

Aetiology and Pathogenesis of Pulmonary Emphysema

A critical study conducted from the real perspective of the lung as a mechanically active autonomic organ.

Abstract

The aetiology and pathogenesis of Pulmonary Emphysema remains unknown, although a great deal of research has been and is carried out. The reason for that is the lack of a scientific theory, which can support its interpretation, since the traditional theory of pulmonary physiology, which considers the Lung a passive organ, does not favor the understanding of a pulmonary physiopathology. Therefore, attention has been diverted to genetic and/or enzymatic factors that could act as a tissue destructive factor

Pulmonary Emphysema must only be considered under the conceptual scheme of the Lung as an active organ, since the anatomo-pathology of emphysema shows results compatible with a systematic cyclic hyper-kinetics able to distend, break down and destroy elastic structures, which become manifest after a long process, not only as respiratory insufficiency but also as Chronic Cor Pulmonale

The basic knowledge to bear in mind is the functional structure and cyclic dynamics of the pulmonary lobules, the bronchioles of which must displace their contained air to expand the alveoli. This expansion must balance a physiological pressure, predetermined in the alveolar design, relative to forces generated by their own muscles, under Sympathetic control. The alveoli are the final destination for the air ejection. They are real functional cul de sacs where expansion of the air molecules takes place to balance structures, alveolar air, and capillary blood pressures. This molecular expansion is the force that becomes destructive when surpassing the limit of physiological resistance in systematic manner.

The primary cause of the named hyperpressure, is based on hyperkinetics of the Sympathetic Adrenergic System, due to endogenous or exogenous agents

There is one exogenous agent statistically pinpointed as a “risk factor”: The habit of cigarette smoking.

An analysis of the facts, from the perspective of the Lung’s dynamics, as evidenced on the Respiratory Pulse, allowed me to conclude that the Nicotine content of tobacco is the exogenous factor, supplied by cigarette smoking, which causes Emphysema, and therefore is the cause of its growing incidence in present day society

Identification of the causal factor enables prevention. Therefore, it is possible to guarantee a World free from Emphysema, if necessary action is taken.

Preface

I discovered, in July 17, 1978, the *Resultant of the cyclic dynamics of the Lung* in the pleural space of the experimental dog. I acquired data and graphs that became the departing point of my analysis and interpretations, physic-mathematical first and physiological after, both with strict logical and experimental basis¹.

These data and graphs have for the Lung and air circulation a similar meaning to those of arterial and venous pulses for the Heart and blood circulation. Therefore, I called it **Respiratory Pulse**.

I obtained the firm objective evidence for the rationale to prove that the *Lung is a mechanically active autonomic organ*.

Consequently, the systematic analysis of those data and graphs, jointly with other simultaneous parameters, led me to create “**The New Theory of the Respiratory Dynamics**”.

Simultaneously, I developed the *Fundamental Equation* of the pulmonary mechanics to achieve the Respiratory Function².

The basic factors for this equation are:

1. Inspired *volume-mas* of air.
2. Successive forces generated in two genres of dynamic cycles, by contraction-relaxation of the muscles of the lobar bronchi and lobular bronchioles.
3. Total Capacity of the lung and that of the successive dichotomised divisions of the pulmonary airways

This equation allowed me to interpret the cause of “*Mountain sickness*”, which is the acute failure of a healthy Lung exposed to low atmospheric pressure at high altitude. The *low air mass per volume unit at that level* is the cause of this failure. This mass of air is inferior to that required by the pulmonary structure, even with its maximal potential

operating force, to finally balance the alveolar air and capillary blood pressures, thus enabling Oxygen diffusion as demanded by the Organism.

We must also apply the understanding of this equation, by analogy, in the interpretation of any chronic respiratory dysfunction, since that can lead us to determine the **causal factor**. This is the present case of Pulmonary Emphysema.

Afterwards, I performed experiments in dogs to establish the real effects on the Lung of selected drugs and biological products. The results serve as a preventive alert to avoid related future accidents in medical practice. As an example, I remember here the effect of Adrenaline on the Lung, which is not a bronchodilator as believed but a bronchiolar constrictor drug³⁻⁴.

*Finally, I have concluded the functional study of the extra-pulmonary air circuit and circulation*⁴.

I completed the analysis of the progressive air displacement, systematically, from the Atmosphere and returning to it, after accomplishing its goal in the alveoli, under physical conditions demanded by the Systemic program.

As a global concept, the Living Being is an Integrated Dynamic Complex, a mechanical System of Fluids including two integrated hemi-systems, of which the Lung and Heart are the primary great pumps to put into circulation their contained fluid masses. The conceptual analogy of the two hemi-systems to achieve circulation of the two different kinds of fluids, and their functional integration is surprising.

As a matter of fact I have opened and paved the way while walking along, with firm steps and certitude in the theoretical interpretation of functional pathologies of the Lung. I have also interpreted their implications with the cardio-circulatory System and Universal Dynamics, as manifested on the Earth. I have also started the study of reasons for related complications and fatal results in medical procedures and anaesthesia³.

The Lung is an organ provided with two simultaneous autonomic activities, one is parallel with that of the Heart and, the other has ventilatory rhythm, both in a functional balance integrating the Organism as a whole, as well as with the Atmosphere.

This final conclusion must place us on a perspective useful for the best understanding of the structural design of the “Global Respiratory System” to perform a dynamics with precise objectives.

These objectives are immediate and long term, also “integrator” of simultaneous and successive actions and reactions of the whole organic mechanical system of fluids, which is the essence of the mechanics for the vital functions.

The global respiratory system

The so-called cell respiration and pulmonary respiration are two complementary phases of the same process: intake of Oxygen offered by the Atmospheric air, its use in tissue combustion and, expelling of carbonic anhydride as its waste.

A complex System of Mechanics of Fluids, composed by two hemi-systems, performs this complex process:

1. Cardio-circulatory hemi-system for the blood
2. Pulmo-circulatory hemi-system for the air.

Both are joined into a somatic structure that answers to demands of the Lung, via reflex, viscerosomatic first and somato-somatic then².

The functional design and structure of each hemi-system is defined by the physical state of each one of the fluids that must be put into circulation, one in liquid state: the blood, and the other, in gas state: the air.

To the former we must add the fact that blood is an organic tissue, therefore circulating throughout a closed circuit, while the air is the gas mixture of the Atmosphere, therefore circulating throughout an open circuit.

Nevertheless, the problem to be solved by the organic design is even more complex since the air has weight and it is relative to gravitational force. Therefore, the Lung must adapt the mass of air per volume unit at the level where the individual lives, to that demanded by their alveoli, which corresponds to that of the adaptation level of the human specie and each individual.

The final functional integration of the two hemi-systems is fulfilled by a dynamic functional specialised structure of the Lung, under Sympathetic control: the pulmonary lobules. These have the alveoli in their respiratory bronchioles and, jointly with the corresponding capillary network, constitute the alveolo-capillary units. These complex mechanical units enable gas exchange that characterises pulmonary respiration.

I must emphasise here that the alveolar air pressure must balance the capillary blood pressure, to accomplish Oxygen diffusion in physiological conditions. I also must emphasise here that *the lobules are mechanical unitary structures achieving the final physical conditions of the air, to be supplied to their own alveoli.*

These mechanical processes for air conditioning is also necessary for the surrounding mechanical structures; also necessary for both, air and blood circulation throughout this vital area.

The cardio-circulatory hemi-system of the blood is the better-known sector.

The traditional interpretation of the *pulmo-circulatory subsystem for air circulation* is wrong, because of the belief of the Lung being a passive organ.

To discover and demonstrate that the Lung is an autonomous active organ is to put into evidence that its potential mechanical activity is unknown. Consequently, I assumed its interpretation.

The scientific re-interpretation of our Organism as a mechanical unit, and the following practical application of my proposed new knowledge, have been and is my utmost task, which I have dedicated to Humankind.

Nevertheless, my individual desires and actions are not enough. It is necessary to break down exterior resistance and to convince, not only of the truth of the new assertions, but also and over all that COMMON GOOD is and must be, ethically, the purpose of all those who live in Society.

Suggested method

As a method to start with interpretation of the proposed *pulmo-circulatory sub-system for air circulation*, I suggest to think it, in abstract first, as similar to the cardio-circulatory sub-system for blood circulation, since they are integrated structures. Therefore, they must obey, and in fact, obey to a specific, proportional and parallel functional design, to succeed in a common goal

Afterwards, one must think that their muscular, elastic and supporting structures, as well as their neurological co-ordination, can port similar or specific problems. Also think that the design of the circulating fluid masses corresponds to the integrator need of Nature, which demand a dynamic balance.

The following step could be to think that:

1. The pulmonary respiratory dysfunction could be caused by any of the factors conveying their own dynamics. These are:

1.1 PHYSIC-NATURAL FACTOR: mass of air per volume unit, at the adaptation level of the individual.

1.2 ORGANO-PHYSIC-NATURAL FACTOR: Pulmonary structure and working design.

1.3 NEUROLOGICAL SYSTEM OF INFORMATION AND CONTROL.

2. The working Organism as a “Mechanical System of Fluids”, composed by two hemi systems:

2.1. The cardio-circulatory subsystem, for blood circulation.

2.2 The pulmo-circulatory subsystem for air circulation.

Both hemisystems need to be full of their respective fluids at appropriate physiological pressure-volume, to warrant their systematic cyclic balanced distribution. These pressure-volumes are named total blood volume and total air volume, better said total air volume mass and, each one is a multiple of the volume used by each ventricular beat and by each pulmonary lobule cyclic contraction, similar to cardiac beat.

3. The consequence of a haemorrhage, which is insufficient mass of blood is similar to insufficient mass of air. Mountain sickness as an example.

4. The physical “obstruction” of the airways as similar to physical obstruction of the blood vessels. Aneurysm as similar to bronchiectasis or great spaces formed by dilatation of air spaces.

5. *Arterial hypertension* and its known consequences, similar to *lobular air hypertension* and its potential consequences, which in this context, the *pathogenesis of Pulmonary Emphysema* must be thought of. This must start with a non suspected air hypertension.

The thoracic and abdominal walls constitute an auxiliary functional structure that responds to pulmonary demand, via pulmo-diaphragmatic reflex.

Diaphragm is a displaceable support *to decrease resistance to intrapulmonary air expansion and balance*, in itself as with blood circulation, while also playing an important mechanical role in the balance of abdominal fluids circulation.

Specific problems of the pulmo-circulatory subsystem for air circulation are relative to specific structures of the pulmonary and extra-pulmonary airways and the thoracic ensemble, as well as to other factors contributing to the dynamic integration for Life.

Lobular air hypertension is similar to blood hypertension

Analytical review of some data and research concerned with traditional understanding of pulmonary emphysema

It is now, after more than twenty years of systematic investigation of the *Lung as an autonomous mechanically active organ*, and once concluded the spectrum of the New theory of the Respiratory Function, that I have decided to think about pulmonary pathologies and, start analysing in which sense and why the factors of the equation were altered to produce such consequences. One exception was Mountain sickness, since it resulted obvious.

Nevertheless, I felt deeply concerned with this circumstance because even though I learned so much about Respiration, from the new perspective developed by me, was unable to directly offer help to those that suffer from respiratory insufficiencies.

Therefore, I started this new era with the study and analysis of anatomo-hystological and pathological observations, as well as interpretations and definitions of Pulmonary Emphysema, carried out by Specialists, and concerned Institutions.

In 1822, Reissenen succeeded in the anatomical demonstration of the smooth muscle of the airways. Since then, many researches have been made to try to interpret its role, dominating the belief that this produces “broncho-muscular tone” to influence the diameter of the pulmonary airways” since “it seems that the lungs and air passages should increase their

volume roughly proportional in response to trans pulmonary pressure changes”⁵.

“Enlargement of the cells can not well be supposed to arise from any other cause than the air being not allowed to common free egress from the lungs and therefore accumulating in them. It is not improbable also that this accumulation may sometimes breakdown two or three contiguous cells into one and thereby form a cell of a very large size”.

This is an excellent interpretation for his time, considering the Lung a passive organ and, obstruction to air circulation the most probable cause for air retention, accumulating destructive expansive forces.

In 1838 Laennec⁷ stated:

1. There is a constant association between chronic bronchitis (catarrh) and emphysema.

2. “*Partial bronchial obstruction raises the pressure in the lung* distal to the obstructed bronchus”.

3. “This mechanical increase eventually leads to *destruction of the tissue*”.

This interpretation is similar to that of Baillie, only that Laennec expresses the implicit concept

of: “*the rise of pressure in the lung*” and “obstruction” as the cause.

In 1929 Loeb⁸ made an excellent actualised resume of prevailing concepts on respiration and analyses aetiology and pathogenesis of Emphysema based on those concepts, many of which are accepted up to now. I quote here:

“The most generally accepted and most plausible theory as to the pathogenesis of the emphysema is that of mechanical obstruction to the air current. From the physical standpoint this would be most likely to result in increased expiratory effort, no matter what might be the nature or the location of the obstructing element. Increased difficulty in inspiration, unless of high grade is easily overcome by a commensurate increase in the activity of the muscles of the wall of the chest and the diaphragm; expiration, on the other hand, being normally a passive process with relaxation of the musculature, offers greater difficulties. Moreover, the air passages open during inspiration and collapse during expiration, so that any stenosis is exaggerated during the latter.

... It is also improbable that emphysema can be due to obstruction alone... there is a great amount of clinical evidence pointing to obstruction as an important factor... it appears, however, that if so a concomitant alteration of the finer air passages is essential...as in chronic bronchitis, which present both infection and obstruction”.

These *muscular geographical design and distribution* shows optimal physical conditions for the muscular fibres to displace the contained air and provide mechanical conditions in the alveoli, to expand their walls with optimal force-effect results to warrant Oxygen diffusion in physiological proportion.

In 1958. Pulmonary emphysema was presented at the Ciba Guest Symposium in London (10). It was considered a condition of the lung characterised by *increase*, above the normal, *of the air spaces distal to the terminal bronchiole*, due to *dilatation* or to *destruction* of their walls”.

This is an anatomopathological definition, which

In 1947, Miller⁹ states that the fibres of the airways’ smooth muscles are distributed as a “geodesic network”, and are thicker in relation to the lumen diameter in the bronchioles and alveolar ducts and have “sphincter-like” appearance round the opening to the atria. He also described the rich elastic network in the alveolar walls and its distribution.

also pinpoints the site of the process: *the air spaces distal to the terminal bronchiole* and, introduces the effect “*dilatation*”, which implies a mechanical factor although not precise. Finally, separates with the disjunction “or” another condition that could be or must be a further step: “*destruction*”. Cause and process are not analysed.

In 1960, Carlton and others¹¹ made a three dimensional analysis of the elastic tissue of the Lung, which conforms to those of others. Quotes to Orsos, Sudsuki, Miller and other anatomists who have described the distribution of elastic tissue in the tracheobronchial tree, terminal air spaces, pleura and pulmonary vasculature. Some important concepts are:

“The elastica of the branches of the *pulmonary artery* is preserved down to about a diameter of 50 microns. The small *branches* are regularly accompanied by bronchioles. An elastic residue corresponding to the *bronchial arteries* is not identified. Elastic fibres of the blood vessels appear to be *continuous with those of the parenchyma*, and this in turn, is *continuous with those of the pleura*.

The pulmonary elastic network appears continuous through. The mural elastic structure of the bronchioles consists of prominent “*hoops*” of tissue, which run *obliquely* around the bronchiolar wall. The *alveolar ducts are slightly larger than the smallest bronchioles* and are defined by distinct “*hoops*” of elastic tissue, which themselves mark the mouth of individual alveoli. These ducts seem to end in club like enlargements representing the sacculi alveolar. *The mouths of the alveoli are distinguished by prominent “hoops” of elastic tissue derived from the walls of the duct.* A network of finer elastic fibres represents the alveolar walls.

The elastica of the visceral pleura consists of an *outer and an inner layer* and in accordance with Miller; numerous elastic fibres from the sub pleural alveoli can be traced into the inner pleural layer and thence into the outer pleural layer.

Studies on whole elastic networks and single fibres from other networks have displayed a typical *rubber-like elasticity*”.

These concepts can be complemented with the followings from Write R.R.¹²

The elastic fibres *unite* the bronchi, alveoli, vessels, interlobular septum and pleura *into an elastic continuum*. Each of these structures possesses a rich supply of elastic fibres, which branch and *intermesh*, as previously described by Orsos and Krahl. The majority of the elastic fibres in a large bronchus were longitudinally arranged. Occasional, small fibres were arranged circumferentially and intermeshed with the thick longitudinal fibres. This arrangement extended to the respiratory bronchiole was the longitudinal fibres divided into poorly defined bundles. The circular fibres were abundant in the bronchioles and formed bundles, which interlaced with the longitudinal bundles.

One can start the analysis and interpretation of a working complex mechanical structure, from the study of their final dynamic Resultant; such was my case twenty years ago. One can also start from the standpoint of its design to achieve a final objective. A viewpoint can also be adopted that embraces the two perspectives, but overall, we must start from the belief in the Lung’s own autonomic activity and its source of energy.

I started my work from scratch, with the conviction that the Lung must be an active autonomous organ, the final resultant of which must be detected in its pleural surface. Having obtained the data and graph I started with the study of the general struc-

ture, the performance of which could produce those results.

In 1961 The Ciba definition was modified by a Committee of the World Health Organisation¹³. They deleted the criterion of **dilatation** of airspaces.

I consider this deletion an error, since I believe, from the mechanical point of view, that the **dilatation of air spaces must precede destruction of their walls**, which characterises the advanced stage of Emphysema, not the process.

In 1962. Write R. R.¹² made a three-dimensional study of the anatomic-pathologic damage in emphysema. I quote here some observations:

“Lungs of individuals in the older age groups frequently showed *alterations in the elastic tissue* which were considered to be *associated with aging*” . “The alterations in elastic fibres were *confined to the small respiratory structures* of the lung tissue, i.e., the alveolar ducts and alveoli”.

“A *generalised and uniform reduction in the number and thickness* of the elastic fibres was observed”. “The *ducts and alveolar openings were slightly dilated* apparently as a result of this *atrophy* and attenuation of elastic

fibres". "Deposit of *granular black pigments* were most concentrated in the walls of the respiratory bronchioles, in the alveolar ducts *and along the courses of vessels*". "The elastic tissue commonly exhibited *degenerative alterations consisting of separation, fragmentation or complete absence of fibres*". "A *slight degree of fibrosis* was often associated with these degenerative changes, and frequently there was dilatation and distortion of the affected respiratory bronchioles and the adjoining proximal ends of the alveolar ducts".

One year later, The American Thoracic Society¹⁴ defined Emphysema as "an anatomic alteration of the lung characterised by an **abnormal enlargement** of the air spaces distal to the terminal, non respiratory bronchiole, accompanied by **destructive changes** of the alveolar walls".

This definition, is similar to that of the Ciba Guest Symposium: and only changes the term "dilatation" for *enlargement* and, merely seems to put aside any possible relationship with any dynamic action, focusing the attention on a *destructive* effect caused by a possible pathology in the pulmonary structure and promote interest in investigations in this sphere.

In 1962, Laws and Heard¹⁵ stated "A *reduction in the calibre of the peripheral pulmonary arter-*

ies, often with an increased transradiancy of the background, due to reduction in the vascular bed, were the most reliable radiological signs of emphysema".

I consider this an important observation, from my viewpoint of the emphysema as caused by Sympathetic hyperactivity which implies the bronchiolar and surrounding structures, among which the pulmonary vessels result narrowing their lumen while being distended, with consequences in tissue feeding.

In 1963, The J. Burns Amberson Lecture, presented by Wright G. W and Kleinerman J.¹⁶ at the annual meeting of the National Tuberculosis Association and The American Thoracic Society stated:

"*Speculation*" is a properly chosen term to describe the state of our knowledge of the cause of emphysema. *The injury was of a vasculonecrotic nature*, leading to necrosis and destruction of tissue with faulty repair. The current state of knowledge will not permit any summarisation that is meaningful. Obviously, we do not believe the necessary causal agent of emphysema has been established".

In 1985. The National Heart, Lung, and Blood Institute, Division of Lung Diseases Workshop,. Presented the report entitled The **Definition of Emphysema**, at the Webb-Waring Lung Institute¹⁷.

This report states "This workshop was convened because of a perceived *need to review* the current status of the definition and classification of conditions in humans characterised by *enlargement and destruction of respiratory airspaces*. Some conclusions were:

The emphysema definition of The American Thoracic Society was retained, but with the qualification that *obvious fibrosis should be absent*.

Three anatomic subtypes were described, *based*

on the portions of the acinus involved: a) centri-acinar b) panacinar and c) Distal acinar.

I agree with the concept relative to fibrosis, since this is a consequence of healing of mechanical, inflammatory or infectious injuries. Pure emphysema leads to a long period of distension elongation and break down, of elastic and vascular structures, where the ends of the broken structures retract, making healing impossible.

I disagree with the classification, because as I have reasoned, emphysema is the progressive damage caused to the lobular structure by mechanical hyperactivity. Therefore, the three named subtypes are only three anatomic-pathologic patterns of average moments in the evolution of the very long-term process, which is unique.

In 1990, The New York Academy of Sciences and The American Thoracic Society held a Conference entitled Pulmonary Emphysema: The rationale for Therapeutic Intervention.¹⁸

“This Conference was organised to evaluate whether the database available to the scientific community is sufficiently solid to justify the initiation of presumable expensive clinical trials to test the

efficacy of protease inhibitors in regarding the insidious progression of lung destruction associated with emphysema”.

This is the present orientation that dominates the field of research in the matter, which I believe could lead to important findings, but not to the cause, pathogenesis, treatment and or prevention of Emphysema.

Cause and pathogenesis of the pure pulmonary emphysema and the “chronic cor pulmonale”.

Suggested definition

Pure Pulmonary Emphysema is the chronic, progressive physical weakening and break down of the lobular structures, beginning by the alveoli and respiratory bronchioles, characterised by successive elongation of elastic tissues, dilatation of cavities and rupture of their walls, *caused* by exaggerated lobular cyclic dynamics, *due* to sympathetic adrenergic hyperactivity, leading to respiratory insufficiency and “Chronic Cor Pulmonale”.

Introduction

The anatomic-pathological damage characterising Pulmonary Emphysema has been well studied and discussed, but neither its aetiology nor its pathogenesis is known. Therefore, the analysis and interpretation of its Aetiology and Pathogenesis is my present contribution to the Welfare of Mankind and to Science.

To understand this *pathogenesis* it is necessary to understand the *normal genesis* –Physiology– of the cyclic dynamics carried out by the integrated autonomic structures of the pulmonary lobes and lobules, as made objective in the Resultant of this dynamics on its visceral pleura¹⁻². Therefore, I offer here an updated synthesis, and the invitation to review histological features.

Normal genesis of the respiratory cycles

The organisation and distribution of the fibres of the pulmonary elastic structure, means, from the

dynamic point of view, *distribution of potential lines of forces (vectors)* in the framework, “*skeleton*” of the lobes and their lobules, which because of their elastic condition must be permanently distended from their fixed ends –the tracheobronchial structure on one side and, the walls of the thorax on the other– to enable cyclic retraction-expansion due to applied forces, which is the working method of Organic Nature.

Consequently, to understand how this structure works, one must “dress” it with its muscular network, since the named structure, like our osseous skeleton works thanks to forces developed by the muscles inserted on it.

The smooth muscular tissue is specialised in generating visceral cyclic mechanical forces and, the muscles of the pulmonary airways are not the exception, although this reality has not been understood and is attributed only with a role in “pulmo-

nary tone to influence the diameter of the pulmonary airways” since “it seems that the lungs and air passages should increase their volume roughly proportional in response to transpulmonary pressure changes”⁵.

Each pulmonary lobule and all together as a unit, *must perform its work* in identical and simultaneous manner. Therefore, its structure must be uniform, in order to generate similar forces and effects. They must obey a common autonomic command, which *I have proved is the Sympathetic-Adrenergic System*, working on basal effects of the Vagus nerve on the bronchial tree, for air renovation.

When the fibres of the Reissesen muscles, distributed as a “geodesic network” contract, they *diminish the airways diameter and length*, decreasing their capacity by the sum of both effects, while at the same time the elastic structures retract. These effects are valid for both *lobar bronchi* and *lobular bronchioles*, although under their specific nervous control –Vagus and Sympathetic– for integrated actions and results.

When the airways retract, they pull the visceral pleura, increasing the pleural lumen, hence, also decreasing the intra-pleural pressure (Boyle Mariotte Principle).

The objective of the *bronchiolar* muscle contraction is to *pressurise* the contained air with the force needed to *eject* and *distribute the air* among the respiratory bronchioles and their alveoli, while opening ways for the alveolo-capillary blood circulation, while sphincters in the alveolar duct close

the alveoli, to favour local expansion of the inner molecules of gases, by which the alveolar membrane become distended at the physiological measure needed to enable physical diffusion of Oxygen and circulation of the capillary blood.

The following muscular relaxation diminishes resistance of the alveolar ducts and bronchioles, to favour alveolar air return and, with it, parallel retraction of the elastic structure, which helps the displacement of the air towards the trachea, while returning to its resting conditions.

Physio-pathological genesis of pure emphysema

The muscles of the airways dispose of potential capacity for generating forces superior to average physiological cyclic organic demands, like the Heart. *Here rests the causal condition for potential generation of “pure” Pulmonary Emphysema*, which is a *pure* mechanical process.

The exaggerated cyclic dynamics of the lobular the finest structures and joined vessels, which repeated throughout the time results in successive and permanent elongation, followed by break-down, and parallel consequent dilatation of air spaces and further mechanical destruction of their walls and consequent retention of air into the now enlarged cavities.

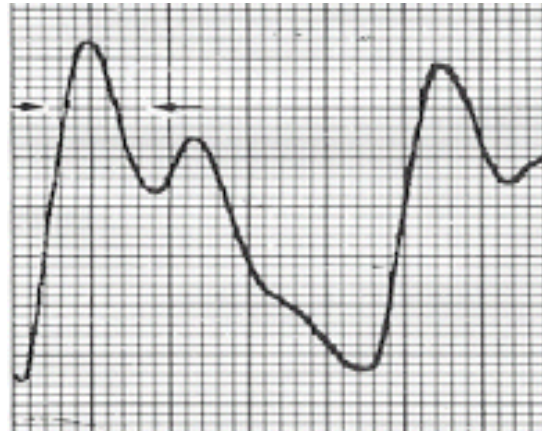
A similar process occurring in the bronchial vessels alters tissue feeding, adding a factor that leads to their destruction.

Emphysema is the consequence of a long lasting systematic increase in intensity and rhythm of the lobular cyclic dynamics, accumulated during years.

To understand this process well, in our contemporary time and evolution of knowledge, it is necessary to know the **Respiratory Pulse** and its interpretation as the *Resultant* of the mechanics described by myself¹⁻²⁻³⁻⁴.

Why has it been so difficult to understand the importance of this evidence?

The answer is given by the history and evolution of the concerned traditional theory not yet well renewed.



Close up of the first graph in history of the Respiratory Pulse

Nevertheless, the light of reason for a better understanding of the matter has arrived.

Today, scientific and logical reflection on the matter is unavoidable, since from this depends a better comprehension of the respiratory functions and pulmonary mechanics to achieve respiration and also to better assess physical damage and insufficiencies like Emphysema, and further more, to prevent or to stop progression of certain damage.

Let me start now with the explanation of the *how and why* of this destructive process, from the perspective of the Lung as an active autonomic organ. I will begin with the named “ageing emphysema”

and will follow the anatomopathological observations generally accepted.

From my perspective, one can infer from this scheme, attributed to the factor age, *that a progressive cyclic weakening* of the elastic structure is produced, which is followed by elongation and breakdown of structural elements. These results represent a half way stage in the evolution of the anatomic damage. Therefore, we must bear in mind that this is a process, a continuum, which must show different pathological degrees in each moment of life and, you yourself could mentally follow its progress up to the point where gas exchange is no longer possible.

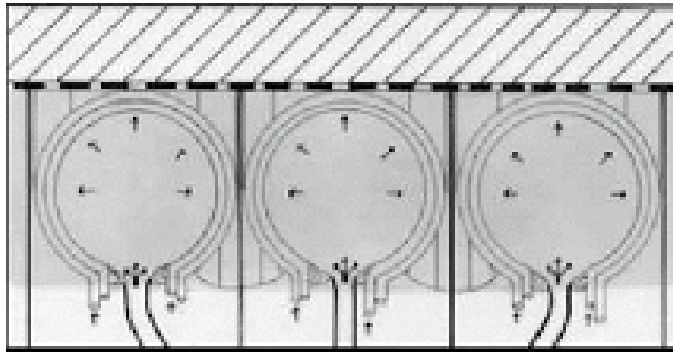
Neither its pathogenesis nor its aetiology is known up to now. Therefore, the nature of the problem has not been well understood.

To start with my interpretation, I would like to express *doubt* that this pathological process, attributed to “ageing”, is caused by the proper physiological function, working between physiological limits, during a long-lasting life.

It is my understanding that the functional design and structure of the vital organs, in any healthy born individual, is programmed to endure, with efficacy, during the vital period of life of each species. I must

also emphasise here that living beings are functionally integrated to their ecosystems, *which also must be healthy*.

In this context, the causal factor of Emphysema can be *organic disorders* involving hyperactivity of the Autonomic Nervous System, or certain Sympathetic-Adrenergic mimetic drugs voluntarily inhale or that could be present in the environment.



Scheme of three alveoli with their capillaries, distended by expansive forces of the contained molecules of gases. The vertical lines represent inter-alveolar walls. The bold segmented line represents the pleural space. The inclined lines represent the corresponding wall of the thorax

*Therefore, I firmly believe that the “ageing” emphysema, in a supposed healthy organism, must have an associated factor of low or medium intensity and, to mention only one probability, I point out minor **cigarette consumption and/or contamination with cigarette smoke**.*

It is necessary to make clear at this point that Adrenaline is not a “bronchodilator” as believed, on the contrary, it increases the rhythm and intensity of the bronchiolar dynamics, as I have experimentally demonstrated³.

The process

It is known that the smooth muscles in the bronchioles and alveolar ducts are thicker than those in the bronchi, relative to the lumen diameter. Therefore, we can expect correlative effects from their potential increase in contraction forces and derived actions. Muscles round the openings of the alveolar ducts are real sphincters, with an important commitment.

I have proved that these muscular networks and sphincters in the lobules are responsible for performing contraction-relaxation with rhythm and intensity relative to sympathetic nerve discharges. This muscular contraction displaces the contained

air up to the respiratory bronchioles and their alveoli, followed by its return at the beginning of the muscles relaxation.

The role of the sphincters in the ducts is to momentarily retain the air in the alveoli, in order to favour its molecular expansion and hence the distension of the alveolar membrane up to the point of balancing the capillary blood pressure. This pressure balance is determinant for Oxygen diffusion and capillary blood displacement towards the pulmonary veins.

Muscular relaxation allows the displacement of the used alveolar air toward regions of lesser pressure, the main bronchi and trachea and, with it, elastic retraction of the structure, which is a simultaneous factor to accelerate the air expulsion. In synthesis:

The bronchiolar muscle responds to Sympathetic nerve discharge and its cyclic contraction-relaxation is the cause of the normal or abnormal dynamic results at the alveoli and nearest structures, with relative consequences.

The final task of the described lobular dynamics is to regulate the tiny masses of air displaced up to the alveoli and, supply conditions for their programmed expansion, thus distending the alveolo-capillary membranes, in balance with the capillary blood pressure.

Increased dynamics augment alveolar distension, which can surpass physiological limits of resistance. Consequently, these structures can become *strongly distended* by each hyperactive dynamic cycle and, *if the process is systematically repeated time and again*, causes successive hyper-distension with progressive loss of elasticity, becoming more and more elongated. Hence, *cavities result dilated* and *rupture* follows.

Hyper-distension of the lobular structures also causes hyper-distension of the outer structures, comprised in the elastic structural framework, such as bronchial and pulmonary vessels, with parallel consequences.

It is easy to understand that dynamic elongation of blood vessels reduce their lumen. This also diminishes tissue feeding, which results in another fac-

tor that lowers its resistance and this leads to rupture, with little haemorrhage, the cause of the pigments found along the site of the vessels.

Similar distension of the capillary network reduces the capillary lumen, with immediate consequences in gas exchange as well as in pulmonary blood circulation, with local and retrograde effects, leading to *Chronic Cor Pulmonale*.

This process, repeated year after year, leads to breakdown in the concerned elastic structures and later on to destruction of alveolar walls, among other parallel effects in the total lobular structure, which characterises the anatomopathology of the advanced stage of emphysema that is known as Pan-lobular Emphysema.

The reason for relative absence of fibrosis is because *emphysema is a pure physical, mechanical process*, with little transient inflammatory effect, without infectious factors, in which the systematic thinning of the structural fibres leads to rupture with elastic retraction of their ends, without the hope of possible repair.

Concerning the matter of classification, it is easy to understand that subjects that die because of emphysema, carry the most advanced stage of destruc-

tion, that is known as “panlobulillar” or “destructive” emphysema, while individuals with non symptomatic emphysema who die from any other pathology or because of accidents in which, emphysema is discovered by autopsy, present degrees of lower evolution, localised to respiratory air-spaces, mainly the alveoli, which are weaker structures and also, those that receive the impact of the expansive molecular forces, as cull de sacs, cyclically closed, where the anatomic damage must be initiated.

The molecular expansive forces of the air previously ejected to pressure into the alveoli, is the final force that acting systematically during years, produce the accumulative and extensive structural damage characterising the emphysema in its different stages.

The pathogenesis of Pulmonary Emphysema is a long lasting process, non symptomatic while the compensatory potential capacity of the Respiratory System balances the effects of this degenerative process. The logical clinical consequences of this

process are air retention. Impairment of breathing. Imbalance in gas exchange. Imbalance in pulmonary blood circulation, with retrograde effects leading to *Chronic Cor Pulmonale*. Imbalance in homeostasis and death.

In synthesis

Emphysema only has one primary or direct cause: Dynamic hyperactivity of the bronchiolar smooth muscles. This hyperactivity also has one cause: Increase in intensity and rhythm of the Sympathetic nerve discharge, of organic origin or produced by action of adrenergic positive mimetic drugs.

Observations on social habits and their statistical analysis has enabled isolation of Pure Emphysema from other associated pathologies, such as chronic bronchitis or asthma, while deriving attention to its relationship with the habit of cigarette smoking.

Clinical and statistical observations coincide on the fact that Pulmonary Emphysema is correlative to the habit of cigarette smoking, to the number of

cigarettes consumed every day and to the number of years smoking. These observations have led to single out cigarette smoking as a “risk factor”.

This benevolence in classifying cigarette smoking as a simple “risk factor” implicitly convey lack of understanding of the real respiratory mechanics achieved by the Lung, as I have demonstrated and interpreted apart.

Nicotine is a causal factor of pure emphysema and “chronic cor pulmonale”

Let’s think about the Nicotine contained in each cigarette and, bear in mind that Nicotine is pharmacologically well known as a potent *Adrenergic-positive mimetic drug*. Let’s also think about the optimal conditions created by the cigarette smoking habit, to generate continuous undesirable actions and effects.

Add to the many millions of smokers the even greater number of “passive smokers”, who simply inhale the environmental smoke containing Nicotine in suspension. And also consider that active smokers are also passive smokers and realise that they are “permanent smokers”.

Nicotine is consumed everywhere by every body

every day of life, thus making this drug responsible for Pure Pulmonary Emphysema, in non symptomatic individuals equally as in those with the advanced disease. In both cases related to the amount of Nicotine consumption.

Add to this that the dynamics performed by the respiratory structure of the Lung (The lobules) and the Heart, are under Sympathetic Adrenergic control and that for the same reason the Heart is directly affected by Nicotine.

Furthermore, blood circulation throughout the very great surface of the alveolo-capillary units is *mechanically controlled by the lobular dynamics*, working as *presses and floodgates*² and you will

realise that the pathogenesis of Pulmonary Emphysema and the pathogenesis of the Chronic Cor Pulmonale is a result of the same process. Therefore, cigarette smoking can clearly be seen as a cause of both morbid processes.

This dramatic conclusion must call to conscience and focus attention on absolute prevention for those

not yet initiated and to beginners. Prevention of further damage in those with long lasting habit and, prevention of environmental contamination, since healthy air is a condition of everybody's health.

To better illustrate the damaging role of cigarette smoking I quote here some pharmacological concepts¹⁹ (Translation and underlines are mine).

“When one cigarette is smoked in one standard machine, the real content of nicotine of tobacco can vary from 02 to 05 % for smoking tobaccos. It is present in ionic manner in nearly all the tobaccos for cigarettes. Due to a more alkaline pH, exist in a non-proton way for easier absorption in cigars and pipe tobacco.

Smoking one or two cigarettes, a significant increase in plasmatic concentrations of noradrenaline and adrenaline is produced.

Nicotine of cigarette smoke suspended on minute particles of tar is easily absorbed in the lung, with nearly the same efficacy as intravenous administration. The medium life of elimination of nicotine is of 30 to 60 minutes. In this manner, the plasmatic concentrations are somewhat larger for the average smoker, at the end of the day”.

“The respiratory excitation is a prominent action. Small doses act in a reflex way, by excitation of carotid and aortic chemoreceptors. (Heymans and collaborators 1931).

The cardiovascular response is due to stimulation of the suprarenal jointly with discharge of catecholamines from the sympathetic nerve ends and cromafin tissues (Gebber 1969)”medulla sympathetic ganglia has a prominent action. Small doses act in reflex way”.

It is easy to understand why this interpretation of pharmacological action of Nicotine on respiration is limited to the concept “respiratory excitation is a prominent action” without any further explanation, since it is not able for the authors to say more than that, due to their lack of knowledge of the dynamics of the Lung, as

long as it is considered a passive organ.

The resultant mechanical damage of the pulmonary structure is irreversible.

To give up the habit of smoking means to stop the progression of anatomic-pathologic damage. That alone is worth enough.

Cigarette smoking is a cause of Emphysema, due to the Nicotine content in tobacco, and is the cause of the increased morbidity and mortality of the destructive pulmonary emphysema.

Cigarette smoking is also cause of Chronic Cor Pulmonale
Prevention of both, based on contemporary scientific knowledge is now possible, more than that, it is a social commitment.

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