BERYLLIOSIS

Summary and Survey of all Clinical Types in Ten Year Period

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THE metal beryllium, in addition to exhibiting unusual chemometallurgic properties, has in the last decade brought to the attention of the medical world its puzzling physiologic and pathologic effects in man. Up to the present the largest number of cases of beryllium intoxication have occurred in plants engaged in the extraction and processing of beryllium and in the manufacture of fluorescent lamps.[1] The least number of cases have been reported from workers engaged in the salvage of fluorescent lamps, in sign tube manufacture, in laboratory research, in the manufacture of ceramic containing beryllium, in the manufacture of beryllium alloys, and in the working of beryllium metal. No known beryllium cases have been reported in the mining, shipping and handling of beryl ore.

Recognition of occupational hazards involving either the derma and/or the respiratory tract came in the early years of the beryllium extraction and processing industry. Since 1940 the authors have observed and treated 461 cases of the various types of beryllium poisoning. Table 1 is a summary of the incidence, mortality and causative compound of the acute manifestations encountered in plants A, B and C. Dermal and ocular manifestations were evident in 202 cases; minor and major respiratory tract involvement occurred in 229 persons. This survey also includes 2 dermal and 31 pulmonary cases of the chronic form of the disease. Many of the cases included have been reported in previous publications.[2,3,4]

The data in this survey are presented to bring to the attention of the toxicologist, the industrial hygienist, and the many other interested clinicians the progress and present status of beryllium intoxication as studied and evaluated by the authors in the last decade. This study has been made possible by the fact that during the last 15 years the major concentration of plants (4) and employees (2200) engaged in beryllium extraction and processing have been located in this area in Ohio.

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A brief resume of the basic operations and uses of beryllium will aid in a clearer comprehension of the factors involved and the magnitude of the toxicologic problems encountered in the occupational diseases associated with this limited but rather vitally important chemical industry.

Elemental beryllium is a light, greyish, brittle and stable metal. Its atomic number is 4 and 1 natural isotope has been established; 3 artificial ones have been developed. It was first identified by Nicholas Vauquelin in 1797 while proving the chemical identity of beryl, emerald and aquamarine. The industrial development of the element has occurred in the last 2 decades.

Ores containing beryllium have not been found in large compact bodies. About 40 classified minerals containing beryllium are known but only 1, beryl (beryllium aluminum silicate) with an average yield of 12.5 per cent of the oxide or 4 per cent of the metal, is of industrial significance. The majority of the ore processed in this country is imported from Brazil.

At the present time the beryllium producers are concentrating their production efforts on the metal, the oxide and the alloys. The extraction methods vary, but the basic concept is to alter the natural beryllium oxide so that it can be extracted from the mineral matrix in pure form. In order to attain this, any one or combination of 2 economically sound basic methods are being used which entail the initial reduction of the ore in furnaces, followed by the use of sulfuric and/or fluoric acids to obtain soluble salts. Intermediate operations may utilize alkaline materials such as ammonium hydroxide. The present rapid research being done on production methods frequently alters the materials and methods used in the various operations so that a standard procedure of today may be altered or discarded tomorrow.

Beryllium metal is lighter than aluminum, is extremely penetrable to x-ray, is an excellent transmitter of sound and an excellent source of neutrons. It is mainly used for windows of x-ray tubes and in nuclear physics development.

Beryllium copper alloy is noted for its unusual resistance to fatigue and impact, for its corrosion resistance, for its freedom from elastic drift and for its high electrical and thermal conductivity properties. Present use includes specialized machine and equipment parts, special springs and safety tools.

Beryllium oxide has a melting point of 2570 C., is an excellent insulator at high temperatures, has unusual resistance to thermal shock plus a high thermal conductivity. Some of the past and current uses of the oxide include: high temperature crucibles and shapes, phosphors in fluorescent lights and neon signs, radiation shields, lining in coreless induction furnaces, cathode heating elements in radio tubes, ceramics and vacuum tube "getters."

Any survey of a toxicologic problem, such as that of beryllium, must not forego the progress in therapy. Foremost in this category one must stress the more important preventative features in the beryllium processing plants and their surrounding environments. These hygienic preventative measures are most important in view of lack of effective or specific therapy, especially with reference to the chronic pulmonary disease. In consideration of these accepted

facts certain engineering and medical hygienic standards have been adopted in order to protect those who are exposed to beryllium or its compounds.

Upon recommendations advanced by Eisenbud and associates[5] and the Atomic Energy Commission, the extracting plants have adopted engineering devices to control the atmospheric concentration of beryllium in order that the plant working environment will not exceed the daily average permissible concentration of 2 micrograms per cubic meter; that no transient concentration will exceed 25 micrograms per cu. M. and that the vicinity of any plant subject to atmospheric pollution by beryllium not exceed a maximum permissible monthly average concentration of .01 microgram per cu. M. Although these figures are tentative and arbitrary, they have added effectiveness since their initial application in reduction of the incidence of acute and chronic disease.

To further maintain a continued high standard of protection for the workers, certain medical procedures and basic control methods have been instituted in a well organized medical department.[6,7]

The present and very effective integrated medical safety and industrial hygiene program adopted in the extraction plants includes rigid pre-employment screening with disqualifications based on certain physical abnormalities or history of pre-existing diseases considered incompatible with the industry. To achieve continued and maximum effective prophylaxis, new employees are instructed in a rigid standard program of health and safety education. All employees are required to have weekly examinations including pulmonary roentgenograms. During the last 4 years this program, mainly under the direction and supervision of one of our co-workers,* has been most effective in the remarkable reduction of the incidence and total elimination of mortality (table 1) with most of the reported cases having been traced to major mechanical breakdowns, personal failures or experimental procedures. Furthermore, these medical and engineering safeguards have aided considerably in the maintenance of better health, better labor management relationship, and a decrease in labor turnover with a concomitant decrease in production costs.

Some of the manifestations of beryllium intoxications have been reproduced by animal experimentation.[8,9] Sufficient evidence has been obtained both clinically and experimentally that beryllium, per se and by its bond with other elements and radicals, is capable of expressing various forms of toxicity in certain environmental concentrations and probably in the presence of certain altered physiologic conditions. The most recent epidemiologic investigations suggest that the beryllium ion is the sensitizing allergen in both the dermal and pulmonary syndromes.[10,11] This aspect is being investigated.

In the various groups of cases studied in the present survey we have emphasized the importance of the urinary excretion of the element and the beryllium content of the necropsied tissues. The spectographic and the fluorimetric, 2 sensitive biochemical analytical technics, were employed by 2 lab-

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oratories* in obtaining the recorded tabulated data of our survey. The value and significance of beryllium determinations in the urine of persons exposed to the element, with or without toxic manifestations, is adequately covered by Dutra and co-workers,[12] and Klemperer and associates.[13] Generally our data are in agreement with the findings and conclusions of the preceding investigators. Table 2 is the survey data on 10 persons having undergone varying periods of exposure without specific occupational disease, all showing evidence of beryllium excretion in varying amounts; and on 2 patients having had constant exposure to insoluble BeO for 5 years who still showed appreciable excretion despite 5 years' removal from contact.

In the course of the present survey we have been able to secure tissue at autopsies of 2 patients having recovered from major respiratory beryllium intoxication with subsequent death from other causes. To the knowledge of the authors no tissue analyses of similar cases have been reported in the literature. Brief case histories are given along with pulmonary roentgenogram plus table 3 tabulating the tissue analysis and beryllium urine determination in case 2 taken during the survey of 1950. It is evident that the analytical figures of these 2 cases strongly support the fact that the quantity of beryllium in the tissues or the quantity excreted in urine after years of freedom from contact with beryllium is merely indicative of previous exposure to the element and not necessarily specific disease. Case histories and findings are as follows:

Case 1. A man 50 years old at time of death, was first employed in a beryllium extraction plant on September 22, 1944, as a mixer in the beryllium copper department and a furnace operator's helper in the beryl furnace department. Exposure was insidious over a period of 64 days and mainly to the dusts of beryllium oxide, graphite and fumes of reduced silicates including $BeSO_4$ and BeF_2. The patient developed an acute chemical pneumonitis on November 24, 1944 (fig. 1, case 1). Clinical recovery, as shown roentgenographically, was apparently complete by March 26, 1945 (fig. 2).

In September 1946 he noticed a severe anorexia, weight loss and a productive cough. Symptoms became progressively aggravated and the patient died in a veterans' hospital on February 14, 1947. The final diagnosis was generalized carcinomatosis with many pulmonary metastases (fig. 3). The beryllium contents of certain autopsied tissues are reported in table 3.

Case 2. A man, 36 years of age at time of his death in 1951, was first employed as a furnace operator in the crystallizing department on January 20, 1942. He was exposed to fumes and mists of soluble salts of beryllium, mainly BeF_2, in varying atmospheric concentrations. He left the industry in the fall of 1946 and had no further exposure to beryllium.

During his employment in the beryllium extraction industry he developed 2 attacks of acute chemical tracheobronchitis due to BeF_2 during the following periods: March 3 to March 12, 1943, and September 3 to September 21, 1943. Recovery was complete in both instances.

The patient was examined for the survey on August 1, 1950, and found to be in excellent physical condition with vital capacity of 5.6 L. or 120 per cent of normal. Roentgenograms taken on July 21, 1950, revealed normal lung findings except for some mild interstitial fibrosis of the right lung (fig. 4, case 2). Urine determination of 24 hour specimen on August 1, 1950, revealed the presence of 0.6 micrograms per L.

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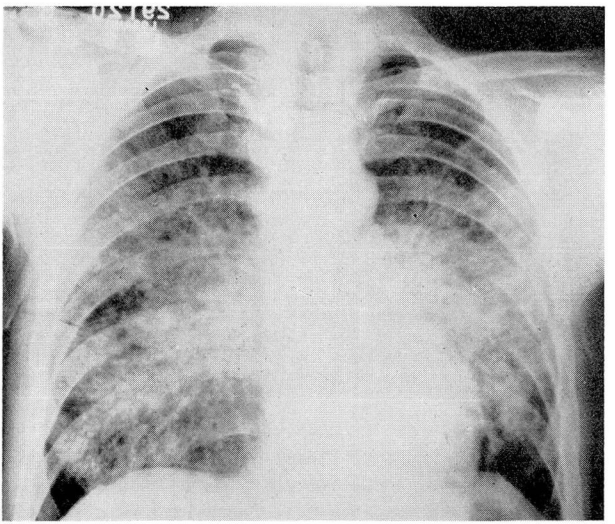

FIG. 1, Case 1. Pneumonitis involving hilar and central pulmonary areas 25 days following onset of illness (12-9-44).

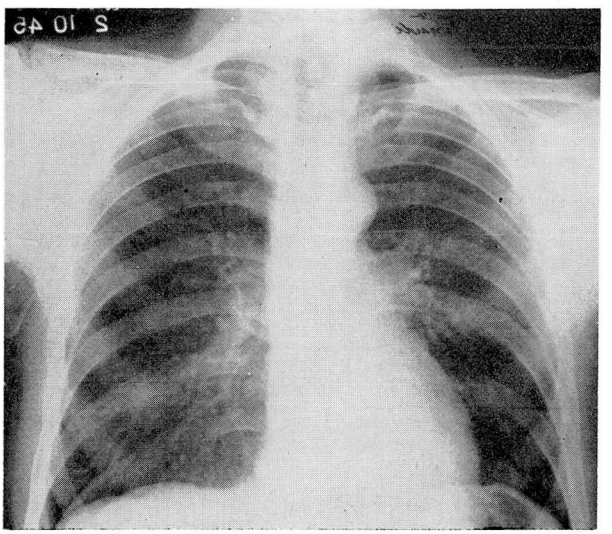

FIG. 2, Case 1. Pneumonitis cleared except for slight hilar residue. Patient fully recovered (2-10-45).

The patient died of acute carbon monoxide asphyxia on June 28, 1951, as verified at autopsy. The beryllium contents of the tissues as reported by 2 separate laboratories appear in table 3.

The preceding and ensuing data are the result of observations and experiments with workers exposed to beryllium and with certain pattern diseases due to toxicity of beryllium and/or its compounds. Important factors encountered in the survey including the present status of each person, exposure data plus analyses of urine and the autopsied tissues, are tabulated under each main heading. Present day therapy is also recorded along with a brief description of the main causative compounds, subjective symptomatology and physical and laboratory findings.

Acute Dermal Manifestations

The dermatitis was usually confined to the exposed parts of the body but in the sensitivity type became generalized. The lesions varied from diffuse papules, and vesiculopapules to macules and irregular areas of edematous lesions with or without vesicle formations. Symptoms of the majority of patients consisted of a burning sensation and pruritis of the affected parts. Usually there was a concomitant involvement of the conjunctivae and eyelids.

Up to the year 1947, due to the rapid turnover of a migratory group of employees, approximately 25 per cent of new workers exposed to the fumes, mists and dusts of the soluble salts of beryllium developed dermatitis of varied intensity depending on individual sensitivity. The subsequent hygienic engineering plant improvements, in addition to a well organized and rigid medical screening of new employees, has reduced the incidence to less than 2 per cent.

The response to treatment varied, the fluoride compound cases being most refractory, but recovery usually was complete in 7 to 14 days after removal from exposure. The present therapy consists of immediate transference from the offending agent, the use of antihistaminics and the local application of mild, soothing, antipruritic and antihistaminic ointments. The concomitant conjuctival involvement usually requires the use of soothing antibiotic ophthalmic ointments and wearing of dark glasses.

Up to the present, 209 acute dermal cases have been observed by the authors over a period of 12 years without any resulting fatalities or local residuum. The dermal manifestations were, with a few exceptions, caused by contact with the soluble forms of beryllium, principally the fluoride and the sulfate. One hundred sixty-four cases were ascribed to the fluorides while the remainder (45 cases) were due to sulfates. Undoubtedly some patients had contact with both compounds.

Sixty-three of the 209 cases were attributed to exposure to the soluble salts of beryllium in sufficient concentration to act as a primary irritant and produce an immediate contact dermatitis. In 146 cases eczematous type of dermatitis, often a severe manifestation, developed as the result of acquired sensitization attributed to longer exposure to smaller concentrations of beryllium salts. The dermatitis appeared on an average of 7 to 14 days after initial exposure.

There were 5 cases included in this dermatitis series in which major respiratory syndromes occurred. Patient 10, table 7 of the chronic berylliosis group, had acute dermatitis due to BeF_2 and patients 1, 2, 5 and 19, table 5 of the recovered pneumonitis series, also had acute dermatitis during their employment in the beryllium industry.

Prior to 1951 it was thought but not demonstrated that the eczematous form of the dermatitis was of the allergic eczematous contact-type. Of 13 patients studied by one of us,[11] 4 had had the dermatitis at one time during the past 6 years and 9 patients had the dermatitis during the period of observation. Cutaneous allergy was demonstrated by the patch test technic with high dilutions of beryllium compounds. In a series of 16 controls who had never been exposed to beryllium and/or its compounds, cutaneous hypersensitivity was produced in 8 (50 per cent).

Beryllium Ulcer—usually an acute localized manifestation due to implantation of the crystals of the soluble salts of beryllium in a pre-existing skin break. It is often a concomitant manifestation with contact dermatitis and the pathologic findings are those of a severe skin reaction to a primary irritant. Untreated lesions may persist for months. Treatment consists of curettage of the ulcer and removal of the offending beryllium salt inclusions. Healing is by second intention and usually complete from 7 to 14 days.

Acute Tracheobronchitis and Pneumonitis

Acute tracheobronchitis, as studied in our series of cases, invariably was caused by inhalation of vapors, dusts and mists of BeF_2, ammonium BeF_2, $BeSO_4$. The onset is either rapid or insidious depending upon the magnitude and duration of the exposure. Symptomatically it is characterized by productive spasmodic cough, substernal discomfort and burning, tightness of the chest, and moderate exertional dyspnea. The objective physical findings reveal normal body temperature, decreased vital capacity with varying degree of dyspnea, injection of the nasopharynx, limitation of chest expansion, and the presence of sibilant rales in the hilar and basilar areas of the lungs; clinical laboratory findings within normal limits. The pulmonary roentgenograms may show increase of bronchovascular markings.

The therapy is not specific and consists of removal from exposure, bed rest, cough sedatives, antihistaminics to relieve bronchiolar spasm, and antibiotics to prevent and control secondary invaders. Recovery is usually complete in 1 to 4 weeks.

Up to the present time 129 cases of acute tracheobronchitis have been observed and treated over a 12 year period. Sixty-two instances were due to BeF_2, 38 to $BeSO_4$, and 29 to inhalation of mixture of the soluble salts. Clinical and roentgenographic recovery was complete in all cases.

Of this entire group, 34 persons were available for the survey study with one nonoccupational death reported in table 3. The majority of the remaining group could not be contacted as this disease occurred largely in migratory

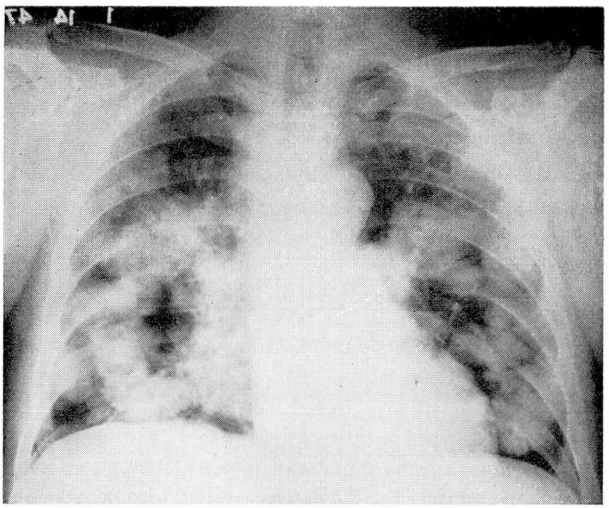

Fig. 3, Case 1. Metastatic tumor nodules scattered throughout both lung fields (1-14-47).

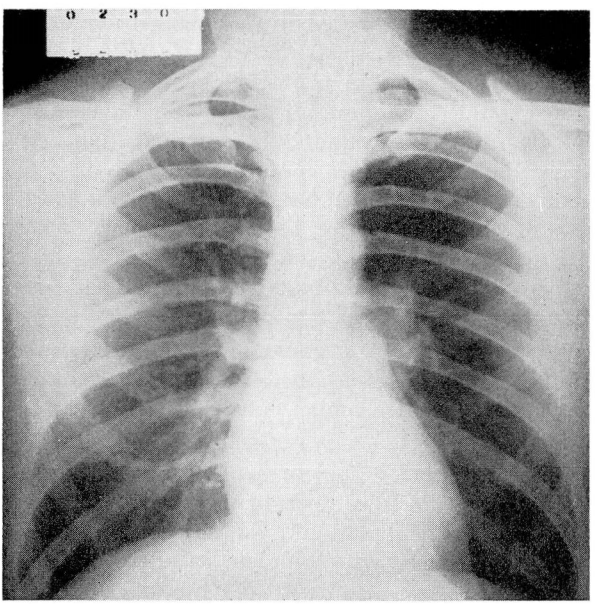

Fig. 4, Case 2. Survey chest roentgenogram reveals essentially normal pulmonary findings (7-21-50).

workers during the war years. Table 4 is a summary of the survey data of 20 of the recovered patients who had had acute tracheobronchitis; 8 persons are engaged in the same industry since recovering from their acute tracheobronchitis. One patient (case 12, table 7) who had two attacks of the disease in 1945 developed chronic berylliosis in 1947. There is also the suggestive history of acute tracheobronchitis in two other persons with chronic berylliosis (cases 8 and 11, table 7) but no confirming medical record was established by either patient.

The data in table 4 reveal the excretion of beryllium in the urine of all the recovered patients. The group still exposed in the processing plants generally show a greater excretion of the element, while in the remaining cases there is suggestive general decrease of the beryllium excreted in relation to the last date of exposure.

Acute Chemical Pneumonitis

Briefly, acute chemical pneumonitis is caused by inhalation of vapors, mists and dusts of BeF_2, $BeSO_4$, combinations of the soluble salts and BeO of high specific area prepared at relatively low calcining temperatures.

Two types have been encountered, namely the fulminating and insidious, depending upon the magnitude and duration of exposure. The symptoms of fulminating pneumonitis usually occurred approximately 72 hours after brief but massive exposures, while the insidious form manifested symptoms several weeks after prolonged exposure to lesser concentrations in the working environments.

Symptomatically it is characterized by progressive, rarely productive spasmodic cough, progressive dyspnea with tightness of the chest and substernal pain or discomfort, anorexia with ensuing weight loss, general malaise and weakness. The objective findings reveal varying degrees of decreased vital capacity with severe dyspnea, rapid pulse and acrocyanosis, hyperemia of the nasopharynx, no increase of body temperature, limited chest expansion with variegated pulmonary rales principally in the lower lobes and hilar areas. Clinical laboratory findings are within normal limits.

Pulmonary roentgenograms become positive in 1 to 3 weeks after onset of symptoms and vary with the stage and intensity of the disability. Findings in chronologic sequences are: diffuse bilateral haziness usually of the lower lung fields followed by irregular soft parenchymal infiltration and finally discrete or conglomerate nodules. Therapy is not specific and consists of hospitalization with complete rest, use of oxygen to relieve respiratory distress, antibiotics as prophylaxis against secondary infection, antihistaminics to alleviate bronchiolar spasm, digitalization in evidence of cardiac decompensation, and the recent use of cortisone and ACTH with some preliminary gratifying results.

This has been the severest manifestation of acute beryllium poisoning which has been observed and treated in 93 instances as result of exposure in the local extraction and processing plants, with 10 deaths during the last 12

years or a mortality of 10.7 per cent. Of this group 35 cases were due to BeF_2, 8 to $BeSO_4$, 17 to mixtures of the soluble salts and 33 to BeO. Clinical recovery and roentgenographic clearing was complete in all but one of the living patients reported in table 5 as case 8. No incidence of chronic berylliosis was detected in any of the cases studied in the survey.

Survey data have been obtained on 40 of the recovered and living patients having had acute pneumonitis and the results of our survey of 20 persons are listed in table 5. Five of this group have continued working with beryllium and generally show a larger urinary excretion of the element than the remaining number. Again, as in the cases of tracheobronchitis, the remaining group reveal the presence of the element in the urine; this, roughly, is in proportion to the number of years since the last exposure.

Autopsy and tissue analyses were obtained in 7 of the 10 deaths in this group and the tissue content of beryllium was considerably higher than the necropsy analyses of the chronic cases (table 6).

Chronic Pulmonary Granulomatosis

As defined by Machle,[14] chronic pulmonary granulomatosis or berylliosis is a generalized disease characterized by pulmonary insufficiency, having the major pathologic changes in the lungs, the most characteristic lesion of which is the granuloma. The outstanding feature of all cases of chronic berylliosis is a delay in onset from a few months to several years after initial exposure. The pathologic aspects of the acute pneumonitis and chronic pulmonary granulomatosis have been adequately covered in several publications and especially by Hazard,[4] Chesner[15] and Dutra.[16]

Symptomatically the disease is characterized by insidious onset with a nonproductive, spasmodic, paroxysmal, persistent cough; chills and fever; anorexia, with asthenia and definite loss of weight; progressive exertional dyspnea with substernal pressure and bizarre thoracic pains. The objective findings are: varying exertional dyspnea; increased pulse rate; decreased vital capacity; "watch-glass" fingernails or clubbing of fingers; acrocyanosis; decreased thoracic expansion and presence of crackling rales throughout both lung fields in the advanced stages of the disease. Routine and special laboratory procedures have failed to reveal any specific common abnormal findings. Serial cardiopulmonary roentgenograms reveal a transition from a generalized "ground glass" or granulation of the parenchyma in the early stages of the disease to the late phases of nodulations, emphysematous changes and cor pulmonale.

The treatment consists of restriction of physical activity below that permitted by the vital capacity; use of antihistaminics to relieve bronchiolar spasm; oxygen for respiratory distress; antibiotics to control any acute respiratory infection; digitalis for cardiac decompensation; cortisone and ACTH in the aggravated state of the disease and in cases showing progression of symptoms. The use of the two latter products in treatment of chronic beryllium

poisoning was reported in detail at a symposium at the Massachusetts General Hospital in December 1950. [17,18]

This chronic type of pulmonary disease first manifested itself in a resident in the immediate vicinity of one of the beryllium extraction plants in January 1944. To date we have observed and treated a total of 31 persons with rather typical clinical and pulmonary roentgenographic patterns of the chronic disease. All gave histories of occupational or nonoccupational exposure to beryllium or its compounds in varying degrees of atmospheric concentration. The nonoccupational cases numbered 12 with 6 deaths; 8 patients in this group were exposed to atmospheric pollution within a radius of less than three quarters of a mile from the beryllium extraction plant while 4 gave definite histories of exposure to the household concentration produced by soiled work clothing of beryllium workers.

Of cases resulting from occupational exposure in the various plants extracting or utilizing beryllium or its compounds, 7 with 1 resultant death occurred in 3 plants engaged in beryllium extraction from the ore, production of the Be alloys and Be research. The total employment of the 3 plants in question was approximately 2200 persons for the period from 1940 to 1952. The remaining cases numbering 12 were from other areas of the country and in plants with occupational exposures to phosphors of beryllium.

The present status of this group is that approximately 50 per cent are static or showing some improvement, 15 per cent are showing progressive regression and, at this time, the mortality is approximately 35 per cent. Of the 8 deaths in this category, 5 autopsies were obtained and the beryllium analyses of the tissues are reported plus the beryllium findings of the 24 hour urine analyses in 2 cases (table 6). Disregarding the inconsistency and disparity in the tissue findings of the various laboratories, it accentuates the fact that beryllium was present in the tissues in all 5 instances. The absence of beryllium in the single 24 hour specimen of urine in 2 cases may or may not be of significance as to possible tissue fixation of the element, temporary retention, or degree of sensitivity of the analytical method utilized.

Table 7 is the survey record of 12 living persons representing various types of exposure and present status. Every recorded urine analysis reveals the presence of beryllium; especially is this consistent by the fluorimetric method of analysis utilized at present by one of the laboratories.

Chronic Beryllium Granuloma is a subcutaneous lesion usually the result of implantation of beryllium phosphor (zinc beryllium silicate) in a skin laceration or puncture produced by a broken fluorescent tube. Lesions are always localized or self limited and usually appear 1 to 4 months after implantation of the phosphor; they are characterized by formation of a subcutaneous nodule which may eventually develop central necrosis and subsequent surface drainage. The treatment is thorough cleansing and debridement of fresh wounds and adequate wide surgical excision of the existing granulomas.

Two cases have been observed and the patients treated by the authors; 1 was previously reported in 1950.[19] The microscopic pathologic change in

both instances is identical with the pulmonary granulomas described in chronic pulmonary berylliosis. Beryllium was found in the involved tissues.

Summary

During the period of 1940 to 1952, the authors have observed and treated a total of 431 patients with various manifestations of acute beryllium intoxication. There were 10 fatalities in the pneumonitis group.

In recent years the incidence of cutaneous berylliosis among workers in the beryllium industry has been reduced from 25 per cent to 2 per cent and the respiratory syndromes almost to zero by engineering and medical hygienic preventive measures.

The eczematous type of dermatitis is caused by allergic sensitivity to beryllium compounds.

Clinical and laboratory data were obtained on more than 75 cases of recovered tracheobronchitis and pneumonitis and detailed tabulation is presented in 20 cases in each group.

From 1944 to 1952, 30 cases of the chronic dermal and pulmonary forms of beryllium have been observed and the patients treated, with 8 resultant deaths. Exposure factors, urine analyses for beryllium and other pertinent data are recorded for this group, plus tissue analyses for the element in 5 autopsied cases.

Significant data are presented of beryllium findings in the necropsied tissue of 2 patients who recovered from major acute respiratory manifestations, but died later from other causes years after removal from exposure.

The presence of beryllium in body tissue and urine is indicative of past or recent exposure to beryllium. The amount detected by present analytical methods does not bear any relationship to existence or severity of specific disease process.

Beryllium remains in body tissues and is excreted for a period of many years after removal from exposure without evidence of beryllium poisoning.

In our survey there is some evidence of proportional decrease of excretion of beryllium with increase of time from last exposure.

No persons included in the survey of recovered cases of acute pneumonitis have developed the chronic or delayed form of berylliosis.

Of the 8 instances of chronic berylliosis of occupational origin, 1 patient had a medically established diagnosis of acute tracheobronchitis while 4 others gave histories suggestive of acute tracheobronchitis during brief occupational exposures to beryllium.

The integrated medical, safety, and industrial hygiene program has been largely responsible for the phenomenal decrease in incidence of beryllium poisoning and total elimination of deaths in the local extraction plants. Therapy is mainly symptomatic and conservative, with recent evidence of therapeutic encouragement from the use of ACTH and cortisone in both the chronic and acute manifestations.

The authors express appreciation for the material assistance given by Dr. John Zielinski.

Table 1

MANIFESTATIONS OF ACUTE BERYLLIUM INTOXICATION

Summary of Annual Incidence and Time Lost Classified According to Probable Causative Compounds (Plants A, B and C)

Year	Pneumonitis				Tracheobronchitis				Dermatitis				
									Contact Hypersensitivity		Contact Only		Lost Time Days
	BeF_2	$BeSO_4$	Mix. of Soluble Salts	Lost Time Days	BeF_2	$BeSO_4$	Mix. of Soluble Salts	Lost Time Days	BeF_2	$BeSO_4$	BeF_2	$BeSO_4$	
1940	....	....	....	....	....	1	....	....	....	....	....	....	....
1941	....	1	1	86	....	1	....	....	....	3	....	....	....
1942	3	3	....	219	3	7	3	81	4	4	1	1	18
*1943	1	....	5	162	5	10	9	397	5	5	....	....	71
1944	....	....	5	477	....	5	2	214	5	5	....	1	92
1945	7	....	....	228	9	6	4	578	12	9	4	....	240
1946	2	....	1	232	9	....	2	208	13	....	5	....	132
1947	14	2	5	644	25	5	7	627	51	9	33	6	740
1948	6	1	....	261	5	2	1	95	7	2	5	....	80
1949	....	....	....	....	....	....	....	....	3	....	5	....	64
1950	2	1	....	93	5	1	1	164	7	....	2	....	86
**1951	....	....	....	....	1	....	....	40	2	....	....	....	15
Total	35	8	17	2402	62	38	29	2404	109	37	55	8	1538

*1943—Three fatalities.
**Complete to July, 1952.

Table 2

SUMMARY OF SURVEY OF 10 WORKERS WITHOUT HISTORY OF BERYLLIUM INTOXICATION*

1952

Case No. Sex Present Age	Length of Service in Be Industry	Exposure	24 Hour Urine Analysis		Present Status
			Date of Analysis and Laboratory	Micrograms Be/L	1) Physical 2) Vital capacity 3) Chest x-rays
1 Female 49 years	4-22-43 to 7-31-48 5 years	Beryllium oxide	3-5-52 (K)	0.10	Normal
2 Female 52 years	4-23-43 to 9-1-48 5 years	Beryllium oxide	3-5-52 (K)	0.38	Normal except for fibrosis of lower lungs present previous to employment.
3 Female 31 years	5-17-43 to January 1950 6½ years	Beryllium oxide	Not obtained		Normal
4 Male 50 years	1926 to present 26 years	All phases of production/maintenance since 1940	1-2-52 (A)*	0.20	Normal
5 Male 58 years	3-14-37 to present 15 years	Mainly beryllium oxide. In office since 1950.	1-2-52 (A)*	1.80	Normal
6 Male 40 years	1937 to present 15 years	All phases of BeO production. Fluoric processes since 1940.	1-2-52 (A)*	3.0	Normal
7 Male 34 years	2-2-40 to present 12 years	Plant production	1-2-52 (A)*	1.80	Normal
8 Male 39 years	5-4-42 to present 10 years	Maintenance	1-2-52 (A)*	0.20	Normal
9 Male 38 years	7-1-47 to present 5 years	Chemist in analytical laboratory.	1-2-52 (A)*	0.50	Normal
10 Male 24 years	10-4-49 to present 3 years	In all phases of beryllium extraction	1-2-52 (A)*	0.20	Normal

*Fluorimetric determinations by Laboratory (A)

Table 3

SUMMARY OF NECROPSY ANALYSES OF TISSUES AND URINE IN 2 CASES OF MAJOR RESPIRATORY BERYLLIUM POISONING (RECOVERIES)

Case No. Date of Analysis & Laboratory	Lung micrograms Be/100 Gm.	Liver micrograms Be/100 Gm.	Heart micrograms Be/100 Gm.	Spleen micrograms Be/100 Gm.	Kidney micrograms Be/100 Gm.	Urine micrograms Be/L
1 1-26-51(K)	182.			0.94	2.15	
2 8-9-51 (K) 8-15-51 (A) 8-1-50 (A)	153.0 2.0	12.5 0.72	0.36 0.17	3.15 0.95		 0.60

Table 4

FOLLOW-UP SURVEY OF 20 CASES OF ACUTE (BERYLLIUM) TRACHEOBRONCHITIS OVER PERIOD 11 YEARS

Case No. Sex Present Age	Length of Service in Be industry	Dates of Occupational Disease	24 Hour Urine Analysis		Present Status
			Date of Analysis and Laboratory	Micrograms Be/L	1) Physical 2) Vital capacity 3) Chest x-ray
1 Male 52 years	Since 1926 26 years	9-20-43 to 9-30-43	4-1-48 (K) 11-15-51 (K) 1-2-52 (A)*	0.80 1.84 0.90	Normal. Still working in beryllium production.
2 Male 48 years	Since 1936 16 years	1-25-44 to 2-9-44 2-21-44 to 3-1-44	4-1-48 (K) 10-30-51 (K) 1-2-52 (A)*	0.60 2.50 0.60	Normal. Still working in beryllium production.
3 Male 39 years	Since 1937 15 years	6-30-43 to 7-7-43 9-9-46 to 9-16-46	7-12-50 (A)*	0.60	Normal. Still working in beryllium production.
4 Male 36 years	Since 1940 12 years	7-10-46 to 7-16-46 4-9-47 to 4-20-47	10-30-51 (K) 1-2-52 (A)*	3.55 2.90	Normal. Still working in beryllium production.
5 Male 32 years	Since 1941 11 years	12-17-46 to 12-26-46	11-15-51 (K) 1-2-52 (A)*	10.60 4.40	Normal. Still working in beryllium production.
6 Male 33 years	Since 1941 11 years	3-20-47 to 3-31-47	11-15-51 (K) 1-2-52 (A)*	0.72 0.20	Normal. Still working in beryllium production.
7 Male 41 years	Since 1945 7 years	6-13-45 to 7-9-45	11-15-51 (K) 1-2-52 (A)*	4.20 1.70	Normal. Still working in beryllium production.
8 Male 45 years	Since 1947 5 years	5-26-47 to 6-9-47	10-30-51 (K) 1-2-52 (A)*	0.18 0.20	Normal. Still working in beryllium production.
9 Male 50 years	From 1940-1944 4 years	4-3-44 to 4-29-44	7-12-51 (A)* 10-16-51 (A)*	0.70 0.20	Normal
10 Male 39 years	In 1942-1943 9 months	6-16-43 to 6-30-43	11-15-51 (K) 10-14-51 (A)*	0.50 3.20	Normal

Table 4—(Continued)

SURVEY OF 20 CASES OF ACUTE (BERYLLIUM) TRACHEOBRONCHITIS OVER PERIOD 11 YEARS

Case No. Sex Present Age	Length of Service in Be Industry	Dates of Occupational Disease	24 Hour Urine Analysis		Present Status
			Date of Analysis and Laboratory	Micrograms Be/L	1) Physical 2) Vital capacity 3) Chest x-ray
11 Male 33 years	In 1943 43 days	3-13-43 to 3-24-43	7-12-51 (A)*	0.40	Normal
12 Male 49 years	In 1943 4 years	11-8-43 to 11-22-43	11-15-51 (K) 10-11-51 (A)*	0.43 0.20	Normal
13 Female 40 years	In 1943 5 months	9-29-43 to 10-6-43	7-13-51 (A)* 1-2-52 (A)*	0.65 0.20	Normal
14 Male 48 years	In 1944 2 months	1-15-44 to 3-20-44	6-17-48 (K) 7-21-50 (A)* 11-15-51 (K) 1-2-52 (A)*	0.04 nil 0.35 0.01 nil 0.20	Normal
15 Male 43 years	In 1944 1½ months	1-29-44 to 4-5-44	6-21-48 (K) 7-12-51 (A)*	0.04 nil 0.25	Normal
16 Male 38 years	In 1945 6 months	6-20-45 to 7-17-45	7-25-50 (A)* 11-15-51 (K) 10-14-51 (A)*	0.60 0.14 0.20	Normal
17 Male 60 years	In 1945 4 months	11-7-45 to 12-17-45	11-15-51 (K) 10-5-51 (A)*	0.05 0.20	Normal
18 Male 28 years	In 1946 2 months	3-20-46 to 4-15-46	11-15-51 (K) 1-2-52 (A)*	1.32 3.00	Normal
19 Male 51 years	In 1947 16 days	2-20-47 to 3-20-47 and 3-25-47 to 4-14-47	7-12-51 (A)*	0.20	Normal
20 Male 25 years	In 1947-1948 11 months	7-20-47 to 7-28-47	11-15-51 (K) 1-2-52 (A)*	0.08 0.20	Normal

*Fluorimetric method of analysis.

Table 5

FOLLOW-UP SURVEY OF 20 CASES OF ACUTE (BERYLLIUM) PNEUMONITIS OVER PERIOD 11 YEARS

Case No. Sex Present Age	Length of Service in Be industry	Dates of Occupational Disease	24 Hour Urine Analysis		Present Status
			Date of Analysis and Laboratory	Micrograms Be/L	1) Physical 2) Vital capacity 3) Chest x-ray
1 Male 46 years	Since 1940 12 years	1-13-48 to 2-2-48	11-15-51 (K) 1-2-52 (A)*	7.40 4.50	Normal. Still working in industry.
2 Male 59 years	Since 1941 11 years	4-4-41 to 4-29-41	4-1-48 (K) 1-2-52 (A)*	1.20 1.10	Normal. Still working in industry.
3 Male 30 years	Since 1946 5½ years	10-20-46 to 11-27-46	4-1-48 (K) 10-30-51 (K) 1-2-52 (A)*	0.40 0.26 0.40	Normal. Still working in industry.
4 Male 37 years	Since 1947 4 years	2-24-47 to 4-29-47	4-1-48 (K) 9-8-48 (K)	0.30 0.30	Normal. Still working in industry.
5 Male 30 years	Since 1947 5 years	12-25-47 to 1-19-48	11-15-51 (K) 1-2-52 (A)*	0.70 0.20	Normal. Still working in industry.
6 Female 27 years	1943 to 1947 4 years	4-5-47 to 5-12-47	11-15-51 (K) 10-26-51 (A)*	0.28 0.20	Normal
7 Female 49 years	In 1943 2 months	8-7-43 to 12-6-43	8-2-48 (K) 10-8-51 (A)*	Nil 0.20	Normal
8 Male 54 years	In 1944 3 months	5-25-44 to 9-21-44	6-29-49 (K) 1-2-52 (A)*	0.04 nil 0.20	Pulmonary fibrosis with decreased V.C. to 60% of normal.
9 Male 57 years	In 1944 6 months	1-16-45 to 4-2-45	No specimen	....	Normal
10 Male 57 years	In 1945 3 months	6-6-45 to 7-5-45	7-12-51 (A)*	0.20	Normal

Table 5—(Continued)

FOLLOW-UP SURVEY OF 20 CASES OF ACUTE (BERYLLIUM) PNEUMONITIS OVER PERIOD 11 YEARS

Case No. Sex Present Age	Length of Service in Be industry	Dates of Occupational Disease	24 Hour Urine Analysis		Present Status
			Date of Analysis and Laboratory	Micrograms Be/L	1) Physical 2) Vital Capacity 3) Chest x-ray
11 Male 28 years	In 1945 3 months	7-13-45 to 9-4-45	11-15-51 (K) 1-2-52 (A)*	0.20 0.22	Normal
12 Male 27 years	In 1946-1947 3 months	11-25-46 to 3-31-47	9-23-49 (K)	0.04	Normal
13 Male 68 years	In 1946-1947 4 months	1-11-47 to 1-28-47 4-1-47 to 4-12-47	7-14-48 (K)	0.04	Normal
14 Male 46 years	In 1947 2 months	3-8-47 to 3-24-47	7-18-50 (A)* 11-15-51 (K) 1-2-52 (A)*	0.40 0.03 0.20	Normal
15 Female 38 years	In 1947 5 months	5-14-47 to 6-30-47	7-12-51 (A)* 11-28-51 (K) 11-12-51 (A)*	0.55 0.034 0.20	Normal
16 Male 29 years	In 1947 3 months	7-3-47 to 8-27-47	11-15-51 (K) 10-26-51 (A)*	0.01 0.20	Normal
17 Male 45 years	In 1947 3 months	9-13-47 to 10-8-47	7-21-51 (A)*	0.60	Normal
18 Male 39 years	In 1947 2 months	11-5-47 to 12-22-47	7-12-51 (K) 1-2-52 (A)*	0.065 0.40	Normal
19 Male 30 years	In 1947 23 days	10-29-47 to 12-9-47	8-13-48 (K) 11-1-51 (A)*	0.04 1.40	Normal
20 Female 46 years	In 1947-1948 2 months	1-6-48 to 1-13-48	10-16-51 (A)*	2.30	Normal

*Fluorimetric method of analysis.

Table 6

SUMMARY OF TISSUE ANALYSES OF 5 AUTOPSIED CASES CHRONIC BERYLLIOSIS

Case No. Sex Age at Death	Type of Exposure and Duration	Dates of Onset of disease to Death	Date of Analysis and Laboratory	Lung Microgram Be/100 Gm.	Liver Microgram Be/100 Gm.	Broncho-pulmonary Lymph nodes Microgram Be/100 Gm.	Spleen & Bone Micrograms Be/100 Gm.	Other Tissue Micrograms Be/100 Gm.	Urine Microgram Be/Liter
1 Female 38 yrs.	Neighborhood: Lived 2 blocks from plant 1940 to 1945	Jan. 1944 to 7-15-46	12-19-47(K) 8-11-48 (S)	Nil 0.4					
2 Female 26 yrs.	Neighborhood: lived ½ mile from plant in 1941.	June 1946 to Feb. 17, 1948	3-23-48 (K) 6-3-48 (R)	.93 .08	1.48 .05	6.5	Spleen 0.17	Kidney .07	
3 Female 7 yrs.	Neighborhood: Lived ½ mile from plant 1941 to 1947.	March 1947 to 9-4-48	9-25-48 (K)	0.237	Nil or 0.008	0.665	Spleen nil or 0.02		
4 Female 53 yrs.	Neighborhood: Lived ½ mile from plant 1942 to 1949.	May 1947 to 8-24-49	12-20-48(K) 3-6-50 (A) Sept.1949(K) Sept.1949(R)	.... 0.2 Nil Nil	....	.... 10.0 0.59 Nil	.... Rib 7.7 Rib nil Rib nil	.... Heart 10.0	Nil or .002
5 Female 26 yrs.	Household: Husband's clothing. Dec. 1942 & Jan. 1943.	Dec. 1943 to 11-27-49	4-1-49 (K) 12-20-49(K) 3-6-50 (A) 3-9-50 (R)	.... 0.99 .... 0.11	.... 0.68 0.40 Nil	.... 5.0 3.3	.... Spleen 0.7 Spleen 0.03	....	Nil

Table 7

SUMMARY OF SURVEY OF 12 LIVING PATIENTS WITH CHRONIC BERYLLIOSIS**

Sex Present Age	Type of Exposure	Dates of Exposure	Date of Onset of Disease	24 Hour Urine Sample		Blood Analyses		Present Status and Therapy
				Date of Analysis and Laboratory	Micrograms Be/L	Date of Analysis and Laboratory	Micrograms Be/100 Gm.	
1 Female 40 yrs.	Nonoccupational. Laundered brother's clothing.	Brother worked at plant in 1941 and 1942	In 1944	8-7-50 (A)* 11-15-51 (K) 1-2-52 (A)*	0.70 0.22 0.20	8-10-50 (K)	Nil	Slight improvement. Symptomatic, conservative therapy.
2 Female 27 yrs.	Nonoccupational.	Lived 1 block from plant 1940 to 1948	February 1947	4-1-48 (K) 8-8-50 (A)*	Nil 0.35	8-10-50 (K)	Nil	Improving. Symptomatic, conservative.
3 Male	Nonoccupational. (Same dwelling as Case 2)	Lived 1 block from plant Feb. 1948 to 1952.	May 1948	10-1-50 (A)*	0.55	8-10-50 (K)	Nil	Condition worse. Therapy unknown.
4	Nonoccupational	Lived 100 feet from plant from Nov. 1940 to April 1945	April 1942	1-2-52 (A)*	3.70	10-23-50 (K)	0.01	Improving. Symptomatic, conservative therapy.
5 Female 33 yrs.	Nonoccupational	Lived 1 block from plant 1942 to 1947.	Fall 1946	4-1-48 (K) 8-8-50 (A)* 11-15-51 (K) 1-2-52 (A)*	0.13 0.35 0.06 0.20	8-11-50 (K)	Nil	Improving. Symptomatic, conservative therapy.
6 Male 24 yrs.	Nonoccupational	Exposed to father's clothing; a plant employee from 1940 to 1952.	March 1949			8-10-50 (K)	Nil	Improving; special therapy.

**Survey, data to July 1952.

(continued on page 192)

*Fluorimetric method used by Laboratory (A) in 1951 and 1952.

Table 7 — (Continued from page 191)

SUMMARY OF SURVEY OF 12 LIVING PATIENTS WITH CHRONIC BERYLLIOSIS**

Sex Present Age	Type of Exposure	Dates of Exposure	Date of Onset of Disease	24 Hour Urine Sample		Blood Analyses		Present Status and Therapy
				Date of Analysis and Laboratory	Micrograms Be/L	Date of Analysis and Laboratory	Micrograms Be/100 Gm.	
7 Female 61 yrs.	Nonoccupational	Lived ½ mile south of plant since 1923 to present.	April 1950	6-30-52 (K)	0.16			Improved in last 12 months. No therapy.
8	Occupational	June 1, 1941 to July 3, 1941	Dec. 1944	4-1-48 (K) 11-15-51 (K) 1-2-52 (A)*	0.14 0.58 1.50			Slight improvement. Symptomatic, conservative therapy.
9 Male 31 yrs.	Occupational	Dec. 1941 and Jan. 1942	Jan. 1946	Not obtained		Not obtained		Some improvement. Symptomatic, conservative therapy.
10 Male 35 yrs.	Occupational	June 14, 1944 to July 13, 1944	Late 1947	11-15-51 (K). 7-12-51 (A)* 1-2-52 (A)*	0.09 0.75 1.40	11-9-50 (K)	Nil	Improving but totally disabled. Cortisone.
11 Female 43 yrs.	Occupational	Nov. 1943 to Mar. 1944	Dec. 1947	12-26-50 (A)* 11-15-51 (K) 1-2-52 (A)*	0.65 0.06 0.42	1-4-51 (K)	Nil	Improving. Partial disability. Symptomatic, conservative therapy.
12 Male 53 yrs.	Occupational	4-30-45 to 5-30-45 7-9-45 to 7-19-45	Oct. 1947	6-21-48 (K) 7-12-51 (A)* 11-15-51 (K) 1-2-52 (A)*	0.04 1.00 0.01 0.20	1-10-51 (K)	Nil	Some improvement. Total disability. Cortisone therapy.

**Survey, data to July 1952.

*Fluorimetric method used by Laboratory (A) in 1951 and 1952.

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