. The principal exceptions to this philosophy are those which are applied to carcinogenic and sensitizing materials. So little is known of the processes of carcinogenicity and sensitization that the tendency is to consider that levels of known carcinogenic and sensitizing materials should be kept as close to zero as possible. The problem, then, is to develop information which can provide a valid basis for establishing levels of toxic materials which can be tolerated in the industrial environment.

TERMINOLOGY

In order to avoid confusion it must be pointed out that there are differences in terminology with refer-

ence to acceptable values for exposures to potential toxic materials. Thus we find such terms as "Maximum Allowable Concentration," which certainly has the broadest usage; "Maximal Acceptable Concentration," which has been utilized by the American Standards Association Z37 Committee (1); and "Threshold Limit Values," which is used by the American Conference of Governmental Industrial Hygienists (2). All of these terms have the same basic implication—namely, that these values are allowable or acceptable or that there is a limit which denotes a fine line between toxic and nontoxic. As a matter of fact, the users of these terms rarely accept the implied connotations. The problem is one of semantics. In 1949 the Committee on Chemical Agents at the 9th Annual Congress on Occupational Health (United States) recommended that the term "Hygienic Guide" was much more descriptive of the actual utilization of the numbers. In September, 1955, the American Industrial Hygiene Association began publishing its

"Hygienic Guide Series" using the term "Recommended Maximum Atmospheric Concentration (8 hours)." In 1956 Smyth (3) proposed the use of "Hygienic Standards for Daily Inhalation." For some time the writer (4) has been urging the general acceptance of the concept of "Hygienic Standard" or "Hygienic Guide," since these terms express much more accurately the actual purpose of the application of such criteria in the occupational health field.

ORGANIZATIONS

In the United States the establishment of hygienic guides is carried on by groups of competent individuals operating within existing organizations and utilizing available technical information. The American Standards Association, a private organization representing American industry, has been sponsoring development of standards in the occupational health field since 1941, chiefly through its Z37 Committee. These "American Standards" include the scope and purpose as well as general physical-chemical and toxic properties, "Maximal Acceptable Concentration," and sampling and analytical methods and references. Since their start 19 such standards have been published, and the Committee is continuing to be extremely active in the field. The basis on which this Committee operates is set forth in the introductory statement provided with all of their standards, as follows:

"The Meaning of Maximal Acceptable Concentration" (1)

It is generally recognized that there are levels of concentration of atmospheric contaminants to which a person may be exposed without known ill effects or discomfort. In view of the impracticability of maintaining uncontaminated air in most industrial environments, it is necessary to establish acceptable concentrations of atmospheric contaminants encountered in industrial operations. These concentrations in themselves do not represent a scale of relative toxicity; they represent the concentrations of contaminants below which ill effects are unlikely to be experienced by any but hypersusceptible individuals.

These concentrations are usually based upon data obtained by one or more of the following procedures:

- (1) Laboratory tests on animals
- (2) Laboratory tests using human subjects
- (3) Environmental and medical investigations in plants

A common feature of these procedures is that the experimental exposure shall correspond to the normal work pattern. This should be taken into consideration also in the application of maximal acceptable concentration values.

Three criteria have governed the establishment of these concentrations:

- (1) Organic or other tissue changes
- (2) Functional reactions which have no discernible untoward effects on health but cause impairments, such as in-coordinations and increased proneness to accidents
- (3) Discomfort or adverse sensory effects

In those cases in which the concentrations have been established on the basis of organic changes, it is logical to assume that repeated exposure to concentrations significantly in

excess of the acceptable concentration probably would produce injury. When the level has been established on the basis of a functional change or discomfort, it is logical to assume that exposure to concentrations not greatly exceeding the acceptable concentration would not produce materially injurious effects. Hence it is important to understand the criteria upon which any such maximal acceptable concentration has been established.

Though the purpose of the acceptable concentration is to minimize health hazards, its immediate use is for guidance in establishing engineering procedures to prevent objectionable concentrations of toxic or noxious materials from being present in the air of work places. Comparison of the results of air analyses with those concentrations indicates acceptable conditions or otherwise the need, extent, and urgency of control measures. Sampling and analysis should be carried out by competent personnel using an acceptable method which will provide a reliable measure of exposure.

Air analyses in conjunction with acceptable concentrations of such atmospheric contaminants as are encountered in industrial operations serve as a measure of exposure—not as a means of diagnosis of occupational disease. Diagnoses should be based on a consideration of all factors including results of clinical and physical examination as well as of air analyses, means of assessing amounts of materials in the body, and a knowledge of toxicologic effects of the materials in question.

In the application of the standards, it should be kept in mind that:

- (1) The acceptable concentrations serve as standards of good practice.
- (2) They serve as engineering guides. Design and operation should aim at maintaining all concentrations below the acceptable maximum.
- (3) They should be applied and interpreted by competent individuals with a full understanding of the basis and limitations of the information from which the standard has been developed.
- (4) It is advised that these standards are considered to be guides toward good industrial hygiene and are not intended as legal requirements.
- (5) The levels are applicable only to exposure to a single substance. In the case of exposure to mixtures, the effect may be increased or decreased, and controls should be based on the specific situation.

The American Conference of Governmental Industrial Hygienists began its work in the standards field in 1947. They publish annually a list of the materials, with values, which they call "threshold limits." The values which are given represent the consensus of a committee of qualified experts in the occupational health field. They are reviewed and brought up to date each year. The most recent published list dated 1959 (2) contains values for 169 gases and vapors; 71 toxic dusts, fumes, and mists; 11 mineral dusts; and a list of 21 so-called tentative values. The basic philosophy of this group is set forth in paragraphs preceding its listing of values:

"Threshold Limit Values for 1959" (2)

Threshold limits should be used as guides in the control of health hazards and should

not be regarded as fine lines between safe and dangerous concentrations. They represent conditions under which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse effect. The values listed refer to time weighted average concentrations for a normal work-day. The amount by which these figures may be exceeded for short periods without injury to health depends upon a number of factors such as the nature of the contaminant, whether very high concentrations even for short periods produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods. All must be taken into consideration in arriving at a decision as to whether a hazardous situation exists. Special consideration should be given to the application of these values in the evaluation of the health hazards which may be associated with exposure to combinations of two or more substances.

Threshold limits are based on the best available information from industrial experience, from experimental studies, and, when possible, from a combination of the two. These values are based on various criteria of toxic effects or on marked discomfort; thus, they should not be used as a common denominator of toxicity, nor should they be considered as the sole criterion in proving or disproving diagnosis of suspected occupational diseases.

These limits are intended for use in the field of industrial hygiene and should be employed by persons trained in this field. They are not intended for use, or for modification for use, in the evaluation or control of community air pollution or air-pollution nuisances.

These values are reviewed annually by the Committee on Threshold Limits for changes, revisions, or additions as further information becomes available. The Committee welcomes the suggestion of substances to be added to the list and also comments, references, or reports of experience with these materials.

In addition to these two groups, the American Industrial Hygiene Association has, since 1955, been publishing the Hygienic Guide Series. To date guides have been published for 97 substances. In many respects this series is similar to the recommendations of Smyth in his report to the A.I.H.A. in April 1956. Information is provided for each material relative to the recommended maximum atmospheric concentrations; severity of the hazards (both health and fire); the short-exposure tolerance; atmospheric concentrations immediately hazardous to life; physical and chemical properties. In addition, under the heading of "Industrial Hygiene Practice," brief statements are given as to recognition, evaluation of exposures and recommended control procedures. Also, under the heading "Specific Procedures," brief descriptions are given of first aid, prophylactic measures, and special medical procedures. Finally, a list of references is given. It is also significant that in each case, under the heading of "Recommended Maximum Atmospheric Concentration," a statement is made as to the basis of the recommendation. This approach represents by far the most desirable way of dealing with the problem of establishing hygienic standards. Mere lists of numbers leave much to be desired. It is extremely important that all available information relative to the establishment of the standard be included with it.

BASES FOR THE ESTABLISHMENT OF HYGIENIC GUIDES

The establishment of numbers for "tolerable limits" in the United States is based primarily on two kinds of information: animal experiments and human experience. The scientific research which produces the basic data is carried on by private industry, universities, research laboratories, and governmental agencies. The results of such investigations are published in many United States technical and scientific journals.

In some cases, particularly new chemicals, the technique of applying analogy with other well-known chemically similar materials has sometimes been used until valid data have been accumulated.

The committees or organizations referred to above utilize all available published and unpublished data in arriving at their judgments as to the kinds of levels which will provide a basis for safeguarding employee health.

Animal Experiments

The technique of evaluating toxicologic and physiologic responses in animals as a means of predicting possible effects of toxic materials, physical agents, or other environmental conditions on man has long been a routine tool in the occupational health field. In spite of this, however, there has been little attempt made to provide a standardized approach to investigative techniques in industrial toxicology. In many respects this is fortunate, for in dealing with the effects of a toxic material on a biologic system considerable flexibility is required in applying established criteria. Usually early tests will indicate the course of further study. The magnitude of acute lethal doses and the effects on different organs will indicate the severity of the acute hazard and the importance of various routes of absorption. Corollary information relative to species variability, sex, age, and possible synergistic effects can be obtained at this time. All of this information will then provide a basis for future, more extensive long-term studies.

In the case of new substances, the first step which is generally adopted by toxicologists or industrial laboratories in the determination of toxicity is the utilization of screening tests on experimental animals. These are usually followed by detailed studies of acute effects resulting from single injection, ingestion, or inhalation experiments. In addition, irritating effects on skin and eyes are evaluated.

In 1956 a complete compilation of acute toxicities for an extensive series of materials was published under the auspices of the Aero Medical Laboratory (5). The purpose of this volume was to bring together available data on "acute toxicity of various substances for several species of commonly used laboratory animals as determined by oral or parenteral administration, or inhalation, of fatal doses." In the introduction to this volume the various significant conditions influencing the acute toxicity for any given compound were discussed. These include the dose, the rate of absorption, route of administration, site of injection, and other influences, including disease, environment, temperature, habit and tolerance, etc. In addition, it was pointed out that the toxicity of chemicals will vary with species of animals and sometimes even with different strains of the same species. Within the same strain the toxicity may differ with age, weight, sex, and general condition of the animals.

Because of all these variables it is virtually impossible to be certain that all experiments are conducted in precisely the same way. In fact, only rarely does one find detailed discussion of all such factors involved in an experiment.

Following accumulation of data on acute effects, long-time chronic effects are then studied through inhalation, feeding, injection, and skin-absorption experiments. The nature of these is determined by the results of earlier screening tests. At a conference on The Toxicological Basis of Threshold Limit Values in 1959 (6) V. K. Rowe and his coworkers presented an extensive summary of the kinds of observations which had been made over a period of more than 20 years by several industrial groups. This discussion summarized and tabulated observations on mortality, food intake, body weight, organ weights, gross pathology, micropathology, hematology, blood urea nitrogen, clinical urine analyses, central nervous system, and cholinesterase.

Tables I-IV summarizing the frequency with which particular effects were observed under various circumstances give an indication of the significance of several biologic and biochemical determinations. The significance of growth studies and cholinesterase in Tables I and II and the significance of the liver and kidney in all of these studies are well demonstrated in Tables III and IV. The authors (6) point out that there is increasing pressure for more and more precise kinds of measurements in the biochemical and toxicologic fields as a means of establishing valid threshold

limits. They point out, however, that while this is an excellent objective and one toward which all should strive, it is essential that one make the most practical use of available manpower and funds to obtain the most meaningful information. The criteria which are set forth in this paper are those which are most widely used and certainly accepted by all workers in the field. The best hope for increasing our fund of knowledge derived from animal experiments must come from the development of new techniques and new criteria. In summary, the authors of this paper state:

In spite of the fact that there are many new criteria being developed and tested today, the data presented herein emphasize the high value of certain of the older criteria. It would seem only prudent to make use of those studies which experience has shown to be most productive. This does *not* mean that *only* those criteria showing a high degree of efficiency in the series of investigations reported herein should be used, but certainly it suggests that they should be basic to any toxicological study designed to determine a threshold limit for repeated exposure.

One other set of criteria which is attracting more and more attention are those physiologic studies which can be made on animals as well as on humans. In the symposium mentioned above, Dr. John A. Zapp, Jr. (7) discussed the importance of utilizing physiologic observations such as systolic and diastolic

TABLE I

FREQUENCY WITH WHICH A PARTICULAR EFFECT WAS OBSERVED AT THE LOWEST DOSAGE LEVEL AT WHICH ANY EFFECT WAS OBSERVED (6)

Criteria of effect	Data from 1952-1959				Data from last 22-25 years	
	Oral		Vapor		All routes	
	*	%	*	%	*	%
Growth	64 (172)	37	16 (38)	42	152 (410)	37
Hematology	1 (79)	1.3	1 (21)	5	5 (170)	2.9
Clinical urines	1 (7)	14	0 (7)	0	2 (43)	4.6
CNS	4 (109)	3.7	1 (32)	3.1	5 (141)	3.5
Cholinesterase	8 (10)	80	—	—	8 (10)	80

*Number of positive findings (number of observations)

TABLE II

FREQUENCY WITH WHICH A PARTICULAR EFFECT WAS THE SOLE EFFECT AT THE LOWEST DOSAGE LEVEL AT WHICH ANY EFFECT WAS OBSERVED (6)

Criteria of effect	Data from 1952-1959				Data from last 22-25 years	
	Oral		Vapor		All routes	
	*	%	*	%	*	%
Growth	25 (172)	15	2 (38)	5	44 (410)	11
Hematology	0 (79)	0	1 (21)	5	1 (170)	0.6
Clinical urine	0 (7)	0	0 (7)	0	0 (43)	0
CNS	4 (109)	3.7	1 (32)	3.1	5 (141)	3.5
Cholinesterase	4 (10)	40	—	—	4 (10)	40

*Number of positive findings (number of observations)

terms of the significance of such information in application to humans.

Human Experience

While animal data provide some basis for judgment about the possible levels of toxic materials which may be used safely in industry, they cannot be extrapolated to humans with complete confidence. The ultimate criteria must come from human experience. The validity of such criteria is based on the amount of experience in terms of both numbers of exposed people and time of exposure, on the methods of evaluation of the effects of the toxic material on people, and on the completeness of the evaluation of exposure levels in the environment and correlation of these levels with human exposure. Data with reference to human effects are obtained from both controlled experiments and industrial environment exposures.

In the case of irritants, for example, such factors as odor detection, sensory response, and levels of exposure which are irritating to eyes, skin, and upper respiratory tract have been studied quantitatively in humans under controlled conditions. In general, such studies, combined with experience gained with actual plant use, provide an adequate basis for establishing or confirming hygienic standards for such substances. It is much more difficult to provide a sound basis of human experience for substances which require relatively long periods of time before producing evidence of injury. Whereas the acute effects can be evaluated relatively rapidly and by simple procedures, long-time detailed studies of controlled groups of industrial workers are required to provide adequate evidence in the case of those substances which may produce chronic injury.

The kinds of information which are available from industrial experience with various chemicals fall into three basic categories. One of these is limited to complaints associated generally with the sensory response or with more severe forms of acute irritation reactions affecting skin, eyes, or upper respiratory tract. The second kind of data result from clinical examination of exposed workmen. The third is the result of human toxicologic or physiologic studies. To be of value in establishing hygienic standards such medical information must be correlated with adequate data relating to the concentrations to which workers have been exposed.

In his paper "Improved Communication. Hygienic Standards for Daily Inhalation" Smyth (3) reviewed 238 values from the 1956 American Conference of Governmental Industrial Hygienists list, together with his interpretation of these values. He has also evaluated the nature of the supporting data—animal and human. An analysis of the four kinds of sources of human data indicates the role of such experience in establishing hygienic standards in the United States. Of a total of 238 values which were analyzed human data were utilized in 108*, distributed as follows:

Clinical Examination of Workmen Was Correlated With Their Exposure	34
Industrial Complaints or Observations Less Quantitative Than Clinical Observations	33
Human Sensory Data	42
Human Toxicologic or Physiologic Data	10

*Of the 119 values distributed in the above tabulation there were 11 duplicates wherein the same material appeared under two or more headings; thus there were actually 108 separate substances analyzed.

In such an extensive list as this there are many materials which are so little used that there is negligible industrial experience available to assist our standards people. For such materials reliance is placed primarily on animal experiments and the use of analogy as guides in setting limits.

For the more common industrial chemicals many years of experience in using them has provided the necessary background to verify existing standards. Such experience is generally of a negative nature. Where it is supported by clinical or physiological data correlated with levels of exposure, as in the case of the ten-year study of butyl alcohol by Sterner and his colleagues (10), the information is most significant.

Such medical programs are designed to evaluate the general physical condition of employees and to include specific physiologic tests which may be expected to provide early evidence of injury. Studies of this type are by far the most valuable for establishing valid hygienic standards.

SUMMARY AND CONCLUSIONS

In summary, it can be stated that hygienic standards for inhalation in the occupational health field in the United States are based on the application of the best known biochemical, toxicologic, physiologic, and pathologic techniques to animals and to human experience. Investigations are carried on by private industry, universities, research laboratories, and governmental agencies. The analysis of such data and interpretation in terms of hygienic standards is done by standards groups composed of competent scientists representing every facet of the occupational health field. The validity of these standards is demonstrated by the low occupational disease attack rate in the United States. Verified cases of such injury are the result of exposures far above the established limits.

Many approaches are being made to the problem of establishing hygienic standards in the occupational health field. It became obvious some time ago that research people in various parts of the world were in some cases utilizing varying techniques. As a result, values for some substances differ by as much as an order of magnitude. In an attempt to get some unification in the basic approach to the problem and to provide a mechanism to permit a much broader exchange of information and data among occupational health workers, the Permanent International Commission on Industrial Medicine set up a Subcommittee to study this problem. This Subcommittee held a symposium on Maximum Allowable Concentrations of Toxic Substances in Industry in Prague, Czechoslovakia, on April 14-17, 1959. The *Transactions* of the Symposium, which appeared in four sections, deal with general areas of agreement among the delegates. This statement of principles is an important first step in establishing international cooperation in this important field. On the basis of this work it is hoped not only that we can look forward to the development of a series of internationally acceptable hygienic standard values but that agreement can be obtained with regard to general principles and to methods and procedures which will be utilized in the establishment of such standards. The present Symposium, which is the second under the auspices of the Subcommittee will, I hope, crystallize even further the thinking of those in the occupational health field concerned with establishing sound standards to be used in assuring safe industrial environments.

Eckardt, Robert E., 7-10, 64-65
 Eckhardt, W., 850-857
 Elkins, Hervey B., 981-983
 Erhardt, J. Th. G., 850-857
 Estadella-Botha, S., 663-668

Fabre, René, 686-692
 Felton, J. S., 413-426
 Ference, Anne M., 12-14
 Ferran, G. H., 486-503
 Fiandaca, S., 353-359
 Finulli, M., 770-772
 Fischer, R., 872-876
 Fisher, R. E. W., 250-256
 Folsom, Marion B., 72-82
 Formánek, J., 714-721, 872-876
 Fornells-Martinez, E., 663-668
 Forssman, Sven, 68-72, 257-258
 Fortuin, G. J., 258-259
 Fournier, Et., 694-698
 Fradà, G., 259-260
 Frantik, E., 714-721
 Frantíková, D., 872-876
 Friberg, Lars, 201-203, 977-980
 Friedland, I. G., 692-694

Gabor, Sylvia, 465-466
 Gasque, Mac Roy, 260-263
 Gaultier, M., 694-698
 Georgescu, A. M., 343-345
 Ghosh, P. K., 426-427
 Gillquist, B., 257-258
 Glorig, Aram, 699-700
 Goldman, Rose, 314-316
 Goldstein, Bernard, 263-266
 Goldstein, David H., 266-270
 Gorospe, Alfredo A., 636-639
 Gradina, C., 700-702
 Grant, Ellsworth S., 118-120
 Greene, Katrine R. C., 314-316
 Grimaldi, John V., 607-608
 Grimlund, K., 703-707
 Gross, Paul, 707-712
 Gucciardi, G., 259-260
 Guymer, R. F., 270-275
 Guyotjeannin, Ch., 694-698
 Gwozdz, B., 795-798

Hamilton, Gilbert L., 656-661
 Hargreaves, Margaret S., 275-278
 Harris, E. S., 281-283
 Harris, William B., 466-472
 Hatch, T. F., 839-845
 Hayes, Wayland J., Jr., 120-122
 Hertig, B. A., 839-845
 Hinchcliffe, R., 712-714
 Hine, C. H., 281-283

Hinkle, Lawrence E., Jr., 283-288
 Hipps, John G., 608-610
 Hogan, Edward J., 610-613
 Holden, F. R., 281-283
 Holm, A., 257-258
 Holmquist, Carl-Eric, 122-126
 Holstein, Ernst, 278-281
 Holtz, John, 783-785
 Horiuchi, Kazuya, 288-289
 Horváth, M., 714-721, 872-876
 Hueper, W. C., 473-486
 Hughes, James P., 879-882
 Hyatt, E. C., 486-503

Inoue, Toshi, 289-290
 International Labour Office, 721-724
 International Symposium on Maximum Allowable
 Concentrations of Toxic Substances in Industry,
 33-39
 Iorga, M., 341-343

Jensen, C. R., 486-503
 Juin, Gérard, 942-947
 Jullien, Georges, 724-726

Kammer, A. G., 427-428
 Kantor, M., 753-755
 Kazantzis, G., 290-298
 Keatinge, Gerald F., 298-301
 Keenan, Robert G., 503-506, 783-785
 Kehoe, Robert A., 126-129, 433-436
 Kesy, Irena, 726-730
 Killens, Richard, 783-785
 King, E., 301-311
 Kingston, James R., 911-917
 Kitagawa, Tetsuzo, 506-512
 Kiviluoto, Raimo, 311-312
 Klein, Irvin, 613-615
 Klutas, Edna May, 428-431
 Kopp, John, 783-785
 Kruger, Daniel H., 615-621
 Krüger, P. D., 971-973
 Kubota, Juko, 313-314

LaBelle, Charles W., 730-735
 Lachnit, V., 947-950
 Laham, Souheil, 686-692, 735-738
 Lammers, B., 876-878
 Landry, A. S., 512-519
 Lavergne, Rafael, 214-217
 Lehmann, Gunther, 878-879
 Leoca-Radu, Mina, 349-351
 Letavet, A. A., 431-433, 891-892, 983-987
 Liber, Amour Fiscus, 738-740
 Lieben, Jan, 316-319
 Lienhard, Wendell F., 879-882
 Lillis, R., 679-681

- Linch, A. L., 580-585
 Lind, A. R., 882-887
 Liniecki, J., 800-801
 Littler, T. S., 712-714
 Lubin, Isador, 621-622
 Lund, O.-E., 740-741
 Lundervold, Arne, 887-891
 Lutier, J., 401-402
 Lutz, Earl F., 184-186
- McCallum, R. I., 741-745
 McClintock, R. S., 879-882
 McKerrow, C. B., 745-749
 Mc Nerney, James M., 707-712
 Magnuson, Harold J., 129-131
 Malysheva, A. E., 891-892
 Manheimer, Robert H., 314-316
 Matthews, James, 131-134
 Matuoka, Syukiti, 893-902
 Maxfield, Mary E., 857-862
 Meiklejohn, A., 134-138
 Meila, I., 677-678
 Metzner, Franz N., 316-319
 Michon, R., 902-904
 Mihaila, I., 904-908
 Mikaelian, Michel, 320-322
 Mikisha, A., 714-721
 Milijic, Bosko, 950-951
 Miller, S. E., 937-939
 Milox, M., 908-911
 Minard, David, 911-917
 Miskolczy, Wilhelm, 322-324
 Mitchell, R. N., 486-500
 Moise, Gh., 676-678
 Molino, F., 952
 Monaco, Alfred, 749-753
 Morris, George E., 324
 Morrow, C. S., 753-755
 Moscovici, B., 341-343
 Moss, N. Henry, 182-184
 Motley, Arthur W., 623-624
 Mountain, John T., 783-785
 Moyer, Burton J., 519-522
 Muica, N., 679-681
 Murray, Robert, 139-145
- Nadudvary, George, 465-466, 755-757
 Nale, Thomas W., 625-628
 Namba, Tatsuji, 757-758
 Nestorescu, B., 679-681
 Newnham, C. T., 324-325
 Niebroj, I., 795-798
 Nixon, James, 699-700
 Noro, Leo, 326-335
 Norviit, Lembit, 952-957
 Norwood, W. Daggett, 335-338
 Nyström, A., 257-258, 653-656
- Olloqui, Fernando Flores, 628-631
 Oyanguren, Hernan, 227-230
- Pafnote, Maria, 845-847
 Paggi, Edoardo, 758-767
 Pancheri, Giovanni, 145-146, 767-768
 Parker, H. G., 147-150
 Patrascu, M., 465-466
 Payne, William W., 473-486
 Pendergrass, Eugene P., 768-769
 Pendergrass, Henry P., 768-769
 Perales y Herrero, Narciso, 631-632
 Pernis, B., 770-772, 817-818
 Pesce, Giuseppe, 958-959
 Petrescu, Leonid, 661-663
 Pettinati, L., 348-349
 Petrovic, Lj., 338-341, 368-371
 Phillips, A. M., 553-556
 Pietschmann, H., 947-950
 Pilat, L., 341-343, 679-681
 Piotrowski, J., 780-782
 Piscator, M., 201-203
 Plumb, Carl S., 260-263
 Plummer, Norman, 283-288
 Poletti, D., 338-341, 368-371
 Potter, A. Lloyd, 150-155
 Powles, William E., 351-353
 Pradel, J., 522-531
 Preda, N., 343-345
 Princi, Frank, 433-436
 Puertas, Benito Nogales, 633-634
- Quer-Brossa, S., 663-668
 Quigley, J. A., 65
- Radcliffe, J. C., 65-66
 Rădulescu, I. C., 343-345, 679-681
 Rae, Stewart, 772-776
 Rainsford, S. G., 345-348
 Rasetti, L., 348-349, 359-361
 Raucher, Karl, 349-351
 Reeve, A. Louise, 634-635
 Renker, K., 917-921
 Riedesel, M. L., 839-845
 Riegért, A. L., 819-825
 Rigner, K. G., 257-258
 Rísquez-Iribarren, Rafael, 155-158
 Rogan, John, 772-776
 Ross, W. Donald, 351-353
 Rossi, Mario, 960-961
 Rossier, P. H., 776-780
 Rotta, C., 353-359
 Rubino, G. F., 359-361
 Rye, W. A., 361-364
- Sakai, Yoshimichi, 158-162
 Salmowa, J., 780-782
 Sands, Frederick W., 531-532
 Santillan, Jose S., 636-639
 Sarfeh, R., 436-438
 Saruta, Namio, 532-535

- Savicevic, M., 338-341
 Sawyer, William A., 438-441
 Scansetti, G., 348-349
 Scheel, Lester D., 783-785
 Schepers, G. W. H., 786-795
 Schermerhorn, W., 850-858
 Schiller, Hans, 961-962
 Schindl, Karl, 364-365
 Schmidt, Heinz-Günther, 365-367
 Schmidt, Marjorie D., 367-368
 Schmidtke, H., 921-923
 Schulte, H. F., 486-503
 Schunck, Karl-Hans, 377-378
 Schwartz, Louis, 639-642
 Seles, L., 237-238
 Serati, A., 963-965
 Sherrill, S. S., 281-283
 Shipman, Thomas L., 642-645
 Shoib, M. O., 85, 162-166
 Sick Absence Statistics Committee of the Permanent Committee and International Association on Occupational Health, 40-55
 Silverman, Leslie, 441-448
 Simpson, H. Marjorie, 448-452
 Simu, George, 755-757
 Smith, Paul E., Jr., 857-862
 Sodergren, David, 122-126
 Sox, Ellis D., 281-283
 Spett, K., 795-798
 Spiers, F. W., 535-540
 Spioch, F. M., 795-798
 Stankovic, M., 338-341, 368-371
 Staskiel, L. J., 753-755
 Steele, Earl C., 371-373
 Steele, Margaret L., 66-68
 Steiner, S. D., 373-377
 Stokinger, Herbert E., 540-544
 Stopps, Gordon J., 857-862
 Stowell, Thomas E. A., 186-191
 Strange, John P., 544-551
 Sumner, Philip, 314-316
 Symanski, H.-J., 798-800
 Szpakowa, T., 800-801
 Szymczykiewicz, K., 801-805
 Tabershaw, Irving R., 11-12
 Taylor, Edmund W., Jr., 182-184
 Teisinger, J., 987-988
 Teso, G. A., 359-361
 Thaxter, M. D., 147-150
 Thom, W. F. J. M., 379-381
 Thoma, George E., 569-572
 Thompson, A. R., 301-311
 Thorpe, John J., 381-387
 Tompkins, Paul C., 551-553
 Tripsa, Rodica, 806-810
 Troisi, Fortunato Maria, 387-397
 Truhaut, René, 33-34, 39, 209-214, 686-692
 Tucker, F. E., 553-556
 Udel, Melvin M., 397-401
 Ursoniu, C., 676-678
 Vacher, J., 401-402
 Valentin, H., 810-817
 Van der Velden, W., 850-857
 Van Liew, Hugh D., 911-917
 Van Valzah, H. J., 678-679
 Vigan, C., 965-971
 Vigliani, Enrico C., 87, 452-457, 770-772, 817-818
 Viles, Frederick J., Jr., 556-563
 Villarroel, Sergio, 227-230
 Viola, P. Luigi, 818
 Voelz, George L., 564-569
 Vosburgh, B. L., 931-933
 Wade, Leo, 7, 61, 88
 Wald, Neil, 569-572
 Walker, Mildred I., 167-169
 Walsh, Richard F., 645-648
 Warnock, Dorothy M., 402-404
 Wassermann, M., 572-580
 Weaver, Neill K., 381-387
 Wechselberger, F., 191-194
 Wells, R. Lomax, 170
 Westrick, Marian L., 707-712
 Wetherhold, J. M., 580-585
 Wheatley, B. M., 585-587
 Whipple, G. Hoyt, 171-178
 Whitney, L. Holland, 283-288
 Wiecek, E., 801-805
 Wieland, H., 740-741
 Williams, Charles R., 988-994
 Williams, Katherine, 587-590
 Williams, May M., 194-197
 Williams, N., 819-825
 Willman, Helvi, 404-405
 Winter, Kurt, 405-410
 Worth, G., 826-827
 Wyndham, C., 924-931
 Yingling, Doris B., 457-459
 Yoder, John D., 590-592
 Yoshimi, S., 827-828
 Yount, Hubert W., 649-650
 Zahorski, Witold, 828-832
 Zanetti, Ennio, 767-768
 Zannini, D., 971
 Zielinski, John F., 592-600
 Zorn, O., 971-973