PULMONARY IRRITANTS*

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CLASSIFICATION OF PULMONARY IRRITANTS

PULMONARY irritant or injurant substances comprise a group of compounds that exist as gases, or as liquids that have a sufficiently high vapor pressure under ordinary conditions to give rise to injurious concentrations in respired air.

Of greatest interest among these, for the purposes of the present discussion, are the acid gases—substances that appear to owe their physiological effects to the fact that they are acids or that they behave like acids under the conditions of their use—these being hydrogen chloride, bromide and fluoride, and chlorine, bromine, sulfur dioxide and certain oxides of nitrogen, together with phosgene, diphosgene and chloropicrin. There are other less common members of this group, and there are also non-irritant, unstable alkyl halogen compounds that exert their primary effect upon the nervous system when inhaled, subsequently, and apparently through hydrolysis, yielding substances that act as irritants, inducing extensive circulatory and pulmonary damage. Whether the pulmonary damage in the latter group is due mainly to circulatory failure, or to the exhalation of an irritant decomposition product of the original compound has not been established, but the lung pathology is so like that caused by the inhalation of an irritant gas as to justify the inclusion of these compounds in this group.

Next, come members of the group classified for the purposes of chemical warfare as vesicants. The best known among these, mustard and lewisite, must be regarded as pulmonary irritants in the toxicological sense, since despite their low vapor pressure, they give rise at ordinary temperatures to highly irritant concentrations of vapor. The serious pulmonary injury sustained by persons who inhale these vapors does

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not lend itself to satisfactory explanation, and nothing will be said concerning its pathological physiology in this discussion. The injurious effects of the inhalation of these vapors must be mentioned, however, because of the pattern of the clinical condition that develops—a pattern that is different in many respects from that associated with exposure to the acid gases. These effects will be dealt with briefly at an appropriate time.

Certain other gases, of which ammonia and formaldehyde may be mentioned as examples, do not fit into either of the preceding groups. Inhalation of these substances in sufficiently high concentrations induces the symptoms and the pathologic picture of acute upper respiratory and pulmonary irritation. They are mentioned only to call attention to the fact that this classification of irritant respirable substances is of necessity somewhat incomplete.

Finally, the carbonyls would seem to come within a toxicologic classification of pulmonary irritants, because of their property of depositing finely divided particles of metal in the lung tissue, thereby inducing an intense pulmonary irritation and edema. Iron and nickel carbonyl represent the best known examples of this group. For a variety of reasons these compounds scarcely seem destined to play an important role in chemical warfare, and therefore they are mentioned only as interesting examples of an additional and apparently unique type of pulmonary irritant.

Certain Properties of Pulmonary Irritants

Correlation and comparison of certain of the physical, chemical, and physiological properties of some of the substances referred to in the foregoing paragraphs will serve to illustrate practical points of importance.

Table I calls attention to the importance of volatility in determining the comparative potentialities of compounds that have about the same toxicity (compare mustard and the potentially more dangerous lewisite), while at the same time it shows how unimportant relative volatility may be when a compound is sufficiently toxic (compare chlorine with mustard).

Table II demonstrates how little relationship there may be between the actual toxicity of one of these compounds, and the immediately painful sensation of upper respiratory and pulmonary irritation that

TABLE I

COMPARISON OF VOLATILITY AND LETHAL CONCENTRATION OF IRRITANT AGENTS

	Concentration in milligrams per liter				
	Phosgene	*Chloropicrin*	*Chlorine*	*Mustard*	*Lewisite*
Vapor in air at 20° C	∝ (gas)	∝ (gas)	∝ (gas)	0.57	4.50
Fatal for 30 min. of exposure	0.36	0.80	2.50	0.07	0.05
Fatal for 10 min. of exposure	0.50	2.00	5.60	0.15	0.12

TABLE II

COMPARISON OF MINIMUM DETECTABLE, IRRITATING AND LETHAL CONCENTRATIONS OF IRRITANT AGENTS

	Concentration in milligrams per liter				
	Phosgene	*Chloropicrin*	*Chlorine*	*Mustard*	*Lewisite*
Minimum detectable odor	0.0044	0.007	0.01	0.0013	0.014
Minimum irritating concentration	0.005	0.009	0.029	0.001*	0.008*
Fatal for 10 min. of exposure	0.50	2.00	5.60	0.15	0.12

* There is a latent period before presence is apparent.

result from exposure to it. In practical terms this means that not all of them give adequate warning of their presence in dangerous concentrations in the respired air.

Still other properties of these substances are important factors in their behavior. Their solubility in water, or the avidity of their combination with water, may be the determining factor in the locus of their action. Thus the primary effect of exposure to the highly soluble chlorine, ammonia, and sulfur dioxide is exerted upon the upper respiratory tract, and if one is exposed to low or moderate concentrations for periods that are not too long, the damage done is confined almost entirely to the nose and throat. In contrast, the chief injury associated with the inhalation of correspondingly irritating concentrations of phosgene occurs in the lung.

The General Effects of Exposure to Pulmonary Irritant Gases

Much has been made of the importance of the time-concentration relationship in exposure to noxious gases, and in general emphasis upon this relationship is justified. A certain caution must be exercised against complete reliance upon it. The duration of the exposure to an highly irritant gas is important, but the severity of the effect cannot be expressed as the product of concentration and time, except within certain limits of concentration, because of the disproportionately injurious effects of brief exposures to high concentrations, as well as the negligible effects of sufficiently low concentrations. This can best be appreciated if it is recognized that there are at least four, and perhaps five, types of effect that result from various combinations of concentration and length of the exposure.

1. The effect of exposure to very high concentrations may be virtually immediate anoxic death. Whether this outcome is the result of direct damage to the respiratory membrane rendering it impermeable to the normal respiratory gases, whether it is due to rapid absorption of the poison with central respiratory paralysis, or whether it is due to circulatory collapse (vagus shock), is not apparent. The pathological picture in experimental animals suggests that the last mentioned possibility is the most likely.

2. Another result of brief exposure to high concentrations of these gases, which may differ only in degree from that previously described, is extensive immediate damage to the pulmonary and upper respiratory tissues. Acute hyperemia, hemorrhage and tissue destruction (coagulation necrosis) may be the prominent features of the pathological picture, or alternatively, if death occurs promptly, there may be acute emphysema, general acute interstitial edema, ischemia and coagulation necrosis. In this and in the previously mentioned type direct pulmonary injury is much more prominent than reaction to injury or the secondary effects, chiefly because death occurs before these have time to develop.

3. The third group of effects is that with which we are most concerned in that it offers an opportunity for survival. Here, there is pulmonary injury of a serious type, and accompanied by upper respiratory damage that varies in degree with the nature of the agent and its concentration in the air breathed by the victim. It is to this general set of effects that we shall give detailed consideration.

4. A fourth type of effect is that following exposure to concentrations of noxious substances that are insufficient to cause immediately serious injury to the respiratory tissues, over such a period of time as to cause accumulation of these noxious substances in the tissues of the body as a whole and thereby to induce systemic intoxication. This type of effect is of no practical importance in relation to chemical warfare. It is of some interest, however, to recognize that a dangerous and even lethal dose of an acid gas may be absorbed from the respired air without doing greater damage to the lungs than to the other organs.

5. A still further set of effects is that produced by mild exposures to respiratory irritants for comparatively short periods, following which the injury is limited almost entirely to irritation of the eyes and upper respiratory tract. There is stinging and burning of the eyes, nose, and throat, redness and weeping of the eyes and the respiratory and pharyngeal mucosa, sneezing perhaps and certainly coughing, with a sore throat and huskiness or perhaps loss, of the voice. There may be headache, originating from irritated accessory nasal sinuses. Nosebleed is not infrequent, and there may be some blood-tinged sputum from the pharynx and trachea, but there will be little chest pain except perhaps the muscular soreness associated with excessive coughing. These effects last from a few minutes to several hours, with more prolonged lesser effects, among which the soreness of the throat and the huskiness of the voice may be the most persistent.

The Effects Upon the Respiratory System of Serious Exposure to Irritant Agents

Immediate effects: The initial symptoms of exposure to irritant gases are those of sharp burning pain in the eyes, nose and throat, with constriction of the throat, irregular respiration, followed by rapid, dyspneic respiration, and subsequently by some degree of relief as the secretions of the eyes and nose begin to flow and bathe the irritated surface. The severity of these symptoms varies with the characteristics of the agent involved, and with the concentration to which one is exposed. Labored breathing with spasmodic coughing may be prominent, and chest constriction and pain, with air hunger and the fear of promptly impending death, may develop. Upon escape from exposures of less than extreme severity, there is some degree of relief from the more acute distress, but the coughing continues for some time, producing considerable mucus

which is likely to be blood-tinged and may be frankly hemorrhagic, and the burning of the nose and throat continues. The voice becomes husky and may be reduced to the merest whisper. Gradually some degree of comfort ensues in most cases.

Effects during following twenty-four hours: After two to twelve hours of relative comfort, respiratory distress, accompanied by the increasing physical signs of pulmonary moisture, may begin to develop, and may reach an acute stage promptly, especially if the victim exerts himself in any way. There may be no interval of relief; in such cases the signs of acute respiratory irritation during exposure are followed by steadily increasing signs of pulmonary congestion and edema or hemorrhage. On the other hand, there may be a gradual subsidence of all of the symptoms of upper respiratory and pulmonary irritation, with little or no evidence of pulmonary edema. Exposed persons, kept under observation over a period of twenty-four hours during which pulmonary congestion and edema have failed to appear, may generally be regarded as free of danger. This period of twenty-four hours following the exposure is crucial, and for such a time the patient must be kept quiet and warm, as comfortable and relaxed as possible, and under careful observation. It is probable also that this is the period during which specific measures for the prevention of pulmonary edema will be indicated, if and when such measures can be developed on a sound physiologic rationale.

Subsequent effects: Exposed persons who do not develop evidences of pulmonary edema within the first twenty-four hours will recover promptly and without further incident, as a rule.

Those who develop pulmonary edema may be ill for periods that vary from a few days to many weeks, dependent upon the severity of the injury sustained. Secondary infection resulting from the invasion of the bacterial flora of the nose and throat into the injured tissues may be expected to develop in the individual who survives the acute chemical injury, and infectious tracheitis, bronchitis, bronchopulmonary abscess, and bronchopneumonia are very likely to follow. Death may occur at any of these stages in the process.

Pulmonary Edema

Since the occurrence of pulmonary edema is the outstanding clinical sign that serious damage to the lungs has occurred as the result of ex-

posure, and since the course and the degree of severity of the pulmonary edema are the most decisive factors in the survival or death of the injured person, we are justified in concentrating our chief attention upon its genesis and development.

Onset: As indicated previously, the onset of pulmonary edema following exposure to irritant gases, may be prompt or it may be delayed for as long as twelve hours. In the young and healthy individual, the longer its appearance is delayed the less likely it is to develop. The outlook is uncertain to some degree in the old or in persons who are the victims of chronic respiratory and circulatory diseases, and therefore the effects of exposure on the part of the civilian population cannot be anticipated with complete assurance on the basis of the experience of armed forces in the last war. The latent period between the occurrence of the exposure to irritant gases and the onset of the edema can best be understood by visualizing the effects induced by contact of the irritant agent with the respiratory tissues.

Pathology: The general character of the injurious effect of the pulmonary irritants (omitting any present references to the effects of exposure to mustard and lewisite) as well as the reaction on the part of the tissues to such effects, is the same throughout the respiratory system. The results differ widely, however, because of the differences in the structure and vascularity of the various parts of the system. Cellular edema, coagulation necrosis and disintegration, hyperemia, congestion, transudation, exudation, diapedesis, hemorrhage, focal necrosis, thrombosis and infarction occur in varying proportions at different sites and times, to make up the whole pathological picture.

In the upper respiratory tract there is a general inflammatory reaction with first a serous, and later perhaps, a sero-sanguineous discharge, and still later ulceration, hemorrhage, exudate and fibrin. Plugs of debris may obstruct larger and also smaller air passages. Later, after the development of pulmonary edema, the trachea will be filled with frothy, watery, perhaps sanguineous fluid, and when pneumonia develops, with a purulent or fibrino-purulent exudate.

In the lung similar damage occurs to the bronchioles and alveolae, on a smaller scale. The picture seen at necropsy depends to a very large degree on the time at which death occurs. The damage is likely to be spotty, rather than general, certain areas being preserved from direct injury by reason of bronchiolar spasm, others being atelectatic or em-

physematous, because of complete or partial obstruction with debris. At first, emphysema, petechial hemorrhage, perhaps confluent hemorrhage, and interstitial edema predominate. Later, large and small areas of deeply congested lung tissue may be seen to be heavy, boggy, and dripping with a thin sanguineous fluid. These may become virtually confluent, the entire lung being large and very heavy, with water running from the cut dark red surface, and with frothy islands of fluid appearing from the cut bronchioles when slight pressure is applied. If death has occurred some days after the onset of the edema, there will be areas of pneumonic consolidation. These may be in any stage of development or resolution dependent upon the time interval between the exposure and death. There may be abscesses or gangrene. Still later, pulmonary fibrosis as well as chronic bronchitis and bronchiectasis may be seen.

The pathological findings are by no means limited to the respiratory system. A later discussion of the pathological physiology of pulmonary edema will show that when death occurs during that stage, it is the result of anoxia and circulatory failure. Accordingly the general signs of circulatory collapse, with widely dilated heart (especially the right side), passive congestion, and venous stasis are very prominent. In addition, the lesions of an acute toxic process—edema, hyperemia, petechial hemorrhage, and focal necrosis—will be found to greater or lesser degree in other organs, notably the kidneys, liver, heart muscle and brain. The systemic effects of the absorption of phosgene, for example, may not be ignored, and would not be reduced to secondary importance except for the overwhelmingly dramatic character of the pulmonary pathology. The blood is dark in color, reduced in volume, and very viscid through hemoconcentration. Capillary thromboses may be seen, and thrombi may be found in larger vessels.

Pathological Physiology: The genesis and the development of the pulmonary and systemic picture may be considered sequentially, in terms of the chief effect—that of the production of anoxia. If it be recognized that bodily requirements in way of oxygen may be met in a variety of normal and unusual circumstances through the joint response of the respiratory and circulatory apparatus, the difficulty presented by gross impairment of the respiratory system will become more apparent. The normal respiratory system can increase its capacity for ventilating the blood some twelvefold or more, while the minute-volume of the circulatory flow can rarely be increased to more than ten times its normal

resting level. The type of injury to the respiratory system with which we are concerned here may deprive the organism of any respiratory reserve soon after exposure, and may well progress to a point where respiration is too ineffectual to sustain life. The large air-ways may be partially obstructed, first by muscle spasm and later by debris, fluid, and froth; large numbers of bronchioles and alveolae may be closed off or filled up with debris, exudate, hemorrhage and fluid; the lung volume is further reduced by atelectasis, consolidation, and fluid; the effective respiratory volume is reduced by maintained, shallow respiration on an expanded, emphysematous chest; the diffusion of oxygen through a greatly reduced area of respiratory membrane is still further hindered by an edematous thickening of that membrane; and the utilization of the limited oxygen supply in the blood is lowered by reason of the reduced oxyhemoglobin dissociation occasioned by the low carbon dioxide tension of the peripheral blood. (The decreased carbon dioxide tension is produced by the relative ease of diffusion of carbon dioxide, aided by the overventilation of intact and unobstructed alveolae.) Every mechanism whereby the available oxygen of the blood can normally be increased is impaired, and the result may well be that the maximum respiratory exchange, in so far as this is mediated by the respiratory apparatus alone, may be greatly reduced below the normal resting capacity. The result obviously is anoxia—an anoxia which can be offset by physiological mechanisms and at normal atmospheric conditions only through increased circulatory activity.

It may be worth while at this point to call attention to the fact that pulmonary edema as we are dealing with it here is the exact antithesis of that more commonly seen in the terminal stages of circulatory failure. The latter arises primarily out of circulatory failure and is a sign of impending death; the former is due to direct chemical injury to the lung, the general circulatory system exclusive of the intrinsic pulmonary circulation being essentially intact. The maintenance of an efficient circulation is seen therefore, to be of paramount importance. Unfortunately the intrapulmonary vascular bed will have suffered damage comparable to that sustained by the pulmonary epithelium, and thereby the circulatory system will have been embarrassed at the point at which the gaseous exchange occurs. With the onset of pulmonary edema there comes further embarrassment in that the water and serum loss into the lung tissue concentrates the blood, decreasing its volume and increasing its

viscosity, thereby promoting stasis and capillary thrombosis. All of these factors, in addition to the reduced interchange of respiratory gases incident to the direct pulmonary damage, throw an increased burden upon the heart.

The sequence of the circulatory changes that may be expected to occur merits special attention. The initial response to anoxia is seen in an increase in cardiac rate and output, the heart remaining approximately normal in size, the arterial pressure increasing in both systemic and pulmonary systems, and the venous pressure showing a moderate increase. So long as the tissue anoxia is readily compensated in this manner, no further qualitative change occurs, but as the edema incident to the pulmonary injury increases, anoxia progresses and the cardiac burden increases. The resistance in the pulmonary circuit increases also, and the load on the right heart becomes disproportionately great. As a consequence of this situation, the right heart increases in volume while the left decreases, the systemic arterial pressure—especially the diastolic—continues to increase, the pressure in the pulmonary artery is still further increased, the venous pressure mounts to high and yet higher levels, the pulse rate increases, and the minute-volume cardiac output decreases to something less than its maximum. At this time there will be capillary dilatation due to the high capillary and venous pressure, and perhaps to some elevation of the carbon dioxide tension, the skin being warm and florid or purplish (cyanosis) in color.

If now the pulmonary edema does not progress, the circulatory system may be capable of maintaining its load successfully, and with the onset of the healing process, survival and recovery may result. If the injury has been sufficiently severe, however, or if the heart begins to fail, the picture changes gradually or perhaps suddenly. The most striking features of the change are dilatation of the right heart, a drop in the venous pressure, a drop in the systemic arterial pressure, the development of a rapid, thready pulse, and the appearance of a grayish, perhaps slightly bluish pallor, with coldness and clamminess of the skin, especially of the extremities.

Clinical Types: An adequate discussion of the variations in the clinical picture that result from exposure to different agents would require much more precise information than is available from industrial experience, from the clinical observations of the First World War, and from animal experimentation. Some few comments may be warranted for

their practical usefulness. Comparison of chlorine, phosgene, and chloropicrin, mustard and lewisite reveal a number of distinct differences.

Exposure to effective concentrations of chlorine results in acute painful injury to the upper respiratory tract, together with somewhat less serious damage to the lungs. Pulmonary edema develops with little or no delay, and reaches its climax within twelve to twenty-four hours. Delayed deaths may result from secondary infection, but apparently not because of general or localized toxic effects in the viscera.

Exposure to phosgene causes little upper respiratory injury or discomfort, and there is a latent period of apparent comfort before pulmonary edema develops. The edema develops rapidly, however, after the onset, most of the deaths occurring within the first twenty-four to forty-eight hours. Delayed deaths occur as the result of pneumonia and also because of toxic damage to the heart muscle and the brain as well as to the liver and kidneys.

Exposure to chloropicrin causes less injury to the upper respiratory tract than chlorine, and more than phosgene. The damage induced by it in the medium-sized to small bronchi is great, with the result that an acute bronchitis develops early. Pulmonary edema also develops promptly, the effect of this agent resembling chlorine in that respect.

Exposure to mustard gas by inhalation of vapors produces acute injury and inflammation of the entire respiratory tract, followed by necrosis and desquamation of the mucous membrane and pulmonary epithelium. A diphtheritic membrane forms on a mucous surface, and a lobular pneumonitis develops, with plugging of bronchioles followed by the formation of bronchopulmonary abscesses that quickly come to the surface, inducing pleuritis and locular empyema. The generalized pulmonary edema associated with exposure to the agents classified as pulmonary irritants, is not a conspicuous part of the picture.

Clinical information on the effects of the inhalation of lewisite by human beings is not available. From observations on dogs it would seem that the type of injury and inflammation resembles that produced by mustard gas, with the exception that there is somewhat greater pulmonary edema. Secondary infection, bronchopulmonary abscess and bronchopneumonia develop promptly and are the most striking features of the pulmonary pathology. Petechial hemorrhages, and other toxic changes in the liver and kidneys give evidence of the general intoxication that might be expected to result from the absorption of this organic arsenical compound.

TABLE III

THE CLINICAL CHARACTERISTICS OF THE BLUE AND GRAY TYPES OF CYANOSIS

Symptom or Sign	*Blue or Florid Cyanosis*	*Gray or Pallid Cyanosis*
Respiratory rate	40—50	50
Pulmonary moisture	Present	Present
Arterial blood pressure	Normal or elevated	Low
Venous pressure	High	Low
Pulse	100—full	130—thready
Temperature	100—101	May be subnormal
Temperature of skin	Warm	Cold—clammy
Headache	Present	Present
Mental state	Restless and apprehensive	Restless and delirious

The clinical types of pulmonary edema that are more commonly referred to, in connection with the effects of exposure to the pulmonary irritants, are differentiated on the basis of the onset and the development of the picture without regard to the specific agent responsible for the injury, as (1) latent, (2) blue cyanotic and (3) gray cyanotic types. There is the more reason for employing this classification rather than that based on the specific agents, since the latter may well be used in mixtures.

1. The latent type has been referred to previously, especially in connection with the effects of phosgene. Despite the fact that the serious symptoms of pulmonary edema tend to develop soon after exposure in most instances, it is necessary to be on the lookout for exposed persons who appear to be practically free of symptoms only to develop labored respiration and circulatory embarrassment within a few hours. This condition may be revealed dramatically by the collapse of an individual who, having attempted some task involving moderate or even slight exertion, has exceeded his scanty respiratory reserve.

2. The type of case classified as having a "blue" cyanosis, is one in which the individual has an anoxemia sufficient to give rise to cyanosis, and obviously, therefore, is suffering from some degree of tissue anoxia. The degree of the anoxemia, and of the general anoxia, is difficult to estimate from the appearance of the patient, since the thickness and

color of the skin, the richness of the circulatory supply, the intensity and quality of illumination, and many other factors, influence one's observation. About 5 grams of reduced hemoglobin are required to produce cyanosis, and therefore, obvious cyanosis must be regarded as evidence of a significant degree of anoxia. The significance of the blue cyanosis, otherwise spoken of as purplish or florid cyanosis, has been pointed out in the discussion of the pathological physiology. The chief clinical characteristics of this state are summarized in Table III.

3. The "gray" cyanotic type is characterized less by the cyanosis, which may be difficult to see, than by the obvious ashen pallor which is associated with circulatory failure. It is thus referred to as the pallid type of pulmonary edema. The associated clinical phenomena of this condition, as given in Table III, show its grave character. When it appears early in the course of the illness, it denotes either extensive pulmonary damage, or the existence of a crippled circulatory system; when seen as a late manifestation, it is only slightly less ominous, since it shows cardiac weakness.

The Sequelae of Injury Induced by Pulmonary Irritants

The sequence of events following exposure to irritant agents has been indicated in sufficient detail to delineate the course of the clinical condition. Death may occur at any of the stages indicated, or the edema may clear up, the pneumonia may be resolved, and complete recovery, without residual effects of any kind may take place. The length of time required for this result depends upon the degree of pulmonary injury sustained and upon the nature of the complications that develop. In addition to the secondary infection which in some degree is almost inevitable, other factors such as age, chronic respiratory disease (bronchial asthma, chronic bronchitis, tuberculosis), diseases of the circulatory system, and trauma, must be considered in the case of civilian casualties.

The sequelae, likewise, will be influenced in frequency and severity by all of the factors mentioned above. The experience of the First World War has shown that complete recovery was the rule among young, healthy persons who survived the acute effects of exposure to pulmonary irritant gases. For a number of reasons the incidence of permanent disability may be expected to be higher among the unselected victims of gas attacks carried out against the general population, but such disability should be relatively infrequent if casualties can be given adequate

care at the proper time. Certain neuroses will be seen, if past experience can be relied upon, and the frequency of these will depend in large measure upon the extent to which the public is taught, led and advised in such matters. In other words, panic and unrestrained fear of mysterious and horrible effects that are thought to result from exposure to war gases, provides a fertile soil for the development of neurotic manifestations.

The sequelae that have been described among soldiers are pulmonary fibrosis, chronic emphysema, chronic bronchitis and bronchiectasis, all of which are the result of infection rather than chemical injury, together with two other disturbances, which in at least some instances are partially functional and which cannot always be clearly distinguished from each other. One of these, generally known as "effort syndrome," is very like "soldier's heart" and is so spoken of by some writers; the other is characterized by recurrent attacks of nocturnal dyspnea. In effort syndrome, as indicated in the expression, the patient becomes exhausted by an insignificant expenditure of effort. Headache, vertigo, precordial pain, dyspnea and tachycardia are the outstanding complaints. The attacks of nocturnal dyspnea are associated with little or no evidence of organic disease of the chest. There is usually an increase in the number of erythrocytes and in the hemoglobin content of the blood. This phenomenon suggests that there is chronic anoxia, due perhaps to rapid shallow breathing, but it is said that no cyanosis is present. Further study of cases of this type would seem to be required to elucidate their physiological background.

The Treatment of Pulmonary Irritation and Edema

First aid treatment of casualties consists of maintenance of quiet and warmth until transportation in the recumbent position can be accomplished. In view of the nature of the condition, persons regarded as casualties should not be permitted to walk or even to sit up, but should be moved on a stretcher as soon as possible to the point at which medical examination and treatment can be instituted. They should be covered up with blankets to prevent chilling, and in addition warm drinks may be administered if desired. Artificial respiration must not be given even to persons in acute respiratory distress, and decontamination should be limited to simple, quickly completed measures such as, clipping off the hair, cutting away clothing, and removal of any agent that may involve

obvious hazard to life or vision.

No treatment for the prevention or relief of pulmonary edema is available at present. Relief of the anoxia may be accomplished satisfactorily in many instances by the administration of oxygen. So long as cyanosis can be prevented by this means, this form of treatment is satisfactory, in that it combats the anoxia, prolongs life, and perhaps tides the patient over a critical period. The administration of oxygen may be carried out in various ways dependent upon the facilities available for the purpose. The use of a nasal catheter is perhaps the best when special equipment is not available. By this means the oxygen tension of the inspired air can be trebled. In well developed pulmonary edema, it may be necessary to resort to the administration of oxygen in a closed inhalation system under pressure. Self-contained portable and fixed inhalation equipment, and various types of masks are available for use with oxygen or with oxygen-carbon dioxide mixtures. The best results can be obtained only by carefully trained personnel. Indeed the success of any efforts made to employ oxygen therapy in this condition will depend upon the training and experience of attendants.

There is considerable disagreement as to the usefulness of venesection in the treatment of pulmonary edema. One may be dubious of the rationale of reducing the volume of the circulating tissue under conditions in which it is destined to be reduced by transudation from a large injured capillary bed. On the other hand, one may be justified in believing that the relief of the high venous pressure associated with the stage of florid or blue cyanosis is a valuable albeit a temporary measure. That any benefit can accrue from attempts at blood-letting in the stage of gray cyanosis, seems impossible.

Prevention and treatment of the infection that may follow this type of upper respiratory and pulmonary injury, will be indicated in accordance with the best methods available. The use of sulfonamide drugs may offer means, not formerly available, to cope with this formidable complication. Perhaps caution against an excess of optimism may be justified here, however, since the organisms involved in such infections will be those harbored in the nasopharynx of the victim, rather than those that would be expected in more common types of nasopharyngeal and pulmonary infections. Arsenicals may be indicated in pulmonary abscess with gangrene associated with spirochetal infections.

Other forms of treatment will be wholly non-specific and presum-

ably symptomatic. General supportive treatment, and careful avoidance of exertion are necessary. Apprehension should be relieved by persuasion as far as possible, but when anxiety and restlessness reach a stage where more vigorous control is required, the disadvantages associated with the use of sedatives, including morphine, will be counterbalanced by their beneficial effect. Heart stimulants may be required and should be used as indicated, caffeine being especially recommended.

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