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Breathlessness

Physicians by tradition have to be students of sensation. Pain, the most compelling of our sensory experiences, has historically usurped the available attention for the total spectrum of perception. Similarly, in the overall physical organisation of somatic feelings in the higher mammal equal priorities appear to exist in that noci-ceptor organs have been designed specifically to evoke and localise the crude and overwhelming sensation of pain. According to Sherrington "in animal forms which partake of mind noci-ceptor organs pertain to sentience and provoke pain. Physical pain is thus the psychical adjunct of a protective reflex. Other of our sense organs evoke their own modes of sensation, sight, hearing, touch, cold, warmth, smell, taste etc. and without pain."

Where in this impressive catalogue of perception would Sherrington have placed the many common symptoms of medicine other than that of pain? In which neurophysiological niche is there room for fatigue, hunger, thirst, exhaustion, apprehension, restlessness and above all dyspnoea? Dyspnoea, next to pain, intrudes itself upon consciousness to the exclusion of all other feelings, somatic or of the mind. One wonders what sort of adjunct appertains to breathlessness, one of the most distressing of symptoms in medicine. It appears that in the course of evolution priorities in sensory organisation were allocated mainly to those modalities which fundamentally and acutely protected and informed the organism. Now that we are hopefully emerging from the procrustean bed of acute pain, will it be possible to unravel sensory mechanisms of a more subtle quality? In a recent book entitled "Breathlessness" experts in medicine, neuro-and respiratory physiology, drawn from two continents, joined forces in an attempt to agree on a definition of dyspnoea and to provide information concerning its genesis. A great deal of time and printed space is devoted to the process of exclusion, a sort of null hypothesis concerning what dyspnoea is not. This in itself is of considerable interest inasmuch as every physician has an intuitive response to his patient presenting with dyspnoea, and he grades his therapeutic response roughly in accordance with the system from which the breathlessness appears to emanate. Respiratory muscle paralysis, upper airway obstruction, overwhelming bronchospasm and acute pulmonary edema would usually dictate immediate therapeutic action or a green light response, while less severe dyspnoea associated with less obvious system involvement or in which there appears to be an overlap, as for instance in an anaemic patient with diabetic ketosis, the therapeutic response might remain amber for some time. Nevertheless, both patient and physician are keenly aware that they are sharing in a dilemma concerning a common sensation which hitherto eluded a neat definition and, therefore, one requiring a classification of nuances other than those of mild, moderate and severe.

The dilemma stems from uncertainty concerning the sensation itself. Is there a single sensation of 'breathlessness' and if not, is there a common mechanism? We are told that dyspnoea is not a single sensation and that different mechanisms subserve different sensations.

Does increased ventilation constitute the cornerstone of dyspnoea? Healthy athletes during exercise apparently enjoy their breathlessness and thus, hyperventilation can, by definition, not constitute dyspnoea.

Can abnormalities of blood gas tensions explain breathlessness? Chemical changes in the blood acting at conscious levels in the brain are not responsible for dyspnoea. They can do so only indirectly through chemoceptors which they stimulate.

Is breathlessness due to excessive activity of the respiratory center? The curious discomfort of breath-holding at low lung volumes can be abolished by vagal block. This interesting fact has now been added to our imperfect knowledge by the courageous and intelligent experiment of Widdicombe from Oxford, who had both vagi blocked at the base of his skull and evaluated the effects with admirable objectivity.

Does breathlessness arise from stimuli originating in the lungs or in the chest wall? The application of resistive loads to breathing shows that lung volume changes still take place and that afferents from the lung, concerned with volume sensing, could not be involved in the unpleasant sensation associated with resistive air flows. Some agreement seems to be crystallizing, however, in favour of a common mechanism attributable to afferents from the respiratory muscles or rib cage, in spite of apparent inadequate afferent action potential traffic. Additional output from motor centers, particularly along the Ω loop, needs to be stipulated in order to experience "length - tension inappropriateness".

The experts who compiled the book, following their long and excellent deliberations, believe that, in the words of Pierre Dejour "There's room for everyone". The sensation is overwhelmingly complex and cannot be straight-jacketed into one single afferent receptor pathway. The center for awareness of dyspnoea defies localisation. Hence "all of us will not describe the symptom faithfully in the patient's own words rather than call every respiratory complaint 'exertional dyspnoea', a term never used by any patient unless he is a physician!" It is also suggested that it would be helpful to the study of dyspnoea to identify unusual patients who should have dyspnoea and don't, and those who do have dyspnoea but logically should not. Such an approach reduces the risk that is involved in espousing a single theory and "a respiratory physiologist offering a unitary explanation for breathlessness should arouse the same suspicions as a tattooed archbishop offering a free ticket to heaven". □

L.C.

References

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Correspondence

Dear Sir:

Can any of your readers help me?

I am keenly interested in finding any original work published in the international Medical Literature by any Canadian Family Physician - during the past 25 years.

If they could please send me the name and reference I certainly would be most grateful. I wish only to hear of work published in journals indexed in the Index Medicus (I understand this excludes all but 2 Provincial Journals.)

Yours sincerely,

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Chronic Obstructive Lung Disease

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Introduction

Increasing interest has been noted in chronic respiratory diseases characterized by productive cough and obstruction to air flow in the bronchial tree, of recent years. These diseases have variably been termed "Chronic non-specific lung disease" and "generalized obstructive lung disease". They are not only receiving increased attention but are also being recognized as major causes of disability and death particularly in the middle-aged and elderly. The clinical diagnoses usually made in such cases are chronic bronchitis, asthma and emphysema, alone or in combination, but there is lack of agreement about the precise clinical conditions to which these terms should be applied. Recent investigation now permit a more complete description and classification of the various disease processes involved, than was previously possible.

In England, these conditions are usually diagnosed as chronic bronchitis. The word emphysema is often added for disabled patients, but deaths from this disease are listed in all international statistics under the heading of bronchitis. There has for many years been a higher mortality from bronchitis in England and Wales than in any other country. It is difficult to be certain of the significance of large international differences in bronchitis mortality because there is wide variation in the terminology on death certification in different countries. It is likely that in some countries with low mortality, doctors are disinclined to attribute death to bronchitis. Many patients who die with chronic bronchitis have terminal pneumonia, and death may be certified as due to this, so for this reason it is helpful to consider death rates from bronchitis and pneumonia together.

If the death rates per 100,000 from bronchitis and pneumonia in men aged 45 - 64 in countries listed by the World Health Organization are studied, a high death rate for England and Wales is seen, with the bronchitis rate being more than twice that of any other country. In the countries with the higher death rates, the ratio of male to female deaths tends to be higher than in the countries with the lower death rates. This possibly could be related to the higher incidence of cigarette smoking as reported by some in these countries. The relatively high rates in Australia and New Zealand may partly be due to the emigration of British subjects who were affected in early life by whatever it is that causes the high British mortality. In the U.S.A. the bronchitis mortality is 1/30th, and the combined mortality from bronchitis and pneumonia is 1/5th that of the British level. However, in recent years the mortality from emphysema has been rising steeply in the U.S.A. Between 1950 and 1959 the deaths per 100,000 from emphysema in the United States rose from 0.7 to 4.2 - a 500 per cent increase. In the United States severely disabled persons are usually described as having emphysema, and no mention is made of the associated or preceding bronchitis, which tends not to be considered a significant disease. (Ciba, 1959[1]; Thurlbeck, 1963[2])

It is therefore important to clarify the confusion of terminology surrounding this group of diseases in Great Britain and the United States.

Definition of Chronic Bronchitis

Diseases may be defined in terms of etiology, morbid anatomy, or functional disturbances. If, as in chronic bronchitis, none of these characteristics are established, it then becomes necessary to base the definition on the clinical features of the disease, in this case, on chronic cough and sputum. The associated conditions of asthma and emphysema may be defined in terms of function and morbid anatomy. A simple classification of the main manifestation of chronic bronchitis is provided in Table I. Chronic bronchitis has been defined as "chronic or recurrent cough with expectoration which is not attributed to localized bronchopulmonary disease". The words "chronic or recurrent" are taken to mean that the symptom "occurs on most days for at least three months in the year for at least two successive years." It is important to distinguish between simple chronic bronchitis and infected bronchitis.

TABLE I

Classification of Chronic Bronchitis

1. Simple Chronic Bronchitis
   - recurrent or persistent mucoid expectoration
2. Infected Chronic Bronchitis
   - recurrent or persistent purulent expectoration.
3. Chronic Bronchitis with Airway Obstruction
   - reversible airways obstruction
     - bronchitis with asthma
   - irreversible airways obstruction
     - with emphysema
     - without emphysema

In simple bronchitis the sputum remains mucoid. The cough and expectoration occur mostly in the mornings, often on first rising out of bed, presumably owing to accumulation of bronchial secretions during the night. Occasionally the cough is entirely unproductive, but a persistent or recurrent dry cough without any expectoration is rare. The

sputum may be swallowed and the patient may deny that cough is productive unless particular enquiry is made. Often patients who admit to sputum production deny cough - the sputum comes up easily upon clearing of the throat. Simple bronchitis causes little disability but its recognition is important since it is often preventable and may be the forerunner of disabling bronchitis. Potentially pathogenic bacteria, in particular *H. influenzae* and *Diplococcus pneumoniae*, may often be isolated from mucoid sputum in simple bronchitis, and this is not simply because of contamination from the upper respiratory tract, as those organisms can also be found at bronchoscopy from the bronchial tree of patients with simple chronic bronchitis, whereas the normal bronchial tree is bacteriologically sterile. Bronchial hypersecretion, characteristic of simple chronic bronchitis apparently permits the colonization of the bronchi by upper respiratory organisms, but the infection is inactive and has not caused an inflammatory reaction in the bronchi if the sputum is mucoid.

In infected chronic bronchitis, the sputum is purulent, either intermittently or persistently. Infected bronchitis follows the rapid proliferation of these organisms, with invasion of the bronchial mucosa so that there is an outpuuring of polymorphonuclear leucocytes which give the sputum its purulent appearance. When the sputum is purulent, pathogenic organisms, especially *H. influenzae*, can be isolated in most untreated cases. These exacerbations of bronchial infection often appear to follow a virus infection of the respiratory tract, and systemic consequences - (fever, leucocytosis and an elevated ESR) are often, but by no means always present. In cases with persistent infection, systemic manifestations apart from a raised ESR are infrequent. Like patients with simple bronchitis, those with infected bronchitis may not regard themselves as ill. The recurrent attacks of purulent sputum are often self-limiting, and the general symptoms may not be sufficiently severe for the patient to absent himself from work or seek medical attention but, since these recurrent infections may respond well to simple therapy and their control may reduce the danger of permanent damage to the respiratory tract, they should be recognized and treated. It is only when they become short of breath on exertion that patients with bronchitis begin to feel significantly disabled. It is usually at this stage of the disease that a doctor is first consulted. The dyspnea is characteristically variable. At first, it may only be noticed as limiting strenuous exertion that was previously managed without difficulty. It is often worse in damp, cold or foggy weather but a few patients are most breathless in hot, humid weather. As the condition worsens, slight exertion causes dyspnea. The patient can only walk slowly on the level and has difficulty walking stairs. At this stage the dyspnea is usually at its worst upon arising from bed in the morning and a marked deterioration between midnight and midmorning may occur. These patients find great difficulty in dressing and getting off to work in the morning, but later on in the day they may be able to walk slowly without distress. The condition in these patients is chronic bronchitis with generalized airways obstruction. Generalized airways obstruction also occurs in asthma, but it is best to restrict the use of the word "asthma" to intermittent or reversible airways obstruction which changes its severity over short periods of time, either spontaneously or under therapy.

In most obstructive cases of chronic bronchitis the obstruction is partially reversible, since it may be reduced by bronchodilator drugs, and this reduction may be sufficient to provide considerable symptomatic relief. But significant obstruction persists in every case of chronic bronchitis so that the term "irreversible generalized airways obstruction" is applicable.

It is these cases that are generally diagnosed as emphysema. There is justification for this in that the word emphysema strictly implies no more than overinflation, and whenever there is generalized airways obstruction the residual volume increases so that at the end of expiration, the lungs are relatively over-inflated. Recently, however, it has been proposed by the World Health Organization and by the American Thoracic Society (1962)[3] that emphysema should imply destructive changes in the alveoli, the definition being "a condition of the lung characterized by increase beyond the normal in the size of the air spaces distal to the terminal bronchioles with destructive changes in their walls". Accounts of the clinical and physiologic characteristics of emphysema have dealt with patients who had irreversible airway obstruction of any type, but it has been shown that emphysema occurs in at least two different anatomic forms. Recent studies have shown that not all patients with severe irreversible obstruction have emphysema and that there are great differences in the clinical findings and functional abnormalities between those patients who do and those who do not have severe emphysema.

In general, patients with severe destructive emphysema usually maintain normal or nearly normal levels of arterial oxygen saturation and of arterial carbon dioxide tension. To do this, they have to achieve a considerable increase of resting ventilation and are often persistently breathless even at rest. Cor Pulmonale usually does not develop until the terminal stages of the disease. In patients with severe, irreversible airway obstruction but without severe emphysema, on the other hand, chronic alveolar hypoventilation tends to develop so that the arterial CO_2 tension is persistently raised, and there is persistent hypoxemia. It would appear

that these patients accept abnormal blood gas tensions in exchange for less severe dyspnea at rest. Patients without emphysema are more prone to cor pulmonale than patients with severe alveolar destruction. They usually have a prolonged history of bronchitis, often originating in childhood, while the emphysematous patients are often well and even athletic until late middle life.

Several symptoms other than cough, sputum and dyspnea may occur in patients with chronic bronchitis. Haemoptysis is not uncommon, though it can never be safely attributed to bronchitis until all other localized causes, in particular tuberculosis and carcinoma of the lung have been excluded. Chest pain is a common symptom. It usually occurs around the costal margins and may be due to muscular strain resulting from coughing. With hypercarbia and hypopnea resulting from hypoventilation, a coarse tremor not unlike the "liver flap" can often be seen.

Pathology

Ulceration and damage to the deeper structures of the bronchial and bronchiolar walls, which may be the sequels of acute bronchitis, results in scarring; in severe cases this leads to total obliteration of some of the small air passages and small respiratory bronchioles may finally disappear leaving no trace. These changes may in part be responsible for causing emphysema. Damage to the surface epithelium of the larger bronchi, though often extensive, is seldom associated with much damage to the deeper structures. During the phase of recovery the damaged surface epithelium is often replaced by

(a) Metaplastic squamous epithelium - this is most common in those suffering from chronic bronchitis particularly habitual sufferers.

(b) Granulation Polyps grow occasionally from the ulcerated surface of a large bronchus and simulate small bronchial neoplasma.

(c) Bronchiolitis Obliterans - these changes occur in bronchitis following the inhalation of irritant gases, e.g., ammonia, N_2O_2 and war gases, also as a complication of pneumonia.

(d) Microscopically the most striking change in chronic bronchitis is the increase in numbers of goblet mucous secreting cells in the surface epithelium, of both the larger and particularly the smaller bronchi and bronchioles. Normally goblet cells account for 1/4 of the epithelial cells lining the larger bronchi and are totally absent in the smaller bronchi and bronchioles.

In chronic bronchitis the epithelium consists almost entirely of such cells which may extend as far as the terminal bronchioles; many of the smaller bronchi become entirely lined by such goblet cells with consequent loss of ciliary drainage. As a result of these changes mucus may spread into and accumulate in some of the alveoli. In addition to changes in surface epithelium, the mucus glands in the walls of the larger bronchi undergo hyperplasia. The dilated bronchial openings of the ducts draining hyperplastic mucous glands can be seen in bronchograms as a series of small diverticula. Accompanying these epithelial changes there is edema, greatly increased vascularity, and swelling of the basement membrane in the walls of the larger air passages. The changes in the bronchial glands can be quantitated by calculating the ration of gland to wall thickness, (The Reid Index). In non-bronchitic subjects this ratio is said always to be less than 0.36 and in patients with bronchitis always higher than this. Infection in chronic bronchitis results from the inability of the bronchial tree to clear itself rapidly of the vast excess of mucus and this enables bacterial proliferation to occur unhindered within the lumen. The resultant mucopurulent inflammation may progress to ulceration and cause a variable amount of destruction of the bronchiolar walls. Repair later results in the formation of granulation and fibrous tissue in the wall and replacement of the normal ciliated epithelium with flattened stratified epithelium. Some of the smaller respiratory bronchioles may become totally destroyed and leave no trace, whilst others become weakened and dilate. This bronchiolectasis may be the main factor in causing the persistence of infection in chronic bronchitis.

Severe damage to the smaller air passages accompanied by peribronchiolar extension of infection may lead to damage to the bronchial and pulmonary arteries. Obstructive changes in the bronchial arteries were regarded by Cudkowicz and Armstrong (1953)[4] as being responsible for the later development of emphysema.

As a result of the structural damage resulting from repeated attacks of bronchitis, it is possible to demonstrate bronchographic abnormalities in the distal air passages. Reid et al (1958)[5] demonstrated that there was failure of some of the peripheral bronchioles to fill due to this destruction, and that others ended abruptly, dilating proximal to their termination with the formation of "pools". Bronchioles which narrow more gradually towards their termination show as "spikes". These radiological changes are almost identical with those found in bronchiectasis though on a smaller scale and involve air passages of much smaller calibre.

Emphysema

The term emphysema, from the Greek, means simply "to puff up". In the present context it refers to the condition described by the World Health Organization and American Thoracic Society as "a condition of the lung characterized by an increase beyond the normal in the size of air spaces distal to the terminal bronchiole with destruction in their walls". The first description of emphysema was given by Laennec in 1819 who observed its close

relationship with chronic bronchitis, believing that the mucus plugs were responsible through allowing air to enter the lungs but preventing it from being expired.

Overinflation of the air spaces with destructive changes in their walls is of two main types, the panacinar or lobular type, and the focal or centrilobular type.

Panacinar or Lobular Type

In the panacinar or lobular type disruption of the lobule extending to the periphery may or may not be associated with severe damage to more centrally situated respiratory bronchioles. The changes may be widespread throughout the lung fields but the lingula, middle lobe, apices and free margin of the lungs are involved. The extent of the change may vary, involving only parts of a lobule in the mildest cases but causing complete destruction of all lobular tissues and interlobular septa in the severest grades. The latter change is responsible for producing the so called "Cotton Candy Lung". In panacinar emphysema, the respiratory bronchioles may be severely damaged or may remain intact; but the alveolar ducts, air sacs, and alveoli are all distended and later are destroyed and form cavities; the bronchiolar orifices, being small and slit-like, seem to behave as valvular orifices preventing expiratory emptying. As these spaces enlarge and form bullae, there is compression of adjacent small air passages with subsequent disruption of elastic tissue and atrophy of the walls of these adjacent units. When changes involve several adjacent lobules the interlobular septa atrophy, and more lung tissue is involved in the destructive process. The large air spaces intercommunicate and the affected lung tissue practically ceases to function as an aeratory organ.

Focal or Centrilobular Emphysema

In focal or centrilobular emphysema the central part of the lobule is replaced by a honeycomb of air filled spaces. This form of centrilobular emphysema is distinct from the occupational focal form of the disease seen in those engaged in certain dusty occupations, in that in the non-industrial focal emphysema there remain small branches of the pulmonary arteries which are found stretched across and exposed in the walls of the emphysematous spaces. Microscopically the walls of the respiratory bronchioles are infiltrated with chronic inflammatory cells including plasma cells and lymphocytes and many of the bronchiolar walls and adjacent alveoli are severely damaged and even destroyed. Despite the extent of the bronchiolar damage, Leopold and Gough (1957)[6] found that in only 60 per cent of the cases was the lumen narrowed and only very rarely was it obstructed: in 40 per cent it remained unaltered. This finding is, however, contrary to that of MacLean (1958)[7] who considered that in emphysema many respiratory bronchioles had been destroyed leaving no trace.

Pathogenesis

It has been shown that chronic obstructive lung disease has a number of components and in discussing the pathogenesis, due consideration must be given to each part of the syndrome and to their relationship with each other. Although the international difference in bronchitis mortality may be partly due to national differences in diagnostic methods, they cannot all be attributed to this. This is shown by the higher male/female sex ratio for mortality in the countries with a higher mortality rate, since diagnostic habits should affect mortality in both sexes equally. Such wide variations must therefore be due, partly, to environmental differences in these countries. We have learned a great deal about the environmental causes of bronchitis from epidemiological studies, but much still is obscure.

Cigarette Smoking and Atmospheric Pollution

Simple bronchitis is usually described as a "smokers cough" and this is in most cases quite true. The steady increase in prevalence of morning cough and sputum, with increasing cigarette smoking shown in studies both in England and the U.S.A. and the decline almost to non-smoking levels in ex-smokers suggest that persistent exposure of the bronchi to cigarette smoke maintains an irritant action whose severity is related to the degree of exposure, but that the effect of this irritation is often reversible. Noted however was that about 50 per cent of the heaviest smokers denied any cough, so there must be varying degrees of individual susceptibility. No study has yet been reported of the simple bronchitis that affects about 5 per cent of the non-smokers, but in some cases this appears to have originated in childhood and the presence of cough has discouraged these people from smoking.

The more serious manifestations of bronchitis, such as recurrent chest illnesses and dyspnea, are less common in U.S.A. than in England, where they are, further, commoner in the urban than rural areas. A high correlation has been found between mortality and morbidity rates for bronchitis and various indices of air pollution by coal smoke in different towns in England (Fletcher et al., 1963).[8] Death rates from emphysema are also much higher in large towns than in country areas in the U.S.A. However, such variation cannot alone be due to cigarette smoking for difference in smoking habits or death rates are very small, and there are fairly small differences between the prevalence of simple bronchitis in town and country. But almost all published reports have shown that cigarette smokers more often have abnormalities of pulmonary function which also are more severe, than non-smokers or pipe or cigar smokers. Studies of the relation of smoking to the presence of emphysema and pulmonary fibrosis at autopsy have shown that these changes are much more common in the smoker than in the non-smoker. Thus in a study of 100 men with chronic irreversible airway obstruction in London and Chicago,

of these only one had never smoked, whereas 15 would have been expected to have been non-smokers, if the patients' habits had been the same as the general population. Severe chronic bronchitis with airway obstruction is a rarity in anyone who has never smoked cigarettes. Doll and Hill (1956)[9] have shown evidence from studies of mortality in relation to smoking habits in Great Britain that chronic bronchitis mortality is related to cigarette smoking. It has also been shown that mortality from emphysema among the non-smoking sect of Seventh Day Adventists living in heavily populated areas in and around Los Angeles, is negligible compared with that among the cigarette addicted population around them.

It is proposed that cigarette smoking, by inducing the bronchial hypersecretion of chronic bronchitis, induces susceptibility to the effects of air pollution, which in some way encourages the development of airway obstruction and thus of infection. Pathologists have suggested that bronchiolar infection is an important cause of the destructive changes that result in airway obstruction and emphysema, and MacLean suggests that in the development of the disease, infection *precedes* airway obstruction and destruction of the pulmonary parenchyma with fibrosis. However, an episode of smog in Britain rapidly aggravates chronic bronchitis and severe dyspnea develops. This must be due to a rapid increase in airway obstruction secondary to bronchial irritation, with increased obstruction interfering with bronchial drainage and thus an increased susceptability to infection - this then suggests that infection is *secondary* to obstruction.

Occupation and Bronchitis

Many authors believe that dusty occupations increase liability to chronic bronchitis but it is difficult to find statistical support for this belief. It is true that bronchitis mortality rates in coal miners and foundry workers in Britain are high, but mortality is proportionally increased among the wives of men working in these occupations, so that it would seem to be a social rather than an occupational effect.

Mortality from bronchitis is five times greater in both males and females in the unskilled laboring group than in the professional group. This may be partly due to air pollution for many of the unskilled laborers live close to the factories in which they work, whilst the professional commutes to and from the countryside.

Bronchial Reactivity

Reactivity of the individual patient to environmental factors must also be considered. It has already been mentioned in relation to cigarettes. It has been shown that when subjects with bronchial symptoms inhale aerosols of acetylcholine, histamine or tobacco smoke, they react by an increase in airway resistance that is much more marked or occurs at a much lower dose level than that of subjects without bronchitis symptoms. Bronchial reactivity is also found to a high degree in asthmatics, so that it is tempting to conclude that all bronchitis is a form of asthma and is basically allergic. The important distinction, however, is that the airway obstruction of chronic bronchitis is irreversible whilst that of asthma is reversible. Another characteristic feature of asthma is the intense eosinophilia that may be found in the sputum, whilst in most cases of chronic bronchitis there is none. There is some basic similarity between the pathogenesis of asthma and that of bronchitis although clinically they are quite distinct.

Mucoviscidosis and Bronchitis

Some studies have suggested that patients with chronic bronchitis may be heterozygous for the gene of mucoviscidosis. Increased levels of sweat chloride have been found more frequently in bronchitic than in control patients, and a higher incidence of bronchitic symptoms have been reported in parents and siblings of patients with overt mucoviscidosis than in the families of control patients. However, most bronchitics have normal sweat chloride, so that this factor cannot be considered a primary one.

The pathogenesis of the destructive changes of emphysema thus remains quite uncertain. Much of the debate has been confused by failure to distinguish between the different forms of emphysema and between cases of bronchitis, with and without emphysema. Airway obstruction and the distension resulting from it are unlikely to cause emphysema because so many chronic asthmatics remain quite free from it and because it is recognized that there is a type of bronchitis with severe irreversible airway obstruction which remains uncomplicated by emphysema. Surveys of orchestra players in Czechoslovakia have dispelled the myth that emphysema is common in wind instrument players. The theory that the stress and strain of chronic cough ruptures alveolar walls deserves consideration because of the close association of emphysema with chronic bronchitis and cigarette smoking. Increased introthoracic pressure during cough would produce tearing stresses in the lung only if there were uneven distribution of these pressures; in the presence of chronic bronchitis, an uneven distribution of ventilation must imply uneven airway resistance, so that the stresses would be unevenly distributed during the expiratory phase of the cough, when air would be more forcibly expelled from some areas than it would from others. This hypothesis will not, however, account for the well documented cases of "primary" emphysema in which dyspnea due to emphysema is the first symptom and in which there is not preceding history of cough. Nor will it account for the absence of emphysema in many patients with chronic bronchitis with a history of many years of severe persistent coughing.

Possible Etiological Mechanisms

"Common pool" theory, (MacLean, 1958[7])

Emphysema is due to obliteration and destruction of respiratory bronchioles causing air trapping, which in turn causes secondary distension and eventually disruption of the alveoli and air passages distal to the obstruction which forms a common pool. This theory depends on a sequence of three events:

(a) the basic lesion is a chronic bronchiolitis which in turn leads to temporary or permanent obstruction of bronchioles.

(b) following bronchiolar obstruction, air passes by collateral ventilation into air passages and alveoli distal to the obstruction.

(c) as a consequence of prolonged "air trapping" in the obstructed acinus, disruption of the air passages occurs beyond the obstruction.

During attacks of bronchitis, the smaller bronchioles become filled with mucus which obstructs the lumen. The further course of events depends on whether the obstruction is temporary or leads to permanent structural damage and occlusion of the lumen. Following obstruction of the bronchiolar lumen by a plug of mucus, air passes collaterally through the pores of Kohn from adjacent acini into the alveoli of the obstructed acinus. Air passes into the obstructed area of the lung during inspiration but during expiration remains trapped owing to the closure of the pores. Now, the pressure distal to a bronchial obstruction in collaterally ventilated lung is raised during expiration and particularly so during coughing; and the pressure during the expiratory phase of coughing in the "air pool" may be sufficient to expel the obstructing plug of mucus into the more proximal air passages from whence it is removed. If, however, this obstruction plug is lodged permanently, the constant repeated expiratory rise in pressure within the pool eventually leads to disruption of the walls of the "pool" and the establishment of a free airway with neighboring acini. The disruption of the alveolar walls whilst restoring once again a free flow of air, leads to the formation of what MacLean has termed the "common pool". The bronchiole which supplies the common pool is no longer the original obstructed bronchiole, but the patent one supplying the adjacent acinus. Further attacks of bronchiolitis leads to further episodes of bronchiolar obstruction with the same dequelae, and in time the "common pool" comes to involve more and more destruction of lung tissue.

Air first pools at a point immediately distal to the obstruction and furthest from where it entered the obstructed portion of the lung. As the obstruction is located mainly in the 2nd or 1st orders of respiratory bronchioles, the first evidence of emphysematous changes is seen in the centre of the anatomical lobules. Later, as disease progresses, the "common pool" involves an ever-increasing amount of the lung lobule, and gradually extends distally to involve the alveolar ducts and air sacs.

The recognition of the obliterated bronchioles may prove difficult or impossible, though elastic stains may occasionally enable the elastic framework of these structures to be visualized. Although the bronchioles may disappear without a trace, their original course may be marked by collections of black pigment. The pigment, usually regarded as consisting mainly of soot particles, was found to contain mainly hemosiderin and other arterial blood pigments, and was thought to have arisen from old peribronchiolar hemorrhages caused by that original bronchiolitis responsible for the obstruction of the lumen. Extension of the "common pool" to the rest of the lobule is thus thought to be responsible for causing panacinar destructive emphysema.

"Stretch Theory (Leopold and Gough, 1957[6])

Emphysema results from inflammatory weakening and destruction of either respiratory bronchioles or more distally situated tissues, the more proximal orders being little changed. The walls of the distal respiratory bronchioles subsequently dilate and eddy currents then occur in the air stream. Once dilatation has started, the walls continue to stretch more readily and, being nearly spherical in shape, dilate according to the formula which governs the expansion of a spherical chamber with elastic properties. The narrowing of the proximal orders of the respiratory bronchioles, probably acts as a protective mechanism and is in no way responsible for the emphysema beyond. Panacinar destructive emphysema, according to Leopold and Gough is due to inflammatory damage involving the respiratory bronchiole, the walls of the alveolar ducts and more distal air sacs with consequent stretching and ultimate destruction of these structures.

"Vascular Necrotic Theory" (Cudkowicz and Armstrong, 1953[4])

Angiographic studies of the bronchial arteries have shown two principal changes in emphysema. First, occlusion of the bronchial arteries apparently led to ischaemic changes in the bronchi and peripheral parts of the lungs supplied by these vessels; a second development was the establishment in some cases of broncho-pulmonary anastomoses causing haemodynamic changes in the pulmonary circulation. In both instances Cudkowicz and Armstrong considered that the blood supply to the lung parenchyma suffered, and that emphysema was due to the ischaemic changes following the obliteration of the bronchial arteries supplying the peripheral supporting tissues and alveoli of the lung.

Spain and Kaufman in 1953[10] after studying cases of "generalized" and "bullous" emphysema, found it was relatively easy to identify the bronchi as far as the terminal bronchioles, but these last-named passages showed considerable peribronchiolar and intramural chronic inflammatory cell infiltration. They considered the rigidity of the walls and the narrowing of the lumen that ensued were responsible for the difficulty in expiration, and

the subsequent dilation of the more distally situated air spaces. Later, enlarging bullae further compressed adjacent bronchioles.

Although the principal theories focus attention mainly upon lesions occurring in the bronchioles, Wright (in 1960) showed that the medium-sized bronchi (the first to the third order of bronchi distal to the segmental bronchi) often undergo dilatation in advanced emphysema. This is caused through atrophy of the mural cartilage and connective tissue, coupled with loss of elasticity in the surrounding lung parenchyma leading to collapse of the bronchial walls during expiration. Normally these larger bronchi remain patent due to their rigid cartilaginous plates and the elastic traction exerted upon them by the surrounding lung. The bronchial atrophy may be caused either by inflammation or ischaemic changes.

The role of infection in the pathogenesis of emphysema is supported by the fact that the type of emphysema most closely associated with chronic bronchitis is the centrilobular type. The distribution of this form of emphysema closely allies the distribution of the inflammatory reaction in bronchopneumonia, which is predominately centrilobular, and it may be that this particular type of emphysema is a post-inflammatory condition.

It has, moreover, been shown in dogs that while insertion of an expiratory check valve in the trachea will not produce emphysema, if there is pulmonary infection present, emphysema may result.

The pathogenesis of cor pulmonale in chronic bronchitis and emphysema has been the subject of much controversy. It does not appear that destruction of pulmonary parenchyma is as important as was once thought, for two reasons. First, because of the vast distensibility of the pulmonary circulation which can for example permit pneumonectomy resulting in loss of 50 per cent of the pulmonary vasculature with no rise of pulmonary artery pressure at rest; and second, because cor pulmonale is not associated with severe destructive emphysema as often as with chronic bronchitis without emphysema. It would therefore appear that pulmonary vasoconstriction must be a major factor. It has been shown experimentally that alveolar hypoxia leads to pulmonary vasoconstriction and pulmonary hypertension. The most important factor in cor pulmonale due to bronchitis and emphysema appears to be chronic hypoventilation with consequent hypoxia and hypercarbia.

In 1963, Gandevia[11] in a study of 42 patients with severe obstructive lung disease, demonstrated tracheo-bronchial collapse during expiration, and correlated this with spirometric data on these subjects. He noted that several of these patients showed an abnormal spirogram with an initial rapid phase followed by a linear phase with slight upward switching at the point of inflection. Others have drawn attention to collapse of the trachea in particular as a clinically significant feature in some cases of emphysema.

The normal forced expiratory spirogram is a smooth and virtually exponential curve, in the first second of which over 3000 cc of gas are exhaled by a male subject of average build. In patients with uncomplicated asthma, expiration is slowed but the spirogram retains its smooth contour; - a similar smooth spirogram is obtained from normal subjects when a sufficiently high external resistance to expiration is placed between the subject and the spirometer. A strikingly different spirographic pattern is consistently observed in some patients with severe obstructive lung disease. Two distinct phases are apparent - an initial almost vertical phase of rapid exhalation (150 ml.) followed by a sharp inflection, and then a second phase of slow exhalation during which flow is virtually constant. Bronchographic studies correlated well with spirometric results.

Rainer et al (1963[12]) performed spirometry and cinefluorographic studies on 28 subjects, both controls and the patients, with varying degrees of emphysema. They found that expiratory reduction of tracheal and major bronchial diameters closely paralleled the reduction in certain pulmonary function tests, especially the F.E.V. They reasoned that the basic defect responsible for airway collapse in emphysema seems to be a weakening of the membranous portion of the trachea and major bronchial walls. The fibromuscular wall between the cartilaginous rings may also be involved. This weakening or thinning probably results from long-standing chronic cough with its repeated sudden, severe increases in intrathoracic pressure. Others have applied the term "expiratory stresses of the trachea and main stem bronchi" to this condition, describing it as an alteration of the elastic fibres of unknown etiology always associated with chronic inflammation and usually found in men over the age of 50 with chronic bronchitis. In addition, some other workers have reported several tracheoplasties using thin slab of bone graft sutured to the membranous portion of the trachea with resultant improvement in respiratory function. Rainer concludes that expiratory collapse of the trachea is a major factor in the pathogenesis of many, if not most cases of chronic obstructive emphysema, especially the diffuse or panacinar type. He feels that it may be this expiratory collapse of major airways that causes patients to advance from chronic bronchitis into the phase of alveolar disruption, parenchymal destruction and rapid deterioration of lung function characteristic of emphysema.

Diagnosis

Differential diagnosis of bronchitis

The diagnosis of simple and infected chronic bronchitis depends on an accurate history, careful

examination of the patient including chest X-ray and examination of the sputum. Clubbing of the fingers should always lead to suspicion of other disease for this never results from uncomplicated chronic bronchitis. Attention to the character of the breath sounds is important in the differentiation between bronchitis and emphysema; in bronchitis with any degree of obstruction the breath sounds tend to be bronchovesicular and relatively uniform while emphysema the breath sounds although bronchovesicular are frequently diminished and distant and vary in intensity and quality from one area to another. It is important to note the volume, consistency and color of the sputum. Not infrequently a false impression of purulence is given by epithelial flakes from the upper respiratory tract, which may look yellow when stained with tobacco. They are, however, more dense and opaque than pus, which is characteristically pale, creamy yellow or green. Bacteriological examination of the sputum is mandatory. The possibility of a fungus infection must be borne in mind as the cause of persistent expectoration. In aspergillosis, the sputum may occasionally have a brownish tinge, and lumps of mycelium may be found and identified under the microscope. Before accepting a diagnosis of simple or infected chronic bronchitis it is essential to exclude other causes of persistent or recurrent expectoration. The chest X-ray should exclude TB, carcinoma, and other localized pulmonary diseases. Often areas of scarring or pleural reaction will be found in the X-rays of long standing cases of infected chronic bronchitis but there are no characteristic, diagnostic appearances of bronchitis in a plain radiograph. There is often difficulty in making a sharp distinction between the diagnosis of bronchitis and bronchiectasis. In clinical terms it is best to reserve the term bronchiectasis to indicate the condition of patients who have gross dilatation of the bronchi which is usually confined to one or a few pulmonary segments. Bronchiectasis may occur without any generalized bronchitis, but it is often associated with it and with generalized airway obstruction. The clinical history may then be indistinguishable from that of chronic infective bronchitis. The presence of bronchiectasis may be suggested by the finding of clubbing of the fingers or by hearing localized rales on auscultation. The diagnosis may also be suggested by X-ray evidence of atelectasis or thickened bronchial shadows but of course a bronchiogram is essential for establishing the diagnosis.

Generalized airway obstruction can usually be diagnosed from a history of dyspnea with wheezing. A somewhat crude but useful clinical test for airway obstruction is to time expiration. If a normal subject is asked to inhale deeply and exhale rapidly and completely the exhalation is completed in less than 5 seconds. With airway obstruction, exhalation is prolonged beyond this and if timed by listening with the stethoscope over the trachea may be heard to continue for many seconds.

A good correlation has been found between this "forced expiratory time" and spirometric measurements of the severity of the obstruction. It is desirable, however, that the severity of the ventilatory impairment and of obstruction should be assessed more accurately than by crude clinical tests. The simplest and most reproductive test of ventilatory capacity is to measure the maximum volume of air that can be expired in one second (F.E.V.) and the vital capacity (V.C.) Normally more than 80 per cent of the vital capacity is expired in one second, but with obstructive impairment, expiration is slowed so that reduction of F.E.V. is proportionally greater than reduction of V.C. and the ratio of F.E.V./V.C. is reduced.

There is also a varying degree of restriction in the sense of a reduction in the V.C.; obstruction to air flow prevents full expiration so that the volume of air remaining in the lung after full expiration (Residual Volume) is increased. Repeating the measurement of F.E.V. and V.C. after administration of bronchodilator drugs will show how far, if at all, the obstruction is reversible. In some cases of asthma, a very large increase in ventilatory capacity is obtained, and the obstruction may almost completely disappear between attacks or after the administration of corticosteroid drugs. In bronchitis and emphysema on the other hand, severe airway obstruction persists. It is here that it is important to attempt to determine how much of the obstruction is due to the effects of the chronic bronchitis alone, and how much is due to emphysema. Perhaps the most useful pulmonary function test in differentiating chronic bronchitis with emphysema from that without emphysema is the steady state diffusing capacity for carbon monoxide (D_{co}). Since this test reflects both the ability to transfer CO across the alveolar capillary membrane and the total surface area available for diffusion; it is logical that the D_{co} would be decreased in emphysema. When the D_{co} is found to be normal at rest and to increase on exercise, it may be stated with confidence that the subject does not have a significant degree of emphysema.

The most important distinction between the two types of obstruction is that the chronic bronchitic type is much more likely to lead to chronic alveolar hypoventilation than the emphysematous. This is readily shown by an elevated arterial pCO_2. A high blood HCO_3 level will also provide evidence of chronic hypercarbia.

Emphysema

There are no clinical signs of emphysema. The so-called barrel chest is of no significance and hyperresonance on percussion is a difficult sign to assess. Any patient with generalized airway obstruction uses

the accessory muscle of respiration. Hoover's sign (in $\frac{1}{n}$ drawing of the lower thorax on inspiration) is due to a flat transverse diaphragm. Many of the classical X-ray signs, such as horizontal ribs, a low, flat diaphragm and a long narrow heart are signs of simple overinflation of the lungs that may occur without any alveolar destruction. Bullae, shown by hair lines may suggest emphysema, but are seen also in its absence. The surest X-ray evidence is attenuation and narrowing of the peripheral vascular pattern of the lung, but this can be diagnosed with confidence only when about 80 per cent of the lung tissue is affected by emphysema, We do not have a clinically reliable method for diagnosing mild emphysema during life.

Heart failure secondary to obstructive lung disease, or cor pulmonale is frequently misdiagnosed as ischaemic heart disease. In this type of cor pulmonale the patient is cyanosed, and the extremities are warm with a full pulse volume of regular rhythm. There may be a coarse tremor of the outstretched hands due to hypercarbia and hypoxia. Sometimes one can palpate a substernal thrust from right ventricular hypertrophy and a third heart sound may be heard in the mitral and tricuspid areas with wide splitting and accentuation of the pulmonary second sound. The E.C.G. shows right atrial dominance with dominant R wave in A.V.R. and chest leads and this dominant R may extend across. Varying degrees of right bundle branch block may be present and obscure the evidence of hypertrophy. Inversion of T waves is also common in the right chest leads, particularly during exacerbations of airways obstruction. The chest X-ray usually shows cardiac enlargement, which is seen on the lateral view to affect predominantly the right ventricle. This enlargement may diminish strikingly on recovery from heart failure. The arterial Pco_2 is almost invariably raised. □

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Bronchospirometry

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In the assessment of a candidate for pulmonary resection, the evaluation of respiratory reserve is of paramount importance. Little is gained if the surgeon cures the patient's tuberculosis, bronchiectasis, abscess or cyst at the expense of making him a pulmonary cripple, and all is lost if extirpation of the diseased tissue leaves insufficient lung for survival.

Fortunately, most individuals undergoing thoracotomy for the removal of lung lesions require only a subtotal resection and at the same time have such a high respiratory reserve that no special pulmonary testing is required as part of their preoperative evaluation. In the remainder, however, the lung tissue that is to be left behind following surgery is abnormal, frequently containing areas of fibrosis and emphysema, or else the motion of the chest wall may be restricted due to the presence of a fibrothorax. Clinically, the patient may not complain of respiratory difficulty but in these cases it is mandatory that a thorough pulmonary function study be carried out before the lung tissue is removed. This will involve the usual ventilatory tests; in some cases, blood gas studies will be necessary and, in a few, resection cannot be undertaken until the function of each lung is individually determined.

Historical

Bronchospirometry was first carried out by Jacobaeus and his associates in 1932. Determinations were made by the use of a double-lumen bronchoscope which was introduced under direct vision and so positioned that air exchange to the two lungs was maintained through the respective channels of the bronchoscope. The ventilation and the oxygen absorption of both lungs were recorded simultaneously. The technique was improved in 1934 by Frenckner. In 1936[1], Bezancon and his associates made a number of observations using a single-lumen bronchoscope recording data first from one lung and then from the other.

The use of these special bronchoscopes posed considerable difficulties, both from the standpoint of introducing them into the proper position and because of the discomfort which they caused the patient. An improvement was made in 1939 when Gebauer[2] introduced a flexible soft rubber double-lumen catheter and, independently of him in 1940, Zavod[3] described a similar catheter. These catheters simplified the procedure to some degree and were much more comfortable as far as the patient was concerned. The catheters contained a flexible steel plate at the tip and the capillary air leads were radiopaque. By means of fluoroscopy, the catheter was placed in the correct position. The usefulness of this type of catheter was limited by the small size of the breathing channels and the consequent increased respiratory effort, which sometimes caused moderate or severe dyspnea during the test. Furthermore, in patients with any marked disproportion between the ventilation of the two lungs, air exchange to the good lung was proportionately more restricted than was the bad one, thus rendering the relative ventilatory determinations inaccurate. In patients with large amounts of thick sputum which obstructed the channels, it was often impossible to obtain a satisfactory record of individual lung function.

In 1948[4], Norris and his co-workers described a single-lumen catheter. This was inserted into the left lung and the exchange to the right lung was maintained around the catheter and through the larynx. The catheter had an inflatable cuff. It was introduced under mirror guidance into the trachea and advanced into the left bronchus under fluoroscopic control. Its advantage was the large size of the lumen which offered only one-fifth the air flow resistance of the largest Zavod catheter. Finally, in 1949[5], Carlens described his double-lumen catheter which proved to be so much superior to the earlier models as to render them obsolete. The Carlens catheter is used universally today in the performance of bronchospirometry, and is constructed of rubber of moderate rigidity, with a double lumen, the diameter of each channel being about 7 mm for use in the male and 6 mm for use in the female. It has inflatable cuffs placed on the tracheal and on the bronchial portions of the catheter. It is provided with a small rubber hook which automatically engages the carina. Before the examination, a curved metal stylet is introduced into the bronchial channel of the catheter. The rubber hook is tied down to the catheter with a silk thread in order to facilitate its passage through the larynx. The slip knot is tied in such a way that it is easy to release by pulling on the free end of the silk thread.

Indications

The indications for bronchospirometry may be summarized by stating that the procedure is required in the individual with a reduced respiratory reserve when it is necessary to know preoperatively what proportion of the total lung function would be lost through the proposed resection or collapse procedure. The roentgenographic findings and the physical examination are frequently quite misleading in regard to the relative respiratory capabilities of the respective lungs. On radiological examination, a

lung may appear completely free of disease and yet because of chest wall fixation or the presence of undemonstrable emphysema it may be contributing but little to the overall respiratory function. Bronchospirometry is especially useful in patients with advanced bilateral tuberculosis or bilateral emphysema, or in the older individual with lung cancer when it may be necessary to perform a pneumonectomy.

Technique

It may be stated at the outset, that even with the Carlens catheter, bronchospirometry is an uncomfortable procedure for the patient. Nothing except the necessary premedication is given by mouth for four hours before the examination. A barbiturate is administered orally 90 minutes, and usually morphine sulfate 10 mgm with atropine sulfate 0.4 mgm. are given subcutaneously 45 minutes before the procedure. Topical anaesthesia is employed, using pontocaine 2 per cent as a spray to the pharynx and impregnated in a small sponge which is placed first in one pyriform sinus and then in the other. About 2 ml of pontocaine are then instilled into the trachea.

The catheter is introduced into the trachea under mirror guidance. When the hook has passed the vocal cord, the stylet is removed and the knot is untied by means of a slight tug on the thread which is then pulled out completely. The catheter is now turned 90 degrees to the left and gently pushed downward until the hook is engaged by the carina. The position of the catheter is checked by a spot X-ray film, the cuffs are inflated with a syringe until the control bags on the upper part of the capillary tubes are distended, the breathing channels are connected with the twin spirometers and the test commenced.

Usually, the determinations are made from both the right and left lungs simultaneously and include minute ventilation, tidal volume, expiratory reserve volume, vital capacity, and oxygen uptake. In a healthy person, the right lung contributes about 55 per cent of the total ventilation and oxygen uptake. When the required information has been obtained, the balloons are deflated and the catheter withdrawn. Generally, there is very little postoperative discomfort aside from moderate soreness in the laryngeal region and hoarseness which may last two to three days.

Results

At the Nova Scotia Sanatorium, bronchospirometry has been utilized since 1956. The necessity for its employment since then has occurred relatively infrequently and, in all, it has been attempted on only 35 occasions. In three instances, the examination was unsatisfactory because of the difficulties in introducing the catheter into the proper position. The procedure, therefore, was carried out successfully on 32 occasions in 31 patients. One repeat undertaking confirmed the findings recorded the first time.

The examination was done in tuberculous individuals on 27 occasions and in patients with bullous emphysema on five occasions. In all cases, it was carried out because of involvement of the nonoperative or better lung, and the conditions present in that lung are summarized in Table 1. It will be noted that in ten instances, previous surgery had been carried out.

TABLE I

Condition of "Better" Lung

PULMONARY TUBERCULOSIS		
MINIMAL		7
Uncomplicated	3	
With resection	4	
MODERATELY ADVANCED		9
Uncomplicated	7	
With thoracoplasty	1	
With resection	1	
FAR ADVANCED		8
Uncomplicated	4	
With thoracoplasty	3	
With extraper.plombage	1	
FIBROTHORAX		3
BULLOUS EMPHYSEMA * (4 patients)		5
		32

*One patient had bullous emphysema in the "better" lung but required surgery for tuberculosis within the other lung.

Ventilation studies were done on all patients who were to undergo bronchospirometry. The figures of maximum voluntary ventilation and vital capacity testing are shown in Table II. It will be seen from this table that although the patients appeared clinically to have adequate total function, this assumption was not justified: one might well seek further evaluation by bronchospirometry.

TABLE II

Pulmonary Function Studies

(a) MAXIMAL VOLUNTARY VENTILATION EXPRESSED AS PERCENTAGES OF NORMAL VALUES

DIAGNOSIS	Less than 30	30 – 49	50 – 69	70 or more	ALL CASES
Tuberculosis					
Minimal				1	1
Moderately advanced		1	2	1	4
Far advanced	1	13	5	4	23
Emphysema	2		1	1	4
ALL CASES	3	14	8	7	32

(b) VITAL CAPACITY EXPRESSED AS PERCENTAGES OF NORMAL VALUES

	Less than 30	30 – 49	50 – 69	70 or more	ALL CASES
Tuberculosis					
Minimal				1	1
Moderately advanced		1	1	2	4
Far advanced		6	13	4	23
Emphysema		2		2	4
ALL CASES	0	9	14	9	32

Fifteen of these patients had a maximal voluntary ventilation of more than 49 per cent, and seven more than 69 per cent of normal expected values. In regard to vital capacity, 23 of them had 50 per cent or more, and only nine were within 70 per cent of

normal. It is always possible that a large proportion of the respiratory function or most of it is being carried out by the lung on which it is proposed to operate. Conversely, the patient who has an extremely low total ventilatory function may withstand pulmonary resection quite well if the lung which is to be resected is contributing only relatively little to the overall respiratory load.

The information gained from this procedure was of inestimable value. While the result obtained was as expected from prior assessment in 27 of the cases, in five it was the direct opposite.

An example is the case of a 51-year old woman who underwent a right upper lobectomy in 1944 for pulmonary tuberculosis. She had an uncomplicated postoperative course and remained well until 1965 when reactivation of disease occurred in the left lower lobe. She was then treated with streptomycin, PAS, and isoniazid, but after nine months it was obvious that extensive residual disease was present in the left lower lobe and so a resection was contemplated for that side. The roentgenogram revealed an essentially normal right lung except for moderate compensatory emphysema. The total pulmonary function was low with a maximal voluntary ventilation of about 45 per cent. Bronchospirometry was carried out and indicated that approximately three-quarters of the total respiratory function was being carried on by the left lung. Obviously, a resection on that side was out of the question.

In this series of 32 bronchospirometries in 31 patients, subsequent surgery was contraindicated by the bronchospirometry in eleven instances. In the remaining 20 patients who underwent subsequent surgery, only one experienced any serious respiratory difficulty and she survived.

Complications were minimal. In one patient, difficulty was experienced in positioning the catheter and several attempts to do so were made. He had some postexamination pain and hoarseness. A second patient experienced hoarseness and pain, and also developed mild subcutaneous emphysema in the tissues of the neck. It would appear that the stylet inadvertently protruded beyond the end of the bronchial portion of the catheter and injured the larynx.

Summary

The history of the development of techniques for measuring individual lung function has been discussed, and the indications for the procedure have been outlined.

The technique of the introduction of the Carlens catheter has been described, and the experience at the Nova Scotia Sanatorium in 32 bronchospirometries carried out in 31 patients has been summarized.

Bronchospirometry is mandatory in the assessment of the respiratory reserve of certain selected patients with bilateral lung involvement for whom pulmonary resection is being considered. □

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Rubella Diagnosis: The Role of the Laboratory

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The first report of the successful *in vitro* cultivation of rubella virus appeared in 1962. Two groups, using different techniques, published simultaneously in the Proceedings of the Society for Experimental Biology and Medicine. Parkman, Buescher and Artenstein, in Washington, used an "indirect" method to demonstrate its presence while Weller and Neva, in Boston, used a "direct" method. Both methods were subsequently tested and used in other laboratories.

Isolation of Virus

In the "indirect" method, the specimen is inoculated to tissue cultures, such as primary African green monkey (AGMK) cell monolayers which will support the growth of rubella virus but show no visible effect of the infection. After a suitable incubation period, the culture is challenged with a virus which under normal conditions causes a marked cytopathogenic effect (CPE); Echo 11 is the type commonly used. If rubella virus has infected the cells an interference phenomenon is set up and the Echo 11 is unable to produce any effect on the tissue cultures. If, however, a rubellavirus is not present there is no interference and the challenge strain quickly produces a marked CPE.

For the "direct" method, cells are chosen which respond to rubella virus infection with the appearance of a visible cytopathic effect. The cultures employed are usually continuous line cells, that is, cells which have been adapted to grow for successive generations in bottles or tubes.

As a general rule, workers on this side of the Atlantic prefer the indirect method for isolation work and most would support Ingalls *et al.*, (1967) in their opinion that for isolation from clinical material no other cell is as suitable as the African green monkey kidney. Several laboratories in England have used the direct method with seeming success and many of them have utilized the continuous rabbit kidney cell line RK_{13} originated by Beale *et al.*, (1963).

Isolation technique used in the Public Health Laboratories

Until recently, the only method used routinely in our laboratory was the indirect one employing AGMK cells, and although the technique was time consuming and rather cumbersome, we were satisfied with the results. In September 1967, however, our supply of these cells was cut off following an accident in Germany among laboratory workers handling tissues from African green (vervet or grivet) monkeys; there were about thirty cases of serious illness with seven deaths. The etiology of the disease has remained obscure although it is thought that a member of either the rickettsia or psittacosis-lymphogranuloma groups may have been responsible, (Smith *et al.*, 1967).

For a few months our isolation work was halted until we could devise an alternative technique for culture, since our experience with the direct method in continuous line cells had not been encouraging. Following a suggestion of Dr. Roger Belcourt, (1967), however, we combined the use of primary rabbit kidney cells with the continuous line RK_{13} cells and preliminary work has been most promising.

AGMK cells have again been released for use, as of June 1967, and now both direct and indirect systems are working well in the laboratory. Positive identification of isolates has created some difficulties but these are under further study, and, we trust will soon be overcome.

Clinical specimens for submission

The following data indicating the periods of time at which virus has been isolated in different laboratories is presented as a guide for the submission of specimens.

A. In clinical cases from –
   - Blood: 6 or 7 days before the rash, to shortly after the appearance of rash.
   - Throat: 6 or 7 days before rash, to 6 or 7 days after rash.
   - Stool: 3 days before rash, to 4 days after rash (Giles et al., 1963).
   - Urine: at time of exanthem.
   - Synovial fluid from a 14 month old child with transient synovitis of the right talonavicular joint. (Hildebrandt and Maassab, 1966).
   - Lymph node excised on the 2nd day of rash. (McCarthy *et al.*, 1963.
   - The virus is most easily recoverable, however, from the throat, (Neva *et al.*, 1964)

B. From the products of conception when pregnancy has been terminated prematurely – brain, heart, skin-muscle-skeletal tissue, lung, kidney, stomach and blood of the fetus; from the placental tissue and from the amniotic fluid. (Alford et al., 1964, Kay et al. 1964; Selzer, 1964).

C. In children born with congenital rubella from –
   - Nasopharynx – up to 6 months after birth (Alford, 1966), 10 months, (Dudgeon, 1967), 12 months (Plotkin, et al., 1967).
   - Urine – up to 6 months of age (Alford, 1966).

Cerebrospinal fluid (Korones et al., 1965), up to 9 months, (Yow et al., 1965, up to 1 year, (Plotkin et al., 1967).

Conjunctiva – up to 6 months (Alford, 1966).

Lens (eye) – material obtained surgically from patients as old as 18 months (Plotkin et al., 1967; Scheie et al., 1967).

Serological Diagnostic Methods

Two tests for evidence of rubella infection are now performed as a routine service at the Public Health Laboratories.

1. *the haemagglutination inhibition (HI) test,*
2. *the complement fixation (CF) test.*

Simultaneously, developmental work is being conducted on two further techniques, namely, the *serum neutralization test* and the *fluorescent antibody (FA) test.* To the latter, must be added a further fifth and possible new diagnostic principle, based on the occurrence of *IgM immune globulins* appearing early in the course of rubella infection. IgM globulins are opposed to IgG globulins, which occur later in rubella and are associated with the FA staining component. This will be referred to later.

The Rubella HI test

This is a relatively new test, first reported in 1967 by Stewart, *et al.*, using newly-hatched chick red blood cells. HI titres start to rise within a day or two of appearance of the rash and reach a peak within a few weeks; in time this level decreases somewhat but remains elevated even after 10 to 20 years. We feel that the combination of HI and CF tests offers excellent coverage, and that while the other serological tests have some value, they would probably add little to the service provided the clinician. The recent survey of Lennette and his fellow workers (1967) and Sever et al., (1967) using the H. I., C. F., F. A. and neutralization tests would bear this out. It is important that two specimens of blood be submitted for study, one collected as early as possible in the illness (acute phase) and the other taken 10 to 14 days later (convalescent phase).

Complement Fixation test

In children and adults infected with rubella virus the complement fixing antibody appears several days to a week after onset of infection, reaches a peak after about 1 month, and declines after 1 to 5 years. (Ingalls *et al.*, 1967; Dudgeon, 1967: Sever *et al.*, 1967). Among congenital rubella babies only 1 in 6 develops CF antibody during the first 8 months of life, and the incidence of babies with positive CF antibody titres reaches a peak towards the end of the first year of life and then falls off again. (Dudgeon, 1967). The neutralizing and HI antibodies appear earlier in the illness than do the CF antibodies (Stern, 1965; Lennette et al., 1967).

The Fluorescent Antibody (FA) test

This test may prove to be of little value in the serological diagnosis of rubella syndrome in babies or in the early stages of clinically acquired infection.

It has recently been discovered that the sera of children with congenitally acquired rubella, not only contain conspicuous IgM fractions (Alford, 1965; Bellanti *et al.*, 1965; Soothill *et al.*, 1966; Soothill, 1967), but lowered IgG levels (Alford, 1965; Soothill *et al.*, 1966; Soothill, 1967). Lennette *et al.*, (1967) reported that in clinical cases of rubella, antibody detected by the FA staining technique was present less frequently than neutralizing and HI antibody when the sera were collected within the first week after onset. They suggested as a possible explanation that early antibody to rubella may consist largely of IgM immune globulin, and that since labelled antihuman conjugate used for the FA tests is directed largely against IgG immune globulins, early antibody may not be detectable by immunofluorescent staining, if it is IgM in nature.

The presence of specific rubella IgM antibody in congenital rubella syndrome of infants and in early acquired infection has prompted several workers to study this aspect more thoroughly. Banatvala *et al.*, (1967), used 2-mercaptoethanol (2ME), a sulphydril-reducing compound, to break down the IgM immunoglobulins; they then titrated the sera in HI tests in parallel before and after treatment with 2ME. They found that 85.7% of acute and early convalescent sera from patients with rubella showed reduction in HI antibody titre after treatment with 2 ME but that all late convalescent sera showed no reduction. Vesikari and Vaheri (1968) used the alternate approach, demonstrating rubella IgM antibody with HI activity in early convalescent sera by sedimentation analysis in sucrose gradients with subsequent recovery of IgM. The latter method, while perhaps the more accurate of the two, is less suitable for routine diagnostic use. As a matter of interest, Schluederberg in 1965 demonstrated the presence of measles, mumps, and Coxsackie B5 specific antibody in the IgM fraction in acute and early convalescent sera by 2ME treatment. Williams *et al.*, (1968) have reviewed some of the work done in the field of interrelationships of viral diseases and polyclonal or monoclonal immunoglobulin abnormality in both lower animals and man. Whereas these methods hold much promise for the future they should be regarded *pro tem* as being in the experimental phase. It is our intention to study and compare HI titres before and after 2ME treatment and if appears to offer additional aid to the clinician in the diagnosis of patients with obscure histories. The test will be made available on a semi-routine basis, meanwhile HI and CF tests constitute the most practical serological method of diagnosis.

The interpretation of results

A fourfold or greater rise in titre obtained on a two-phase sample of blood is considered to be diagnostic of recent rubella infection. Much difficulty in interpretation may arise if the first specimen of blood is collected late after the onset of rubella when the titre may already have reached its peak, and the

second sample taken 2 weeks later may not show a further rise. Prior rubella infection may also leave a high normal residual titre.

Experience has shown that the rise in rubella antibody titre occurs very quickly and that when the suspicion of rubella is aroused in early pregnancy, only too often the specimen is collected after the antibody rise has occurred and is thus too late to be of diagnostic significance. A more practical answer to this problem would be to perform serological tests for rubella simultaneously with routine tests for syphilis, as part of a routine prenatal serological program. The administration of gamma globulin may also complicate the results of serological tests. Blood samples for testing should therefore always be collected before administration of gamma globulin.

The introduction of rubella serological tests is a relatively new innovation and a much greater background of experience and accumulated data is desirable to evaluate them accurately. The ideal arrangement in the case of pregnant women, as suggested above, would be to collect the first sample of blood from all pregnant females at their first prenatal visit. Subsequently, a second sample should be collected if and when suspected rubella illness did occur during pregnancy. The greater the number of such specimens which are forwarded to the laboratory, the greater will be the backlog of experience the laboratory can draw upon, for the interpretation of results.

Collection of Specimens

Isolation. Specimens for isolation of virus should be collected from clinically ill patients as soon as possible after onset of symptoms: they should be kept refrigerated and transported to the laboratory as quickly as possible. When such specimens cannot be delivered within one or two hours, they should be frozen and shipped in dry ice. This also applies to tissue collected at operation or at autopsy.

From clinically ill patients or rubella syndrome babies, collect throat washings and urine. In the event of an abortion, either spontaneous or therapeutic, send the products of conception. If a rubella syndrome baby dies and a post mortem is conducted, collect sections of lung, heart or other organs thought to be infected. If an operation for removal of cataract is performed on a congenitally infected baby send lens material.

Serology. Collect the acute phase specimen of blood as soon as possible after onset of symptoms and the convalescent phase 10 to 14 days later. For pregnant women, collect the first phase blood at the first prenatal visit and the second phase if a suggestive rash or illness develops during pregnancy.

Obtain 10 ml of venous blood and place in any sterile, glass, stoppered tube. Allow to clot at room temperature and then refrigerate but do not freeze. Send to the laboratory to arrive, when possible, within 12 to 14 hours of collection. If forwarding over long distances through the mails, it is wise to centrifuge the specimen, discard the clot and red blood cells and ship only the serum. The laboratory will hold the acute phase serum until the convalescent phase serum is received and carry out the tests on both sera at the same time and under the same conditions.

History of Illness. This must accompany all specimens. A sample requisition form is reproduced below for use when submitting specimens from a pregnant woman or suspected rubella syndrome baby.

PROVINCE OF NOVA SCOTIA
PUBLIC HEALTH LABORATORY
5800 UNIVERSITY AVENUE
HALIFAX, N. S.

Phone: 422-9661 Ext. 229 **VIRUS SECTION**

Request for serological or direct evidence of Rubella virus infection. (German Measles)

Patient's Name..... Doctor's Name.....
ADDRESS..... ADDRESS.....
AGE..... MARRIED..... SINGLE..... Phone No.....
SPECIMENS: (1) Blood*..... (2) Throat washings or swab.....
(3) Urine..... (4) Cerebrospinal fluid.....
(5) Placenta..... (6) Products of conception.....

*Children 5 CC Adult 10 CC

CLINICAL DATES:

If pregnant Woman:

1. Last menstrual period.....
2. Fever.....
3. Headache.....
4. Sore Throat.....
5. Rash.....
6. Adenitis.....
7. Differential leucocyte count.....

If suspected Rubella Syndrome Baby

1. When did mother have rubella.....
2. Length of term.....
3. Birth weight.....
4. Clinical abnormalities.....

Dr..... Date.....

Summary

The laboratory study of rubella has made rapid strides since the first reported isolation of the virus in 1962. We are now prepared to offer diagnostic service for the isolation and identification of virus from clinical specimens, as well as serological studies if 2 phase sera are received. *It should be clearly understood that no conclusions can be drawn from the results of a single sample of blood.* To establish an accurate diagnosis *at least two samples of blood collected 10 - 14 days apart,* or in the case of pregnant women, a prenatal specimen and one collected post infection, must be submitted in order to determine whether or not a rise in titre has occurred.

We have attempted in this report to explain some of our procedures and to assist in the interpretation of results. A close liaison between the laboratory and the practicing physician will build up an extensive backlog of information for future use as well as assist with the immediate diagnostic problem.

□

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How long can an old stand-by* stand fast?

P.G.A. oral penicillin G is just as effective against penicillin-sensitive infections now as it was 16 years ago. "For pneumococcal, streptococcal and 70% of the staphylococcal infections, Penicillin G is the agent of choice and for the pneumonias that elderly patients may get, this would always have to be the first choice."**

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*Stand-by: Any person or thing that can be relied upon in time of stress or emergency . . . New College Standard Dictionary—Funk & Wagnalls.

**Cardiac Drugs and Antibiotics, GUNTON Ramsay, Ontario Med. Rev., 34:227, 1967.

Pulmonary Embolism*

Reprinted from The Canadian Medical Association Journal, Vol. 93, p. 1172, Nov. 27, 1965

A 20-year-old white married woman was pregnant for the second time, and had had no prenatal care when she presented herself for admission to hospital on March 5, 1961, her expected date of confinement. The previous pregnancy had terminated April 15, 1959, with the vaginal delivery of a healthy 5 lb. 3½ oz. male infant. Thirteen days before that delivery she had had two eclamptic convulsions from which she apparently recovered satisfactorily.

When admitted to hospital she was having irregular uterine contractions five to seven minutes apart; her blood pressure was 114/90 mm. Hg, her pulse was 100/min., her hemoglobin was 14 g. %, the urinalysis was normal and the fetal heart rate was 136/min.

On physical examination she was a mildly obese white woman about seven months pregnant who had dyspnea and pitting edema of the ankles and abdomen.

An internist was called in consultation because of the possibility of underlying heart disease. He noted a Grade 2 systolic murmur which was maximal over the pulmonic area; there was no associated thrill. The liver was not enlarged. The consultant suggested that the patient be allowed to deliver spontaneously and recommended a cardiac reassessment in the postpartum period because of a possible atrial septal defect or other cardiac lesion. The patient was placed on 500 mg. of chlorothiazide daily, ½ grain of sodium phenobarbital twice daily, a low-salt diet and bed rest. During her hospital stay the uterine contractions ceased, and the dyspnea and edema improved. The patient was discharged from hospital on March 12, 1961, one week after admission. She was advised to continue the above regimen at home and return to the prenatal clinic on March 16.

When seen in the prenatal clinic, four days after her discharge from hospital, the uterus was four fingerbreadths below the ensiform process, the fetal heart rate was 148/min. and the blood pressure was 100/70 mm. Hg. She had slight dyspnea and ankle edema. Radiographic pelvimetry at this time revealed a gynecoid pelvis with adequate obstetrical measurements; however, the fetus was presenting as a transverse lie with the head to the right, the breech to the left and the back over the pelvic inlet.

The patient was readmitted to hospital on March 17 at 4:30 a.m., having had uterine contractions for 12 hours. The blood pressure was 110/70 mm. Hg, the fetal heart rate was normal and the fetus was presenting as a transverse lie. The membranes ruptured shortly after admission and a prolapsed cord was noted. A consultant obstetrician was notified, oxygen was administered and the patient was prepared for immediate Cesarean section.

Under spinal anesthesia a low transverse Cesarean section was attempted. A constriction ring was present above the lower uterine segment, and the lower transverse uterine incision had to be extended vertically to allow the delivery of the baby. A 3 lb. 4 oz. male infant was delivered with some difficulty at 5:10 a.m. and the baby sustained a fracture of the left clavicle and the left humerus. The infant's condition was poor and he died at 41 hours of age. An autopsy revealed that death was due to intracranial hemorrhage.

The immediate postoperative condition of the mother was satisfactory. She was given 300,000 units of procaine penicillin G, 100,000 units of potassium penicillin G, and 0.5 g. of streptomycin sulfate (Strep-Dicrysticin) at 10:15 a.m. on March 17.

Her condition was good for 12 hours postoperatively, when she suddenly became nauseated and had a prolonged cold sweat. The blood pressure was 88/66 mm. Hg, and at this time the patient stated that she was allergic to penicillin. She was given 50 mg. of diphenylhydramine hydrochloride (Benadryl) intramuscularly. An intravenous infusion of 500 ml. of 5% glucose and water was started. The patient continued to sweat profusely and intra-abdominal bleeding was suspected. At 6:00 p.m. on March 17 (13 hours postoperatively), 500 c.c. of blood was started intravenously and a second bottle of blood was begun at 11:00 p.m. The blood pressure was 100/85 mm. Hg throughout the night and the urinary output gradually increased to normal.

During March 18, the patient remained in a shock-like state, complaining of weakness and having cold sweats; her blood pressure was 100/85 mm. Hg and her pulse rate was 98/min. On the morning of March 18, she had received 50 mg. of diphenhydramine hydrochloride and 50 mg. of hydrocortisone (Solu-Cortef) in an intravenous infusion of 5% glucose and saline.

On re-evaluation during the afternoon of March 18 (36 hours postoperatively), the internist noted "a harsh, Grade 3 pulmonary systolic murmur with a snapping second sound". The liver was not palpable and no rales or rhonchi were heard on auscultation of the chest. Tenderness was noted in the right flank. He considered that intra-abdominal bleeding might

*This series of articles arranged by an editorial subcommittee of the C.M.A. Committee on Maternal Welfare, and originally published in the Canadian Medical Association Journal, is being reproduced in the Bulletin at the request of The Medical Society of N. S. Committee on Maternal and Perinatal Health, by kind permission of the Editor of the Canadian Medical Association Journal.

have occurred and that early heart failure was present. The patient was digitalized and another 500 ml. of whole blood was started. The hemoglobin was 14.4 g. %; the white blood count was 32,000/c.mm. with 85% neutrophils and 15% lymphocytes. The blood urea nitrogen was 24 mg. %, the serum sodium was 136 mEq./l., the serum potassium was 5.3 mEq./l. and the serum chloride was 103 mEq./l. On March 18, additional hydrocortisone was given and 500 mg. of chloramphenicol (Chloromycetin) was administered, with 250 mg. to be given every six hours thereafter.

On March 20 (third postoperative day), the patient was seen by a cardiologist. An electrocardiogram at this time was suggestive of acute cor pulmonale associated with pulmonary embolism. At 8:50 p.m. on March 20, the patient was transferred to the intensive care unit and heparin was given intravenously.

At 3:00 a.m. March 21 (94 hours postoperatively), the patient complained of severe right-sided chest pain. Examination of the chest revealed diminished breath sounds over the right lung field. Despite an intravenous drip of metaraminol (Aramine) and continuous oxygen therapy, the patient became very restless and died at 5:45 a.m. March 21 (96 hours postoperatively).

A complete autopsy was performed and revealed a pulmonary embolus obstructing the right main pulmonary trunk and small recent emboli with infarcts of the right lower lobe. The origin of the embolus was at the junction of the right uterine and internal iliac veins. There was cor pulmonale with right ventricular hypertrophy, pulmonary arteriosclerosis and marked venous congestion of the organs. The heart weighed 370 g., and the right atrium and right ventricle were dilated. However, there was no lesion of the heart valves. There was no blood in the peritoneal cavity.

Decision of the Provincial Committee on Maternal Welfare

The conclusions reached by the Provincial Committee on Maternal Welfare after a review of the case were: "This is a preventable direct maternal death. There is a patient factor in that the patient did not seek prenatal care; however, it is unlikely that adequate prenatal care would have altered the outcome. Pulmonary embolism probably had occurred 12 hours postoperatively when she became nauseated, had a prolonged cold sweat and developed shock. This is substantiated by the pulmonary infarcts found at autopsy. Death was caused by the massive embolus found in the right pulmonary artery. This probably occurred some two hours prior to her death when she complained of sudden chest pain. It is possible that if the diagnosis of pulmonary embolism had been made when the process began 12 hours postoperatively, and adequate anticoagulant therapy had been instituted at this time, this maternal death may have been prevented. A low vertical intrauterine incision was indicated in this case of fetal transverse presentation.

"This maternal mortality has been considered ideally 'preventable' under the terms of reference of the Provincial Welfare Committee and there is no implication of any negligence."

Discussion

The pulmonary arteriosclerosis in this 20-year-old woman was evidence of pulmonary vascular disease which antedated the present pregnancy and in turn was responsible for the right heart hypertrophy. The prominent pulmonary conus, the dilated right atrium and ventricle, and the acute engorgement of the organs reflected terminal acute right-heart failure which resulted from the postoperative pulmonary embolism.

In this patient, no pathological cause was found for the pulmonic systolic murmur. In retrospect the accentuated second heart sound in the pulmonic area associated with the murmur (heard by the internist) indicated increased pulmonary hypertension secondary to pulmonary embolism.

The differential diagnosis of shock developing 12 hours postoperatively included: delayed penicillin reaction, intraperitoneal or extraperitoneal hemorrhage, and pulmonary embolism. It was unfortunate that an electrocardiogram was not done then because a tracing at that time might have been similar to that obtained on the third postoperative day which suggested acute cor pulmonale associated with pulmonary embolism. With this tracing and the finding of an accentuated second heart sound in the pulmonic area, the diagnosis would have been obvious, and if immediate anticoagulant therapy had been instituted the continuing and fatal embolic process might have been prevented.

Pulmonary embolism must always be excluded in the differential diagnosis of shock following obstetrical delivery or pelvic surgery. Pulmonary embolism in the first 24 hours following delivery or surgery is unusual; however, it does occur, as in this case. A maternal death was recently described due to pulmonary embolism 22 hours following normal spontaneous delivery; however, this catastrophe does not usually occur until seven to 14 days after delivery or surgery.

This patient was given penicillin some 12 hours before she mentioned that she was allergic to penicillin. Whenever possible, patients should be questioned about known drug sensitivities.

With a transverse presentation, it is prudent to perform a low vertical uterine incision to extract the fetus. The fetus is often impacted in the pelvis, and the lower transverse uterine incision does not provide a uterine opening adequate for the extraction of the fetus.

Summary

A maternal death was reviewed by the Provincial Committee on Maternal Welfare. The cause of death was pulmonary embolism, the embolic process originating in the right internal iliac vein. The preventable factors are discussed. □

Public Health News

Alcoholism Research Upgrading Needed

A Dalhousie psychiatrist has called for the upgrading of research efforts "to improve both our methods of treatment and prevention of alcoholism."

Dr. Benjamin K. Doane told the annual meeting of the Nova Scotia Branch, Canadian Public Health Association, his appeal was "not just for an increase in research but for an upgrading of the quality of research particularly in psychiatry."

Recent work in physiology and biochemistry, he said, was "telling" us much about the physical effects of alcohol within the body, particularly in the liver and nervous system. This is important in helping us as medical men to treat the physical aspects of alcoholism."

However, progress was "painfully slow in dealing with the psychological variables." The most important area for research in this direction was the "exploration of factors affecting the motivation of alcoholic patients. Patients do differ and it is upon their points of difference that we must concentrate."

New Health Guide for Elementary Grades

A new health guide for the elementary grades is now being tested in several parts of Nova Scotia.

The guide, written by Clem Crowell, former inspector of schools, with the assistance of a committee of representatives from the Departments of Public Health and Education, is now in use in Digby, Annapolis, and parts of Colchester counties, New Waterford, and parts of Halifax City.

This new curriculum guide for teachers covers a number of major health areas including: social development, nutrition, body and reproduction, and play and exercise.

The family life and reproduction section was tested in two classes in Digby early in 1968. Inclusion of this section in the health course, however, will remain the option of the local school board in cooperation with the parents concerned.

Sister Frances Traynor, one of the two teachers involved in the Digby trial last year, said that when she was first approached about teaching the family life aspect, she had a feeling of uncertainty but after the teaching experience she had become convinced it should be taught at the grade five level (her own grade).

National TB Centre Opened

The National Tuberculosis Reference Centre in Ottawa has been officially opened.

Staffed by scientists from the Department of National Health and Welfare's Laboratory of Hygiene, it is responsible for establishing and maintaining uniform standards in testing for resistance to the primary drugs.

These tests are currently done in provincial laboratories but centralization of these services will assure a uniform standard of investigation.

Another important objective of this new service is to conduct investigations on resistance to the second line anti-tuberculosis drugs for the whole of the country.

The centre is located in facilities made available by the Royal Ottawa Sanatorium.

Nova Scotia Hospital

Victor F. Simpson has been appointed the first administrator of the Nova Scotia Hospital.

The appointment reflects changes in the administrative structure at the hospital to bring it in line with that of general hospitals in the province.

The changes are believed to be the first in a provincially-operated mental hospital in Canada.

Mr. Simpson was formerly a counsellor in hospital administration with the Nova Scotia Hospital Insurance Commission. He has been with the commission since 1966 and has more than 20 years experience in the field of hospital administration.

Dr. Harry Poulos, clinical director, becomes the first medical director of the hospital and Dr. C. H. Bentley, assistant superintendent, becomes assistant medical director.

The first step in the administrative change took place last September when it was placed under the jurisdiction of the Nova Scotia Hospital Insurance Commission. The present changes constitute the second step.

The appointment of a board of management will complete the change in administration.

Local CPHA Elect New Officers

Paul MacDonnell, a public health inspector from St. Peter's Nova Scotia, was elected president of the Nova Scotia Branch, Canadian Public Health Association, at its annual meeting. He takes over from Dr. Lloyd Hirtle, Department of National Health and Welfare.

Mrs. Marilyn Cole, assistant director of nutrition, Department of Public Health, was elected first vice-president, and Dr. Peter Gordon, Dalhousie University, second vice-president.

Other members of the new executive include: Miss Helen Miller, Dr. C. E. Tupper, Mrs. E. M. Bentley, and John Wilson, all of Halifax, and Dr. V. K. Rideout, Yarmouth.

National CPHA To Meet In Halifax

The Canadian Public Health Association will hold its annual national meeting in Halifax May 21 and 22 at the Hotel Nova Scotian.

Close to 600 delegates from across Canada are expected to attend. Dr. Chester Stewart, Dean of Medicine, Dalhousie University, is national president. □

News Flashes

"Did you hear Erica is marrying her X-ray Specialist?"

"Well, she's lucky; nobody else could ever see anything in her."

Nova Scotia Medical Bulletin, 14: 306, 1935.

SURGICAL SECTION NEWS

The Surgical Section of The Medical Society of Nova Scotia held its annual meeting in Sydney on November 9, 1968. Twenty-five members attended the scientific and business sessions.

The scientific sessions were held at St. Rita's Hospital. Dr. C. E. Kinley of Halifax discussed esophageal carcinoma and its present management. Dr. G. W. Bethune of Halifax reviewed the results in breast carcinoma and presented a plan of management. Dr. M. R. Rajani of Glace Bay presented three cases of postvagotomy atony. Injuries of the spleen were presented by Dr. D. M. Nicholson of Halifax. Dr. J. H. MacLeod of Halifax reviewed abdominal injuries related to the use of seat belts. A case of splenectomy performed in the management of neutropenia was presented by Dr. B. J. Steele of Halifax. Dr. P. J. Gouthro of Sydney presented a case of multiple malignancies. Dr. K. Raz discussed dislocations of the upper extremities.

The business meeting was well attended. Among the topics discussed were proposed changes in the Medical Act and the new Fee Schedule. Committee reports were received and discussed. The following slate of officers was elected:

President	Dr. G. W. Bethune, Halifax
Vice-President	Dr. F. Kelley, Sydney
Secretary Treasurer	Dr. J. H. MacLeod, Halifax
Past President	Dr. B. K. Coady, Halifax

Executive members at large:
Dr. F. Markus, Shelburne
Dr. J. A. Myrden, Halifax
Dr. D. H. MacKenzie, Sydney

A very pleasant dinner was held at the Isle Royale Hotel for the members and their wives. This was followed by an enjoyable evening at the Royal Cape Breton Yacht Club. The success of the program was due to the efforts of the local committee headed by Dr. D. H. MacKenzie. The ladies' program was arranged by Mrs. Lloyd Allan and Mrs.D. H. MacKenzie.

ANNOUNCING

The Third Annual Symposium of The Nova Scotia Division of THE CANADIAN SOCIETY OF INHALATION THERAPY TECHNICIANS to be held at The Holiday Inn, Dartmouth, on February 20, 21, 22, 1969.

* * * * * * * * * *

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* * * * * * * * * *

Registration Fee — $5.00 *
Banquet on Friday Evening — $4.00
For information call 429-7368, Department of Inhalation Therapy Victoria General Hospital

AUDIO-VISUAL AMATEURS

Those producing stills, films audio or video tape recordings for educational purposes in medicine will be glad to know that the C.M.A. has decided to continue the program of awards begun last year. If you plan to enter material for this competition, the deadline for completing the application is March 1st, while completed material must be submitted by April 1st. For further details see the C.M.A. Journal of November 16, 1968, or write the C.M.A. direct.

Congratulations to Dr. and Mrs. Benvie, who, on September 10th, celebrated their arrival at another milestone on the road of marital happiness.

Nova Scotia Medical Bulletin, 14: 541, 1935.

Shown are members of the Executive of the Surgical Section of The Medical Society of Nova Scotia.
From left to right: Dr. F. Markus, Shelburne; Dr. J. A. Myrden, Halifax; Dr. J. H. MacLeod, Halifax; Dr. B. K. Coady, Halifax; Dr. D. H. MacKenzie, Sydney.

News Flashes

FORTHCOMING MEETINGS

Forthcoming Events, Courses and Meetings

Dalhousie University is offering the following short courses:

Radiology	February 14 - 15
Psychiatry	February 24 - 26
Physiology for practicing physicians	February 28 - March 1
Obstetrics	March 14 - 15
Anaesthesia	March 17 - 20
Paediatrics	March 21 - 22
Surgery	March 28 - 29
Urology	April 25 - 26
Workshop in Cancer	April 28 - 29

Full information on these courses from: The Division of Continuing Education, 15th Floor, Sir Charles Tupper Medical Building, Halifax.

The American College of Physicians announces the following postgraduate courses:

Physiological Concepts Of Clinical Disease	March 3 - 6
The Doctor: His Patient and the Illness	March 3 - 7
Recent Advances in Cardiovascular Disease	March 17 - 21
Modern Pathology for Internists	March 24 - 28
Three Days of Gastroenterology	March 26 - 28
Internal Medicine: the Good That's Old, the New That's Vital	May 12 - 16
Adolescent Medicine	May 19 - 22
Intensive Care Units	May 19 - 23

Full information on these courses: Edward C. Rosenow, jr., M.D.F.A.C.P., Executive Director, American College of Physicians, 4200 Pine St., Philadelphia, Pa. 19104

The Province of Quebec Medical Association, Convention, Queen Elizabeth Hotel, Montreal, April 17. 18, 19, 1969.

". . . as suggested by one newborn infant,"
NEJM 279: 570, 12/9/68

POSITION WANTED

Pakistani Doctor M.B.B.S. D.A. (London) with four years all round English Hospitals and G. P. Experience. Immigrating to Canada, seeks opening in Hospital General Practice in Nova Scotia. Registered with Provincial Medical Board of N. S.

Contact: S. Qureshi, Moorgate Hospital, Rotherham, U. K. Tele., Rotherham, 2171. England.

SKI-TOURING

Through cross country skiing, winter can become a time of special beauty. If you want to keep in shape this way, consult **Ski-Fun for Everyone,** published by the Dept. of Health and Welfare, and available through the Queen's Printer, Halifax.

OFFICE SPACE
DARTMOUTH, N. S.

We are reserving 3,000 square feet of office space for doctors in the expansion of our shopping centre on Main Street in Westphal.

Size, layout and finish to your requirements.

Address enquiries to

J. D. Fraser
SOBEYS STORES LIMITED
King Street
Stellarton, N. S.

CASE REPORTS

Readers of the Bulletin have expressed a wish to see more reports of interesting cases and of diseases of particular importance in the Maritimes. However, many who encounter such cases state also that they have insufficient time, writing ability or library resources to compile case reports in a form suitable for publication.

Recently an Editorial Service was set up for the Faculty of Medicine at Dalhousie, to prepare medical reports for publication. For a trial period, any doctor who is a member of the Medical Society of Nova Scotia will be eligible to use this service after 1st July, 1969. Members who wish to take advantage of this should send manuscripts to The Editor of the Bulletin with a request for this service: a draft of the suggested version is sent to the author for his comment, and his approval is obtained before the paper is forwarded for publication in the Bulletin.

FRIDAY, November 29, 8.00 p.m.

Dalhousie History Club—Professor J. M. S. Careless

"Canada: History's Error?"

GENERAL PRACTITIONER WANTED for a group of General Practitioners, Surgeons and Anaesthetist in the Province of Nova Scotia. Modern Hospital facilities are available and a new Medical Centre is in the process of construction. The Hospital has active teaching program of Ward Rounds, monthly Journal Club meetings, Mortality Conferences and Lectures by visiting Physicians. Interested candidates should apply in care of The Nova Scotia Medical Bulletin, P.O. Box 100.

News Flashes

TO ALL PHYSICIANS

Re: Early and Continued Supervision of Your Pregnant Patients with Rh Incompatability

We continue to lose babies due to Erythroblastosis because their mothers were referred too late in their pregnancy for anything constructive (e.g. intrauterine transfusion or early induction of labour) to be done. This, we feel, is a tragedy and a judgement against our profession. In some of these cases, however, it is the patient's fault for not reporting to her doctor early in pregnancy.

May we respectfully suggest a continued "all out" effort in protecting these unborn? We owe it to ourselves—the Medical Profession of N. S. — and particularly to the unfortunate babies who are at high risk.

A Recommended Outline of Management

1) All pregnant women to be Rh tested – 5 c.c. of blood is all that is needed.
2) Any Rh negative multigravida to have her blood tested for antibodies every month.
3) Any Rh multigravida with Rh antibodies to have an Amniocentesis at the 28th week, or **earlier** if she has a previous history of stillbirths or neonatal deaths or previous babies requiring transfusion at birth.

We are here to help in any way we can. Please use us. Phone us (collect) or write

The Rh Committee
5821 University Ave.
Halifax, N. S.
Phone 422-6501, local 241

OFFICE SPACE

6411 Quinpool Rd., Halifax (over Drug Store) Previously occupied by Doctors.
(Waiting Room, Sect. Office, Office, Exam. Room and Work Room also two extra rooms could be used)
Phone: 422-4479

A NEW OTOSCOPE

Beginning mid-November, Smith Kline & French, Montreal pharmaceutical company, will market the Hotchkiss Otoscope in Canada. The Hotchkiss instrument is a new otoscopic system with coaxial lighting (the same principle as the head mirror), designed to improve and simplify ear examinations and instrumentation.

Designed by Dr. John E. Hotchkiss, a San Francisco otolaryngologist, the new system eliminates parallax error – a basic deficiency of standard otoscopic systems. It also provides greater illumination, up to four times brighter than traditional otoscopes.

Young Boy, to Mother, in car passing blond, long-haired youth who is 'thumbing' a ride:
"What's the thumb out for?"
Mother: "It means he wants a ride".
Young Boy: "She, stupid!"

WANTED

Practice Partnership or Long Locum wanted in Nova Scotia. By 37 year old married London Graduate. 9 years experience. Obstst, Anaesthetics & General Pract. Surgery in Australia.
Apply Box No. 101,
The Medical Society of Nova Scotia.

WE STILL HOPE SO

"After taking off my winter clothing," says Dr. Hammond, of New York, "I wouldn't appear on the street for a while." Not immediately, we hope—certainly not.

PROVINCIAL MEDICAL BOARD SUSPENSION OF PHYSICIANS

Dr. Javendra Arvindlal Shah of 6736 Quinpool Road, a general practitoner, was suspended following an investigation on Nov. 2, by the discipline committee of the Provincial Medical Board.

He was found guilty of "improper conduct," the charge — "being registered under the Medical Act and at the relevant times being a participating physician under agreement number 3043 with Maritime Medical Care Incorporated, you improperly and wrongly submitted and received payment for accounts sent to Maritime Medical Care Incorporated" . . . for three persons.

Dr. Shah must not practice in Nova Scotia for six months, beginning on the date of the hearing.

In the meantime the only other suspension made by the provincial medical board in the past year, is under appeal.

Dr. Shahnaz Mahboob of New Waterford, has given notice of appeal regarding a decision on Nov. 18 and 20 of last year finding her guilty of incompetence.

The board held the two-day investigation at Sydney. Dr. Mahboob was given notice — after being found guilty on four charges and not guilty on five other — that she, must serve a 12-month internship in a Nova Scotia hospital before she is permitted to practice again.

TROUBLE-TRIPS

For information on a trip of a different kind, through L.S.D., the Dept. of Health and Welfare publishes an informative monograph "L.S.D.: Problems and Promise" which may assist in explaining the problem to parents and young people. These are available at 25c a copy from the Queen's Printer.

On Elevators

As I waited for seemingly an eternity, pacing back and forth while scanning the mocking arrows and numbers, I thought how perverse elevators are. Why do they trick us so often? It seems more than coincidence that when we want them, elevators are invariably on the next floor down, about to descend, or else every available elevator is right at the bottom of the building. There is a hint of poltergeistic activity in an elevator rising two floors, then descending to our original level for no apparent reason, before taking us to our planned destination. My little boy was aware of this extra-mechanical activity, and his tears were evidence of this.

Perhaps the answer is that elevators are indeed imbued with some kind of mindful function. They lead a life of their own, while we, pretending to be their masters, are really only parasites distracting them, disturbing their way of life. When we consider how we mistreat them, their perversity is hardly surprising.

Observation of one's fellows leads one to conclusions which, like elevators, are sometimes depressing, sometimes elevating. We recognize human types: the elevator, in this mechanical age, draws us out. The person who cannot refrain from impatiently pressing the button while waiting, the person who uses the elevator to descend one floor rather than walk, the one who invariably steps onto the upgoing elevator to go down, the woman who is reduced to a jibbering state of anxiety lest she be the sole passenger, and, at the other extreme, the man who wants to appear as though he is taking absolute control, with a profound knowledge of the precise function of all the buttons and knobs: these are ourselves. Elevators offer us opportunities for gratuitous graffiti, corridor consultations (often unnecessarily public), flighty flirtation, and mystical meditation; and we accept them to overflowing.

Elevators portray a moving scenario, before which we flounder; as Emerson said, "The machine unmakes the man". How few of us know the secret of coaxing these mechanical maidens into our service, how few of us can accept with patience their vertiginous vagaries! In this lunar and lunatic age, when but few of us as it is would qualify as passengers to the moon, fewer still seem to understand that machine so much less complex and so much more down-to-earth than the lordly rocket: our humble, friendly, but much-abused servant, the elevator. □

D. A. E. S.

DOCTORS VERSUS EDITORS

A Doctor can call on another man's wife any time of the night or day, and charge for the visit, if an Editor does, he gets a charge of buckshot.

A Doctor can get out a word a foot long without himself or anyone else knowing what it means. If an Editor uses the same word, he has to spell it.

If an Editor makes a mistake there is lawsuit, if a Doctor makes one there is a funeral, cut flowers and perfect silence.

Any old College can turn out a Doctor but an Editor has to be born.

ODD EPITAPHS

And am she dead, and are she gone
And have she left I all alone?
Oh cruel fate, you is unkind
To take she fore and leave I (be) hind.

Here lies my wife Samantha Proctor
Who ketched a cold and wouldn't doctor
She couldn't stay, she had to go,
Praise God, from whom all blessings flow.

She had two legs and a baddish cough.
But it wasn't her legs that carried her off.

Medical Review Literature

We hope to publish in each issue of the Bulletin a selection of symposia and review articles of interest to the general practitioner. Listed below are those which had appeared in 1968 at the time this issue went to press.

SYMPOSIA PUBLISHED IN *THE PRACTITIONER* IN 1968

January: Clinical pharmacology
February: Drug and alcohol addictions
March: The toddler
April: Endocrinology
May: Disorders of the skin
June: Care of the elderly
July: "Retrospect and prospect" – Changes in all areas of medicine
August: Diet and nutrition
September: Renal disease

A new series, entitled "Everyday problems in general practice," was started in *The Practitioner* in the January 1968 issue.

REVIEW ARTICLES

Burns: Management of the burn patient in a general hospital. M. B. Sullivan, Jr, *et al.* Surg. Clin. N. Amer. 48: 79–86, Aug. 1968.

Cancer chemetherapy and surgery. Higgins G. A. and White G. E. Surg. Clin. N. Amer. 48: 849–850 Aug. 68.

Deficiency diseases: Undernutrition in children and subsequent brain growth and intellectual development. Nutr. Rev. 26: 197–9, July 1968.

Dermatology: Contact dermatitis. D. S. Wilkinson. Brit. J. Derm. 80: 482–3, July 1968.
Current review of psoriasis. E. M. Farber *et al.* Calif. Med. 108: 440–57, June 1968.

Diet: Overfeeding lean and obese individuals. Nutr. Rev. 26: 202–5, July 1968.

Gall stones: D. M. Small. New Engl. J. Med. 279: 588–93, 12 Sept., 1968.

G. I. system: Drug action on digestive system. S. Holz. Ann. Rev. Pharmacol. 8: 171-86, 1968.

Gout: C. J. Smyth. Clin. Orthoped. 57: 69–80, Mar./Apr. 1968.

Heart failure: Use of sympathomimetic amines in heart failure. L. I. Goldberg. Amer. J. Cardiol. 22: 177–82, Aug. 1968.

Infection: Wound infection; etiology, prevention, and management, including selection of antibiotics. J. C. Todd. Surg. Clin. N. Amer. 48: 787–98, Aug. 1968.

Liver disease: Preoperative management of patients with liver disease. F. C. Jackson *et al. Ibid.* 48: 907–30, Aug. 1968.

Metabolism: Calories and activity in children. Nutr. Rev. 26: 239–41, Aug. 1968.

Pain: The autonomic nervous system and pain. F. P. Haugen. Anesthesiology 29: 785–92, July/Aug. 1968.

Pancreatitis: principles of management. Y. H. Zimberg. Surg. Clin. N. Amer. 48: 889–905, Aug. 1968.

Paraplegia: Adjunctive care of spinal cord injury. H. S. Talbot. *Ibid.* 48: 737–57, Aug. 1968.

Pulmonary disease of vascular origin: D. E. Dines. Dis. Chest 54: 3–12, July 1968.
Virus, fungus and parasitic infections of the lung. Quart. Med. Rev. 18: 1-44, Jan. 1968.

Rheumatic fever: Optimum therapeutic program in seropositive nodular rheumatoid arthritis. C. J. Smyth. Med. Clin. N. Amer. 52: 687–98, May 1968.

Sociology: Sociocultural factors in health and illness; selected review of the literature. B. Schlesinger. Can. Med. Ass. J. 99: 274–6, 10 Aug., 1968.

Tetanus: Prophylaxis and therapy. N. L. Robles *et al.* Surg. Clin. N. Amer. 48: 799–806, Aug. 1968.

Thromboembolic disease: Management of acute arterial insufficiency. H. B. Wheeler. *Ibid.* 48: 851–68, Aug. 1968.
Pulmonary embolism. R. Fontaine. J. Roy. Coll. Surg. Edin. 13: 205–16, July 1968.

Unconsciousness: Management of head injuries. E. Mannarino *et al.* Surg. Clin. N. Amer. 48: 723–36, August 1968.

ADVERTISERS' INDEX