Pulmonary Aspects of Some Toxic Experimental Space Fuels

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With the advent of the space age, a number of new compounds have been introduced for potential use in various scientific and military fields. Among such compounds are the boranes which consist of chemical combinations of boron and hydrogen and serve as intermediary agents in the formation of high energy fuels to propell aircraft beyond the stratosphere. The relative frequency of pulmonary symptoms in a number of individuals employed by a local industry, who were exposed to these agents, has motivated this present study. Previous reports on the respiratory involvement in boron hydride intoxication have been published by Rozendaal1 and Lowe and Freeman.5 We believe our study represents the first to deal in detail with the various pulmonary problems encountered, including the altered lung function patterns.

Foremost among the noxious agents from the bronchopulmonary aspect was diborane with a chemical formula of B2H6. Decaborane, B10H14, and pentaborane, B5H9, were associated with fewer toxic reactions referable to the respiratory tract and provoked unusual and almost unique neurologic abnormalities.

Diborane, a gas with a boiling point of minus 92.5° C. has been found to be perceptible in the atmosphere at three parts per million, and its toxicity has been comparable to that of phosgene, according to the work of Krackow.3 Pentaborane has been equated in potency to hydrogen cyanide by the same author. Decaborane, a crystalline solid, is less noxious than the other two boranes. The excessive heat evoked upon hydrolysis of these agents has formulated the basis of their use as fuels.

Materials and Methods

This study extended over a five year period (1956-1960). Among the total of 26 cases of acute diborane toxicity, 18 patients were seen primarily with respiratory involvement. Of 33 patients with subacute exposures, eight became ill with chest symptoms. Five of 35 patients with decaborane intoxication had pulmonary manifestations. Pentaborane poisoning with bronchabor pulmonary findings occurred in three patients from a total of 166. Two individuals had repeated exposures to diborane, whereas one had recurrent exposures to all three agents. These three patients were chronically ill over a prolonged period of time.

Routine laboratory studies included chest x-rays, complete blood counts, urinalysis, liver and kidney function tests. The cephalin flocculation, thymol turbidity and urine for bile and urobinogen comprised the liver studies and the bromsulfalein and the SGO-T and SGP-T tests were added in the latter part of the investigation. The blood urea and the phenolsulphonphthalein tests constituted the kidney function workup.

All patients had pre-employment chest x-ray films. Subsequent chest films were taken in those individuals who were heavily exposed, but in most instances not commensurate with the time of immediate exposures, since this facility was not available in the immediate plant area at the beginning of this study. Likewise, pulmonary function tests

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were not available at the outset of this investigation and therefore were not done routinely. Those patients tested included the three chronic respiratory cases and ten other individuals with prolonged electroencephalographic abnormalities and pulmonary symptoms. The studies performed on the latter group were the ventilatory tests, whereas the chronic cases also had arterial, alveolar and lung volume determinations including residual volumes. They also had additional studies consisting of total eosinophile counts, postprandial blood sugars, total proteins with A-G ratio and chest x-ray films at approximately six month intervals. Sputa were unobtainable in all three individuals. A bronchogram was done in the sickest patient of the chronic respiratory group. Electrocardiograms were taken in two of these patients.

One of the chronic patients was lost to followup examination, having to move from the immediate area for economical reasons, and therefore only had one set of lung function studies.

Electroencephalograms were done in 23 individuals who had prolonged nervous system abnormalities.

**Results**

Three patients with protracted respiratory distress had obstructive ventilatory insufficiency in the pulmonary function tests. One individual showed a constant hyperventilation pattern. The lung volumes were normal in these patients and the results of other patients tested were normal.

Electroencephalographic abnormalities found in all three chronic cases were characterized by a temporal dysrhythmia. The abnormal graph present in the sickest individual, (P.K.), cleared completely when re-examined one and one-half years later. This patient's chest x-ray film remained normal, but his bronchogram revealed diffuse narrow-
ing of many bronchi, compatible with bronchospasm.

The consistent electroencephalographic abnormality of the other patients tested was also a temporal area disturbance.4

The other laboratory finding of significance was a three plus cephalin flocculation found in 6 per cent of patients which persisted for several days. No clinically detectable jaundice was present in any of these cases.

Two patients with pentaborane exposures showed increased pulmonary vascular markings. All of the other chest x-ray findings were unremarkable except those in two patients with acute diborane exposure which revealed pneumonitis and each cleared from one to two weeks. One of these two individuals (T.T.) had lung function studies subsequent to complete recovery and his results were normal. All the patients seen in the three different types of intoxications recovered.

Graph 1 reveals the air trapping in the vital capacity spirogram of P.K.

SIGNS AND SYMPTOMS

Diborane intoxication in the acute phase was accompanied by generalized chest tightness, dyspnea, nonproductive cough and wheezing, lasting from three to five days in the majority of patients. Nausea, anorexia and hypersalivation were present in 10 per cent of the patients. In individuals exposed to lower concentrations of this gas over longer periods of time, light-headedness, headache, fatigue, and drowsiness were prominent features. Cough and chest tightness were present in 25 per cent of these subacute exposures. These patients were ill for approximately five days and a few patients were sick for two to three weeks. The major physical findings on chest examination of the diborane cases of acute and subacute exposures were inspiratory and expiratory rhonchi throughout the lung fields.

The major symptoms of the three chronic diborane patients consisted of wheezing, dyspnea, moderate chest tightness and dry, nonproductive cough. Dyspnea was associated with moderate exertion while wheezing, aggravated by effort, was rather constant in one patient and intermittent in the other two. Hemoptysis, chills and fever were not present at any time.

The salient physical findings were inspiratory and expiratory sibilant rhonchi, frequently predominant during inspiration. Inspiratory and expiratory rhonchi were less prominent and frequent.

The duration of illness in the two patients who were followed closely ranged from three years (R.K.) to four and one-third years (P.K.). The former individual has been asymptomatic during the past four months. The third patient was symptomatic for approximately two and one-half years up to the time of last examination in May, 1959.

Treatment was continuous throughout the period of disability in the above two patients. There was no previous history of pneumonia, pleurisy, recurrent or chronic bronchitis, chronic rhinitis or allergies of any kind in the chronic cases.

Decaborane intoxication was associated with generalized chest tightness which lasted seven to ten days. The prominent features of the decaborane cases were primarily referable to the nervous system and consisted of gross tremors of the extremities, bizarre positional movements of the hands and feet, hypoglossal spasms, generalized nervousness, light-headedness and drowsiness. Nausea and anorexia were noted in approximately 10 per cent of the cases.

Pentaborane intoxication resulted in respiratory symptoms in a small percentage of the total number of patients that became ill. Striking neurologic features were rather dramatic and were characterized by chronic movements of extremities and neck, generalized muscle spasms, diffuse fasciculations, opisthotonus and catatonic-like reaction. In two patients a severe cough persisted for five days and the x-ray films of these two patients disclosed increased pulmonary vascular markings.

CASE REPORTS

CASE 1

This 32-year-old white man (T.T.) who was exposed to diborane at 9 p.m. on September 11-
16, 1956 shortly thereafter developed extreme difficulty in breathing, severe tightness in the upper mid portion of the chest, weakness, and slight twitching of the hands. These persisted over an approximate two-hour period.

Physical examination upon admission to the hospital Saturday 11, 1956, revealed an acutely ill, flushed, white male with a temperature of 101°F., respiratory rate of 28, pulse of 128 and blood pressure of 110/60. Examination of the head and neck and special senses were negative. Over the lungs inspiratory crepitant basal rales were heard posteriorly. There was also increased intensity of the breath sounds in these areas. The remainder of the examination was negative.

Dyspnea and cough continued over the next 72 hours and on September 13 fine rales were heard anteriorly in both bases. The patient gradually improved from September 13 and on September 16 his lungs were clear to examination and the cough, wheezing and shortness of breath had completely ceased. The laboratory work on this admission revealed the white blood cell count to be 21,000, with a differential count of 80 polymorphonuclear leukocytes, 6 lymphocytes, 2 monocytes and 12 stabs. This patient was discharged on September 17, 1956, asymptomatic. The hemoglobin was 15.4 grams and the serologic tests were negative. Urinalysis was negative, except for three to four pus cells per high power field. The cephalin flocculation was negative in 48 hours; BSP revealed 8 per cent retention in 45 minutes. The total van den Bergh was 0.35 mg. per cent. The sputum examination was negative. The cold agglutination test was also negative. Chest x-ray film revealed infiltrations in both bases, predominately in the right side. (Fig. 1).

Treatment consisted of penicillin, one million units daily, oxygen by tent, which was administered over the first 24 hours, and general supportive care.

This individual was readmitted on September 24, 1956, having been subjected to the fumes of diborane gas immediately prior to admission and at this time complained of recurrence of severe shortness of breath and diffuse chest tightness. The salient findings on examination were limited to the lungs, namely, medium dry rales at the bases anteriorly, slightly more so on the right side. A few fine rales were also heard at the right base posteriorly. These abnormalities remained until September 27, 1956. On September 29, 1956 the patient developed urticular lesions which disappeared in 48 hours. The laboratory work revealed WBC count of 21,000 with 90 polymorphonuclears, 16 stabs, 8 lymphocytes, 2 monocytes. The hemoglobin was 14.9 grams and the red cell count was 4.85 million. The urinalysis was again negative and chest x-ray film disclosed pneumonitis of the right lower lobe and increased markings in the left lower lobe (Fig. 2). The treatment received again was penicillin 600,000 units b.i.d. and chloramphenicol was added on September 26 when his initial fever of 102°F. recurred. Oxygen was again administered by tent. Penicillin was stopped on September 29, 1956 and chloramphenicol was discontinued September 30, 1956. The patient was discharged asymptomatic on October 1, 1956. A chest x-ray film obtained approximately two weeks later showed complete disappearance of the lesions, (see Fig. 3).

CASE 2

This patient (O.R.) was exposed on August 18, 1958 to diborane fumes and immediately afterward developed shortness of breath, vertigo and dry cough and was given O2 by mask in the infirmary of the plant, obtaining relief 20

**FIGURE 4A**

minutes thereafter. Six days later the dry cough recurred after again being exposed to diborane and he developed concomitant generalized chest tightness. At this time he was given oxygen and ammonium chloride. However, the symptoms persisted and gradually became worse. On August 31 isoproterenal hydrochloride (Isuprel) inhalations with intermittent positive pressure breathing were instituted. Examination of the chest disclosed moist rales at both bases. X-ray film on September 2 revealed pneumonitis in both bases, more on the left side. The patient was treated at home with 200,000 units of penicillin q.i.d. for three days. In addition he received isoproterenal by IPPB on September 3 and 4. Chest x-ray on September 9, 1958 showed considerable improvement with clearing of both bases. Laboratory findings: hemoglobin, 15.5 gm., red blood cells 5.1 million and white blood cells 10,400. Differential count showed 55 polymorphonuclears, 27 lymphocytes, 4 monocytes, 12 stabs and 2 eosinophiles. Urinalysis within normal limits and the blood urea was 12 mgm. per cent. Sputum examination was negative. See Figs. 4A, 4B and 5.

Discussion

Chronic respiratory embarrassment from repeated diborane exposures in two patients and repeated triple gas exposure in one patient resulted in obstructive ventilatory insufficiency which has been reversible. Hyperventilation, present in two of the chronic patients and most prominent in the sickest individual, has decreased somewhat in the latter patient, but still persists. It has been increased by 80 per cent helium, 10 per cent carbon dioxide and exercise and has decreased minimally with oxygen and heavy sedation (three grains of sodium amobarbital.) Moderate sedation with one and one-half grains of sodium butabarbital has produced no effect. The mechanism of hyperventilation is not completely known at present. Two possibilities may be considered, namely, a factor of central origin, which has not been demonstrated by a persistent dysrhythmia of temporal lobe patterns in two of the chronic patients and secondly a psychogenic or neurogenic factor. A remote possibility also is an increase in pulmonary resistance. The psychogenic aspects of this problem have been tested in detail and have not yielded conclusive results. An alveolar capillary block syndrome is untenable since normal arterial oxygen saturation studies were obtained before and after exercise on two occasions when tested at a one year interval. However, the last results performed revealed borderline low readings with an arterial O2 saturation of 92.9 per cent before and 93.8 per cent after exercise. Another perplexing finding in this same individual has been a persistently low alveolar P02.

The mechanism of chronic respiratory disability could be attributable to one or all of three factors: (1) prolonged hypersensitivity reaction to the offending agent; this is the most logical explanation in our opinion; (2) chronic irritative bronchitis on a thermal basis; diborane has an exothermic property which is the basis of its use as a high energy fuel; this reaction in lung tissue has been postulated by Lowe and Freeman; (3) bronchospasm, on a neurogenic or psychogenic basis; this is always difficult to prove, but nevertheless is a strong possibility particularly in the one patient with prolonged hyperventilation. As was mentioned previously, this patient did have a slight depression in the hyperventilation pattern after large doses of sedation were given.

The pneumonitis in the two acute patients appears to represent secondary infection provoked by the physical and possibly by the chemical properties of the boranes. Previous cases of pneumonia related to these com-

Figure 5: PA chest x-ray film of O.R., September 9, 1958.
pounds have been cited by Rozendaal and Lowe, and by Freeman. Furthermore, in experimental animal studies, Krackow produced both pneumonia and pulmonary edema.

The treatment of the acute exposures has been with oxygen by mask or with intermittent positive pressure breathing and the additional use of methocarbamol in many of the cases of pentaborane and decaborane intoxications. Severe neurologic involvement was managed by combined administration of meperidine hydrochloride (Demerol), promethazine (Phenergan) and chlorpromazine (Thorazine) intramuscularly. The chronic cases of diborane were treated with long-term bronchodilators, oxygen with intermittent positive pressure breathing at varying intervals, and expectorants. In addition, in the severest case, prophylaxis with sulfanilamides was instituted during the fall and winter of the year.

**Summary and Conclusions**

1. Acute diborane intoxication is associated predominantly with bronchopulmonary involvement, whereas acute decaborane and pentaborane toxicity is manifested primarily by neurologic abnormalities.

2. Two cases of acute diborane intoxication with pneumonitis were encountered.

3. Chronic respiratory distress was present in two patients from recurrent diborane exposure and in one patient from combined triple borane exposures. This chronic disability is most likely on a hypersensitivity basis and appears clinically as an asthmatic bronchitis. This is borne out by the obstructive ventilatory patterns demonstrated in the pulmonary function tests.

4. The cause of the hyperventilation in one chronic patient thus far has not been ascertained.

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**Resumen**

1. La intoxicación aguda por diborano se asocia predominantemente con compromiso pulmonar broncopulmonar en tanto que la toxicidad aguda con decaborano y pentaborano se manifiesta por transtornos neurológicos.

2. Se encontraron dos casos de neumonitis aguda por intoxicación con diborano.

3. Hubo transtorno respiratorio crónico en dos enfermos con exposición reiterada y en un enfermo con triple exposición combinada al diborano.

Esta afección crónica es muy probablemente debida a una hipersensibilidad y aparece como una bronquitis asmática. Esto es afirmado por los cuadros de obstrucción ventilatoria, demostrados en las pruebas funcionales.

4. La causa de la hiperventilación en un enfermo crónico hasta ahora no se ha aclarado.

**Resume**

1. L'intoxicacion aigue au diborane est associee essentiellement a une atteinte broncho-pulmonaire, tandis que la toxicite aigue au decaborane et au pentaborane se manifeste d'abord par des anomalies neurologiques.

2. L'auteur rapporte deux cas d'intoxicacion aigue au diborane avec pneumonie.

3. Il existait une d'etresse respiratoire chronique chez deux malades provenant d'une exposition repetee au diborane, et chez un malade, provenant d'exposition aux trois boranes associs. Cette incapacite chronique est fondee plus vraisemblablement sur une hypersensibilite et apparait cliniquement comme une bronchite asthmatique. Ceci est mis en evidence par les tracdes de l'obstruction ventilatoire montres par les tests de la fonction pulmonaire.

4. La cause de l'hiperventilation chez un malade chronique n'a pas ete verifiee jusqu'a present.

**References**


