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THE PHYSIO-PATHOLOGY OF STATUS ASTHMATICUS

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The asthmatic crisis can be produced by various agents—(inhalants, foods, infections, meteorological conditions, etc.) acting alone or in association with another. When the asthmatic crisis is prolonged or severe enough we call this crisis: status asthmaticus.

Whether there is spasm of the smooth muscles of the bronchioles or edema of the bronchiole mucosa is a question not yet settled notwithstanding numerous discussions concerning the subject. Either of them: edema or spasm would be the result of a series of reactions, with liberation of histamine or a histamine-like substance, the different phases of which, however, are not well-known. It seems to us that the theory of the mucosal edema of the bronchiole, with spasm of smooth muscles as a subsequent factor, is more in accordance with the clinical observation.

The report of Warren and Dixon (1) based on experimental studies, strongly supports the edema theory. They determined anaphylactic shock in guinea-pigs, using an antigen traced by radioactive iodine and were able to demonstrate the antigen fixation in the edematous fibrous tissue of the bronchioles. It should be pointed out that they also observed spasm in the initial phase of shock, but at that moment the edema was already present.

In a general way, we may consider the following pathogenic conception of asthma:

(1) spasm of the bronchiole muscle, supported among others by Laennec, Biermer, Trousseau, Paul Bert and F. Franck; (2) diaphragmatic spasm (Wintrich and Bamberg); (3) combined action of a mucous plug and nervous asthma (*asthma convulsivum*) as was first admitted by Willis. The origin of the mucous plug was traced to a hypersecretion of the bronchiole glands by Steinberger; (4) a special type of neurosis of the exudative variety (Traube, Weber, Bretonneau). In the same line of thought is the conception of Strumpel, who speaks of *urticaria bronchica* when referring to asthma (2).

The discussion has mainly been concerned with the theory of muscular spasm of the bronchioles. Cooke, Walzer, Jimenez Diaz, Unger and others accept the edema theory held by most modern authors. A careful analysis of each of the theories mentioned above will show that the authors have analysed only part of the problem, giving an extreme and exclusive value to their observations and having disregarded the problem as a whole; as a result of such policy a great number of pathogenic interpretations of asthma have appeared in the literature, but very little has been done for the elucidation of the real pathogenesis of the asthmatic crisis.

How can we explain the different phenomena observed in the status asthmaticus?

The dyspnea mainly expiratory in the beginning of the crisis but may become inspiratory and expiratory at more advanced stages. It is a well-known fact that inspiration is made easier by the intervention of accessory inspiratory muscles. Expiration, on the other hand, is accomplished with extreme difficulty. The elements that habitually come into action in expiration, such as pulmonary elasticity, elastic tension of ribs and cartilages, intra-abdominal pressure and so on, are not enough to overcome the obstacles to expiration that are found in asthma. That is why other elements which normally do not interfere in respiratory dynamics become active, such

as the following muscles: muscles of abdominal wall, *m. serratus*, *m. ileo-costalis lumborum*, *m. intercostalis interni* and the *m. triangularis sterni*.

The flow of air through the narrow passages and the presence of thick, tenacious mucus are responsible for the production of wheezing respiration. There are cases where nothing can be heard on auscultation; in such cases the thorax is extremely inflated with air—the thorax is in maximum inspiration—the dyspnea being extremely severe, which bespeaks the serious hindrance of the normal aeration of the lungs (3).

The vital capacity of an asthmatic patient during the crisis, more especially in the status asthmaticus, is extremely reduced. The following alterations are observed:

(1) increased residual air; (2) reduction of tidal air; (3) absence of complemental and implemental air. The fact is easily understandable if we realize that the patient is making the deepest inspiration he can, the same being true in expiration (4).

To overcome the crisis various mechanisms are used. The inspirations are made deeper and deeper and the respiratory frequency is diminished. The respiratory exchanges are altered; there is an increase in the alveolar CO_2 and a reduction in O_2 tension. The greater tension in the alveolar CO_2 determines greater stimulation of the respiratory bulbar centre while the reduction of CO_2 has the opposite effect. The reduction of the O_2 alveolar tension and the fall of the capacity oxygenation of hemoglobin are responsible for the increased amount of reduced hemoglobin in the capillaries. When the amount of reduced hemoglobin is 5 g. per 100 cc. of capillary blood cyanosis may appear.

The variation of the CO_2 tension will be responsible for the changes in the respiratory activity either increasing or decreasing this activity and as a consequence maintaining the ionic balance of carbon dioxide in the respiratory centre.

The chemical stimulation of the nervous centre results in hyperventilation and hypocapnia. A state of gaseous alkalosis is gradually established. If the status asthmaticus does not

subside, but on the contrary is aggravated or prolonged, the carbon dioxide is not eliminated and its concentration is increased, and we pass from hypocapnia to hypercapnia, and as a result the dyspnea which was predominantly expiratory becomes inspiratory and expiratory. We also observed that the bradypnea as replaced by tachypnea. The gaseous alkalosis is followed by gaseous acidosis. In this instance the urine is highly acid.

From a clinical point of view we observed a positive expiratory hyperpressure and a negative inspiratory hyperpressure. As a consequence of the latter we observed the aspiration of the structure of the base of the neck.

It is not enough to characterise the status asthmaticus in its severe form and describe its various aspects as we have done. It is necessary to remind of the fact that Hilding (5) in 1934 demonstrated the importance of the ciliary insufficiency which is responsible for the lack of drainage of the thick, tenacious mucus which adheres to the walls of the bronchi, constituting a real mucous plug, which is not rarely the cause of death in these patients.

In 1946, Jacobs demonstrated that in the fatal cases of asthma a greater number of goblet cells and extreme damage of ciliae were found and these alterations should be traced mostly to recurrent infection. In our opinion the indiscriminated use of epinephrin nebulizations, specially when self-prescribed, is one of the contributing causes of damages to the ciliae; in the beginning the drug is quite effective.—Two or three pumpings prevent the crisis and the patient counting on his "pump", neglects his treatment. But the asthmatic process advances regardless of his false impression of improvement. The patient will soon spend hours "pumping" without relief. This is the explanation of severe circulatory disturbance which calls for emergency treatment. So, we think, with Benson and Perlman (1948) (6) that not only infection but also this wild self-medication injures the ciliary epithelium.

In 1947, Mack et al. (7) showed how dyspnea is in-

fluenced by pulmonary congestion. Pulmonary congestion diminished pulmonary contribution to increase of the respiratory obstacle. In the fatal cases of asthma this congestion was a constant factor, which must be considered in the physiopathology of status asthmaticus.

In asthma and in its most severe aspect—status asthmaticus—there are a high venous pressure and sometimes also arterial hypertension. In Brazil, di Piero (8) has studied the venous pressure in asthmaticus patients without emphysema and without heart failure, observing alteration in the normal value, ranging from 1.5 to 6.4 cms water (normal values from 10 to 14 cms water) above the higher normal levels. Di Piero also observed that after the crisis the venous pressure returns to normal at a rate proportional to the amount of right heart involvement. This venous hypertension would be the result of the alteration of intrathoracic pressure determined by the distended lungs in forced inspiration. Another factor to be considered is the venous hypertension in the right heart arteries caused by permanent pulmonary distention. We observed in one of our young patients an increase in the arterial tension during the crisis, from 100×70 to 220×140 , two hours after the first arterial pressure determination, despite the fact that no ephedrine or adrenalin was used.

The faulty oxygenation and biochemical changes resulting from hypoxemia is compensated by an increased work of the heart, which beats more rapidly (increased minute volume); giving thereby to the organism its due oxygen supply.

As the hypoxemia progresses the consciousness becomes dull and cyanosis becomes apparent. Significant changes such as hyperglobulia and hyperhemoglobinemia are readily verified. The former could be explained by the contraction of the blood venous lakes which increases the circulating blood volume. On the other hand we might say that it results from a severe loss of fluid and passage of plasma to the tissues through a vasocapillary reaction (plasmorrhagy as Alvaro de Bastos says (9)) with the characteristics of a serous inflammation (Pescador) (10). Eppinger has already pointed

out the close resemblance between acapnia, vaso-motor failure and serous inflammation.

If we take an X-ray picture of the chest of an asthmatic patient during the crisis, we shall see that the pulmonary area is clearer, the diaphragm lower and the hilar portions dense, which means circulatory stasis; atelectatic areas can also be detected.

One of our asthmatic patients has undergone a bronchoscopy and we have seen the following picture: "normal trachea, sharp limit of the carina, which was vertical and freely movable. Congested mucosa of main bronchi with sticky, white secretion. Secondary bronchi partially closed by the same white and adherent secretion. Mucosa of the bronchial tree congested and distinct reduction of the lumen of the secondary bronchi. Cough with poor expelling power" (11). This mucus, cause of not a few deaths, will result in Curshmann's spirals under the action of perpendicular expelling forces. These spirals are composed in their centres by refracting fibrils and adhere to the bronchial wall through its outer layer. The expelling forces acting in one direction and perpendicular forces acting in the periphery, where the mucus adheres to the bronchiole wall, create a circular movement around the central part and is responsible for the spiral form (3).

From the pathological point of view the following alterations have been verified in cases submitted to post-mortem examination: (1) bilateral pulmonary emphysema; (2) hypertrophy of bronchial muscles; (3) areas of atelectasis; (4) extraordinary infiltration of eosinophiles; (5) thickening and hyalinization of the basal membrane of the bronchi; (6) mucus in the lumen of the bronchi; (7) dilatation of bronchioles and alveoli.

Cordier and Croizat (12) among others attach great importance to the mucous transformation of the elements of the bronchial epithelium which become goblets. These French authors say: "Les grandes bronchiques, normalement sereuses, participent à cette hypercrine muqueuse; elles réalisent

au plus haut degré l'aspect mucipare décrit par Renault au cours des états d'inflammation chronique." In a recent paper Hilding (13) stresses the importance of the fact, stating: "This may have a profound and dangerous affect upon the patients."

It is well to remember the mechanism of mucous expulsion and the mechanism of bronchial secretion. The following factors are considered as responsible for the elimination of mucus: (1) the ciliary mechanism, whose importance is capital, as Policard and Galy (14) have pointed out; in the presence of a too heavy and thick mucus the ciliary mechanism may be insufficient; (2) the cough mechanism; (3) the peristaltic movement whose existence is controvertial. The ciliary epithelium may undergo a metamorphosis and be replaced by goblet cells. Of 31 fatal cases of asthma Hilding (13) found 12 in which the cause of death can without any question be solely attributed to asthma. In these cases he found a great increase in the goblet cells which lined as much as 100 % of certain areas. He also observed that these goblet cells showed mucous hypercrinia to a point where the cells could not completely eliminate the secretion material which obstructed the lumen. A vicious circle is thus established: transformations of the ciliary epithelium into mucous cells → hypercrinia → cough entertaining hypersecretion mucous → harbouring in the lumen of goblets cells → difficulty of expectoration → adhesion of bronchial walls to the mucus during expiration. When this stage is reached, the case becomes very severe and death will not be surprising if there is no elimination of the plug by mechanical aspiration.

The origin of the eosinophils found in the lung has been much discussed. A local genesis has been maintained and one of the supporters of this view has written: "*infiltration composée des cellules à granulation éosinophiles, cellules nées sur place le plus souvent, car les vaisseaux congestifs ne contiennent souvent pas une proportion anormale de leucocytes oxyphiles.*" The medullar origin of the eosinophilia has had the strong support of the majority of authors. They believe that

the local eosinophilia is very rare if it exists at all. This point of view is in accordance with the knowledge that local eosinophilia is a consequence of the mobilization of the eosinophiles from the bone marrow.

Castex (15) in a lecture delivered at the Academia Nacional de Medicina of Buenos Aires, mentioned that he had found eosinophiles in the urinary sediment of asthmatic patients after an acute crisis of asthma.

The status asthmaticus may end in one of the following ways: (1) spontaneous remission; (2) remission by the action of drug therapy; (3) intercurrent infection, pneumonia, etc.; (4) death (asphyxia, exhaustion, circulatory crisis, infection, etc.).

It is of importance to emphasize that the use of certain drugs may aggravate a condition already very severe. This is the case of morphine and opium derivatives, atropine, demerol, and even oxygen when not suitably wet.

REFERENCES

- (1) *Warren, Shields & Dixon, Frank J.*: Antigen tracer studies and histologic observations in anaphylactic shock in guinea pigs. *Am. J. Med. Sc.* 216: 136, Aug. 1948.
- (2) *Cruciani, Julio A. & Etchemayt, Pedro & Cavlin, A.*: Autopsia de una asmatica morta in crisis. *La Prensa Médica* 28 (4): 247, Jan. 22, 1941.
- (3) *Jimenez Diaz, C.*: Lecciones de Patología Médica. Vol. 1, ed. 4ft. Ed. Científica Médica. Barcelona, Madrid, 1947.
- (4) *Best, Charles H. & Taylor, Norman S.*: As bases fisiologicas da pratica médica. Vol. 1. A Casa do Livro Ed. Rio, 1942.
- (5) *Hilding, A. C.*: The relation of ciliary insufficiency to death from asthma and other respiratory diseases. *Ann. Otol. Rhin. Laryng.* 52 (1): 5, March 1943.
- (6) *Benson, R. L. & Perlman, F.*: Clinical effects of epinephrine by inhalation. *J. All.* 19 (2): 129, March 1948.
- (7) *Mach, I. & Grossman, M. & Katz, L. N.*: The effects of pulmonary vascular congestion on the distensibility of the lungs. *Am. J. Phys.* 150 (4): 654, Oct. 1947.
- (8) *Di Piero, Fioravanti*: Sistema Venoso. Flores & Mano Ed. Rio, 1934.

- (9) *Bastos, Alvaro de*: Morte por asma - síntese patogénica. Folha Médica ano XXX, numero especial de Alergia, pag. 30, May 15, 1949.
- (10) *Pescador, L.*: Medicina aeronáutica. El vuelo de alta cota. Tomo I. Editorial Científico Médica. Barcelona, Madrid, 1941.
- (11) *Dias Da Costa, Paulo, Guimarães, J. C. & Vianna, Theobaldo*: Estado de mal asmático, Medidas terapêuticas práticas. Oportunidade da broncoscopia. Med. Cir. Farm. 152:737, Dez. 1948.
- (12) *Cordier, V. & Croizat, P.*: Crise d'asthma mortelle avec autopsis. Soc. Méd. des Hôp. de Lyon 11-1-36, pag. 225.
- (13) *Hilding, A. C.*: The respiratory epithelium as a vital organ and some pathological changes in it due to common diseases. Acta Oto-Laryng. Vol. XXXVII, fasc. 2, pag. 138 (reprint).
- (14) *Policard, A. & Galy, P.*: Les bronches. Structures et mechanism a l'état normal et pathologique. Masson et Cie. Paris 1945.
- (15) *Castex, Mariano R.*: Las manifestaciones alérgicas del aparato urinario. Bol. Acad. Nac. Med. Bs. Aires. 54:406, Julio 1939.

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