Air Pollution Impact: Modeling, Simulation and System Identification of the Human Respiratory System

Bernhard Quatember, University of Innsbruck, Institut für Informatik,
Technikerstraße 25, A-6020 Innsbruck, Austria

Abstract It is necessary to investigate the health effects of ambient air pollution. Population studies of the damage caused by air pollution have to be carried out. In these studies, the initial stages in the development of chronic bronchitis play a decisive role. However, these initial stages cannot be assessed appropriately by using the parameters obtained by performing classical lung function tests. We developed a simulation model that allows us to perform thorough investigations of the effects of the pathological changes in these initial stages on breathing mechanics. We will focus on the lining of the small airways with a layer of secretion (mucus). The simulation results which will be presented show the consequences of this pathophysiological manifestation. We will propose a parameter identification procedure which permits an assessment of the severity of these pathophysiological changes. This method can be used in population studies and will allow a better evaluation of the health effects of airborne contaminants.

1. INTRODUCTION

The inspired polluted air carries harmful substances into the body, causing a serious health risk. The airborne contaminants lead very often to an impairment of the lung function. Although the health effects of the airborne contaminants are not always confined to the respiratory tract, the possible development of lung diseases will be the focus of our attention. Almost all industrialized countries have become concerned with the effect of ambient air pollution (particulate matter, sulfur oxides, ozone, nitrogen dioxide etc.) on the development of chronic obstructive lung disease, especially chronic bronchitis. Several population studies have apparently confirmed the opinion that the development of chronic bronchitis is related to the air-pollution level of the environment.

Population studies of the possible damage caused by ambient air pollution are complicated and it is particularly difficult to obtain reliable results. Nevertheless, reliable data are urgently needed. For instance, legislators insist on proof of effect as a basis for legal definitions of acceptable air quality. Acceptable air-quality standards as well measures to improve the air quality should not be based solely on a simple proof of respiratory morbidity. The population studies should be based on a more thorough investigation, not confined to the advanced stages of the chronic bronchitis, but rather include and concentrate on the development of the disease. Hence, the progression of the disease must be determined by carrying out a sequence of pulmonary function tests. In all the contemporary population studies of this kind, as for instance those described by Detels et. al., [1991] and by Schwartz [1989], the deterioration of the respiratory function is assessed by using classical pulmonary function test data, as total airway resistance and FEV1. However, we are able to show in the following that these parameters are not ideally suited to describe the variation of the patient's state over time.

In the following, we will focus on an improved method of assessing the development of a chronic bronchitis caused by ambient air pollution. The characteristic manifestation of this disease is excessive secretion (mucus) in the small airways. We developed a special simulation model of the human respiratory system and carried out a series of simulation experiments for varying quantities of secretion (mucus) accumulated in the small airways. We introduced a specific parameter to describe the extent of such a layer of mucus and thus the severity of pathological changes in the development of a chronic bronchitis. This parameter is essentially better suited to assess the impact of ambient air pollution than the classical lung function data, as total airway resistance and FEV1, used in contemporary investigations.

2. AIR POLLUTION AND LONG-TERM CHANGES IN LUNG FUNCTION

In the following, we will concentrate on the development of a chronic bronchitis solely caused by air pollution. Hence, we will exclude smokers and persons that already suffer from lung diseases, since those persons my have different sensitivities to air pollution.

2.1 Development of Chronic Bronchitis Caused by Air Pollution

The initial stages of lung damage caused by air pollution are characterized by inflammatory and obstructive changes in the peripheral airways. Especially in the small airways,

resulting in the development of a chronic bronchitis. A persistently increased secretion of mucus takes place, lining the airways and eventually causing chronic cough and recurrent expectoration. This lining of the airways, especially the small airways, with secretion (mucus) in the development of chronic bronchitis leads in more advanced stages to a progressive airways obstruction which can be recognized by a decline in lung function test parameters. Further remarks on the progression of the disease can be found in the descriptions of an expert system for chronic pulmonary disease of Jahn [1990] and Quatember[1990].

In the development of a chronic bronchitis, the assessment of long-term pathological changes is very difficult. This is particularly true for the initial stages. We have to realize that the peripheral airway (small airways) have an enormous functional reserve. This is clearly pointed out by Pride [1990]. The pathological changes in the initial stages may cause few symptoms and negligible decline of the parameters in classical tests of the overall lung function, such as total airway resistance and FEV1. The development of chronic bronchitis is thus characterized by an insidious course of chronic airways obstruction. Initially, even considerable pathological changes (lining of the airways with secretion) will not become evident over a long period of time. However, further changes my then lead to progressive airway obstruction. For studying the health effects of air pollution, the investigation of the pathological changes in the initial (pre-clinical) stages of the development of a chronic bronchitis plays a decisive role. For further details we refer to the descriptions of Gardner [1994], Hongg [1990], and Schwartz [1994].

2.2 Assessment of Pathological Changes in the Development of Chronic Bronchitis

In population studies of the development of chronic bronchitis caused by air pollution, the initial (pre-clinical) stages are, as already mentioned above, by far more important than the established disease.

With conventional lung function test procedures, as for instance described by Hoppin [1991], Laszlo [1994], and Ulmer et. al., [1991], the reduction in cross-sectional area of the small airways in the pre-clinical stage cannot be reliably detected. In very early stages, these pathological changes cannot be detected at all. Typical lung function test parameters that are frequently used in population studies are, as already mentioned above,

(a) the total airway resistance measured by whole body plethysmography and

(b) the parameter FEV1 which is measured with a spirometer; it is the volume expired in the first 1 second interval of forced expiration.

The total airway resistance is a single parameter that is used to indicate the degree of obstruction. It is determined on the basis of pressure-flow loops measured with a whole body plethysmograph. With this single value, the flow during the whole inspiration phase and expiration phase is described. In the normal respiratory system (physiological conditions), the small airways do not contribute significantly to the total airway resistance. This is still true in the case of small to moderate reductions in cross-sectional lumen areas of the small airways caused by lining with secretion (mucus) as this is the case in the initial stages of development of chronic bronchitis. Therefore, the total airway resistance cannot be used to describe the progression of the disease in the initial stages. For the same reasons, the parameter FEV1 is not suited to identify the pathological changes in these initial stages of a chronic bronchitis. Hence, we need other lung function test procedures that are sensitive to minor pathological changes in the small airways. The single breath N_2 test has been proposed in the literature. However, Pride [1990] pointed out that its value was not as strong as originally hoped.

In the following we will propose another method for the evaluation of the pathological changes in the small airways.

2.3 Basic Characteristics of the Proposed Method

The total airway resistance which is obtained in classical lung function tests is based on the idea that the airway resistance remains constant during breathing. However, the resistance to flow in the tracheobronchial tree will change in the course of breathing. The small to moderate reduction in cross-sectional lumen areas by the lining with secretion (layer of mucus) in the initial stages of chronic bronchitis will only increase the resistance significantly at the end of the expiration phase and the begin of the inspiration phase, but during the main part of the respiration cycle the reductions in lumen cross-sectionals areas of the small airways will have almost no influence on the resistance to flow. The proposed method is based on a newly-developed very detailed simulation model of the tracheobronchial tree. At this stage of development, the simulation model allows us to evaluate the change of flow patterns in the tracheobronchial tree caused by the lining of the small airways with secretion (mucus). More specifically, the model allows us to perform such investigations in the case of varying reductions in cross-sectional lumen areas of the small airways caused by the lining with secretion (mucus). In doing so, we are able to assess the above-mentioned significant influence of the narrowing of the luminal areas on the resistance to flow at the end of the expiration phase and the begin of the inspiration phase. This influence is represented by the specific shape of the pressure-flow loop. The pressure-flow loops obtained by individual simulation runs can be compared with the pressure-flow loops of a person measured with a whole body plethysmograph. These comparisons allow already a coarse assessment of the reductions in cross-sectional lumen areas. More accurate results can be obtained by applying the formal method of parameter identification. However, at this stage of development the applicability of our simulation model is still limited, since we are not yet able to consider the pathophysiological changes of the dimensions and mechanical properties of the walls of the bronchi and bronchioles.

In the following, the new simulation model will be described and it will be pointed out how the model can be exploited to assess the development of a chronic bronchitis in its initial stages.

3. SIMULATION MODEL OF THE HUMAN RESPIRATORY SYSTEM

The newly developed model is a nonlinear pulmonary simulation model that describes the fluid mechanical characteristics of the human respiratory system. The model is based on the morphometric analysis of the geometry and dimensions of the human tracheobronchial tree performed by Weibel [1964]. It is a lumped parameter model in which each of the 24 zones in Weibel's scheme is represented as a separate component. In doing so, the nonlinear character of the relationship between transmural pressure and volume (cross-sectional area, length) of each of these zones has been taken into account. The model was programmed in ACSL. On the basis of this ACSL simulation program, several simulation experiments were carried out in order to investigate the effect of alterations in the mechanics of breathing which are caused by pulmonary diseases, especially by a chronic bronchitis. Moreover, the simulation experiments which have already been carried out and which will be described later constitute the conceptual basis for the accomplishment of parameter identification tasks in the field of diagnosis.

3.1 Objectives And Salient Features of our Modeling Approach

The range of applicability of the known pulmonary models, as for instance those described by Fry [1968] and Verbraak et. al., [1991], is limited. This is particularly true when attempting to identify parameters of disease (pathophysiological parameters) that are closely related to the location, the degree and the extent of a pathophysiological process. Our modeling efforts aim primarily at a simulation model that can be used in the area of diagnosis. More specifically, our objective is a model that can be taken as the basis for an identification of pathophysiological parameters that would allow an assessment of the patient's condition. The intended purpose of our development is the construction of a simulation model with the following salient features:

(a) It contains all system variables necessary to analyze pathophysiological changes in the degree of detail physicians would require for an exact functional and morphological description of these alterations that will cause an impairment of the respiratory system.

(b) No concessions have been made: We avoided the oversimplifications inherent in previous models, namely an excessive lumping together and a linear treatment of the breathing dynamics.

(c) Our model also allows system identification methods (parameter identification methods) to be employed appropriately, thus achieving a diagnosis guided by parameters of disease that are directly related to the morphology of the pathophysiological manifestations.

In the first step, we built a model of the normal respiratory system (healthy average adult). This model can be adapted to specific pathophysiological changes. These adaptations are easy to carry out, even interactively at run time between individual simulation runs. At this stage of development, we will only deal with chronic bronchitis and pulmonary edema. In addition, we will restrict ourselves in the following to a single but very important pathophysiological manifestation, namely the lining of the small airways with an excessively thick layer of secretion (mucus). In the very early stages of chronic bronchitis, this lining of mucus, which is strictly limited to the small airways, is the only significant pathophysiological alteration, since at least at the beginning of chronic bronchitis, the effect of pathophysiological alterations of the bronchi walls and especially of the walls of the bronchioles within the region of the small airways is not predominant. Moreover, in the initial stage the contribution of all the other sections of the tracheobronchial tree to the pathophysiological process is insignificant. Although the design principles of the newly-developed model would permit an application for all kinds of breathing maneuvers, we will restrict ourselves in this stage of development to the case of quiet breathing (respiratory flow characteristic of resting conditions). Moreover, we will confine ourselves to a version of the model for pure mouth breathing that occurs in a subject with an occluded nose cavity and a piece of flexible tubing held firmly in his mouth. We assume (at this stage of development) that humidified and warmed air (BTPS conditions) is breathed in, as is usually the case in lung function tests with a whole body plethysmograph. The model was programmed in the simulation language ACSL. We also used the facilities of the ACSL language system for the visualization of the simulation results. For further details of we refer to the description of the newly developed model by Quatember et. al., [1994] and Quatember et. al., [1995].

3.2 Simulation Experiments

In this stage of development, several simulation experiments have already been carried out. A comprehensive experimental program is planned for the future. The simulation experiments described below include simulations of the normal respiratory system as well as simulations of the respiratory system in the presence of an excessively thick layer of secretion (mucus) in the small airways. The lining of the walls of the airways with a layer of liquid results in an obstruction. The experiments were based on the assumption of a uniform reduction of cross-sectional area in all sections of the small airways. In our investigations, we introduced a specific parameter to describe the extent of such a layer of secretion. This parameter, denoted by RED_A, represents the uniform reduction of cross-sectional area in sections of the tracheobronchial tree from generation 11 to generation 23 caused by the amount of accumulated mucus at the end of the expiratory phase.

Figure 1 depicts the variation of the alveolar gas pressure p_{alve}, the total flow (mouth) f_{mouth} and the flow into the alveolar space f_{alve} with time in case of a normal respiratory system.

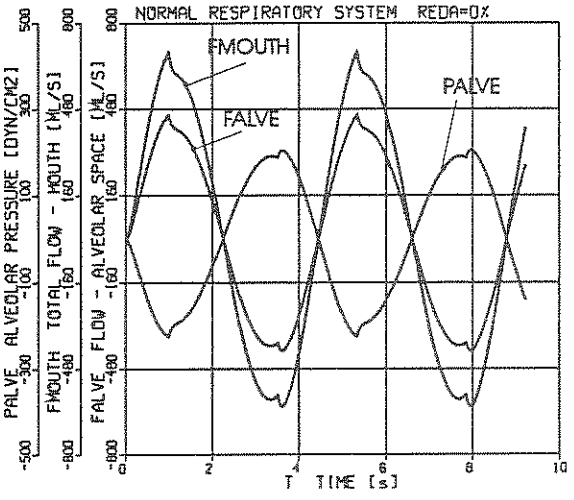

Fig.1. Variation of p_{alve}, f_{mouth} and f_{alve} with time - normal respiratory system

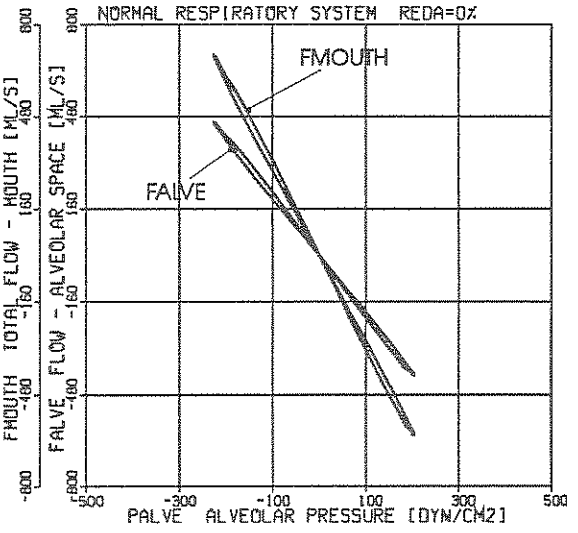

Fig.3. Pressure-flow loops: $f_{mouth}=F_1(p_{alve})$, $f_{alve}=F_2(p_{alve})$ - normal respiratory system

Fig.2 shows the variation with time of the same variables as in Fig.1; however, this is a case of a uniform reduction in cross-sectional areas of all sections of the small airways specified by the parameter value RED_A =75%.

Figures 3 and 4 show the same simulation results represented in another way.

The alveolar gas pressure is now recorded on the axis of abscissa and the rates of gas flow at the mouth and the gas flow into the alveolar space on the ordinates. The curves in Fig.3 and 4 are called pressure-flow loops. This method of representation corresponds with the usual way of representing the measurement results obtained from a whole body plethysmograph. A direct comparison of simulation results and measurement data is thus possible.

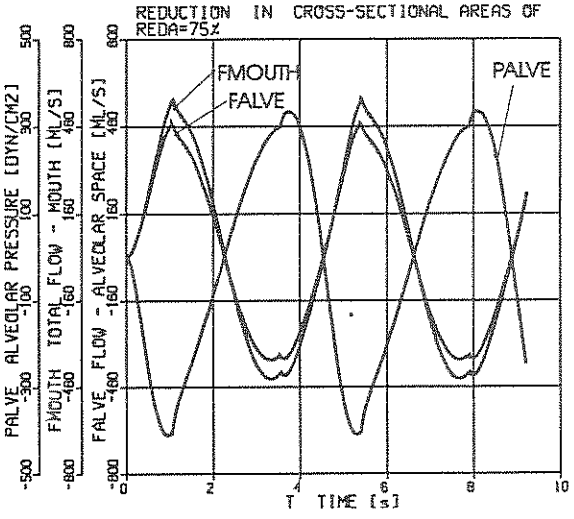

Fig.2. Variation of p_{alve}, f_{mouth} and f_{alve} with time - reduction of RED_A=75% in cross-sectional areas of small airways

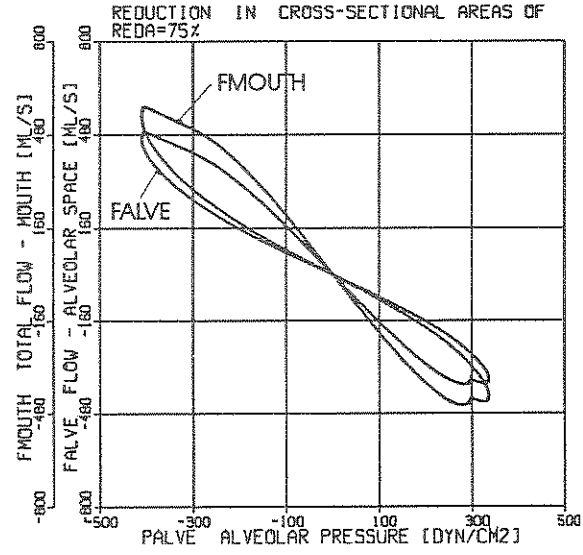

Fig.4. Pressure-flow loops: $f_{mouth}=F_1(p_{alve})$, $f_{alve}=F_2(p_{alve})$ - reduction of RED_A=75% in cross-sectional areas of small airways

4. EXPLOITATION OF OUR SIMULATION MODEL FOR THE ASSESSMENT OF HEALTH EFFECTS ASSOCIATED WITH AIR POLLUTION

The comparison of a patient's measured pressure-flow loop with simulated pressure-flow loops for different values of the parameter RED_A as described in the previous paragraph is still a rather crude way to arrive at a parameter value for the patient's condition describing the pathological change, namely the thickness of the layer of secretion in the small airways. However, there are proven formal methods to reliably identify the value of RED_A that describes the just mentioned pathological change. The methods are based on the aforementioned whole body plethysmographical data. It is thus possible to exploit much more of the potential physiological and diagnostic information contained in the plot of the pressure-flow loop delivered from the whole body plethsymograph than would be possible with a conventional analysis of the body plethysmographical data, since such an analysis would only result in parameters like, for instance, the total airways resistance and the parameter FEV1. However, these parameters are not suited to assess the pathological changes in the initial stages of chronic bronchitis.

5. CONCLUSIONS

The pulmonary model which has been presented in this paper will be extended and refined. In this stage of development it is already possible to simulate the effect of an accumulation of secretion (mucus) in the small airways on the breathing process. This pathological change is decisive for an appropriate assessment of the health effects of ambient air pollution. Already in this stage of its development, the model can be used to study the impact of air pollution. In the future, the model will allow more accurate investigation. It will be possible to study further pathophysiological processes. We also plan to improve parameter identification (parameter estimation) programs and to extend the capabilities to include the identification of further significant parameters of disease.

6. REFERENCES

Detels, R., D.P. Tashkin, J.W. Sayre, S.N.Rokaw, F.J. Massey, Jr., A.H. Coulson, and D.H. Wegman, The UCLA Population Studies of CORD: X. A Cohort Study of Changes in Respiratory Function Associated with Chronic Exposure to SOx, NOx, and Hydrocarbons, *American Journal of Public Health, 81(3),* 350-359, 1991.

Fry, D.L., A Preliminary Lung Model for Simulating the Aerodynamics of the Bronchial Tree, *Computers and Biomedical Research 2,* 111-134, 1968

Gardner, D.E., Direct and Indirect Injury to the Respiratory Tract, in *Air Pollution and Lung Disease in Adults,* edited by P. Witorsch, and S.V. Spagnolo, pp. 19-47, CRC Press, Boca Raton, 1994.

Hogg, J.C., Airway Pathology of Functional Significance in Chronic Bronchitis and Chronic Obstructive Airway Disease, in *Inflammatory Indices in Chronic Bronchitis, AAS Agents and Actions Supplements (Vol. 30),* edited by C.G.A. Persson, R. Brattsand, L.A. Laitinen, and P. Venge, pp. 11-20, Birkhäuser Verlag, Basel, 1990.

Hoppin, Jr., F.G., Pulmonary Function Tests for Diagnosis and Evaluation of COPD, in *Chronic Obstructive Pulmonary Disease,* edited by N.S. Cherniack, pp. 363-373, W.B. Saunders Company, Philadelphia, 1991.

Jahn, O., Medical Foundations of an Expert System for Chronic Obstructive Lung Disease, *Cybernetics and Systems, 21,* 337-349, 1990.

Laszlo, G., *Pulmonary Function: A Guide for Clinicians,* Cambridge University Press, 245 pp., Cambridge, 1994.

Pride, N.B., Assessment of Long-Term Changes in Airway Function, in *Inflammatory Indices in Chronic Bronchitis, AAS Agents and Actions Supplements (Vol. 30),* edited by C.G.A. Persson, R. Brattsand, L.A. Laitinen, and P. Venge, pp. 21-34, Birkhäuser Verlag, Basel, 1990.

Quatember, B., Development of an Expert System for Chronic Obstructive Lung Disease, *Cybernetics and Systems, 21,* 351-365, 1990.

Quatember, B., O. Jahn and R. Schindl, Simulation and Parameter Estimation Relating to the Diagnosis of Pulmonary Diseases Based on a Nonlinear Model of the Human Lung, in *CISS-First Joint Conference of International Simulation Societies Proceedings,* edited by J. Halin, W. Karplus and R. Rimane, pp.595-599, The Society for Computer Simulation, San Diego, 1994.

Quatember, B., O. Jahn, and R. Schindl, Simulation Studies and Parameter Estimation Based on a Non-Linear Model of the Human Lung: Possible Contribution to the Diagnosis of Lung Diseases, in *The Proceedings of the 1995 Summer Computer Simulation Conference,* edited by T.I. Ören, and L.G. Birta, pp. 677-684, The Society for Computer Simulation, San Diego, 1995.

Schwartz, A.M., The Pathology of Environmental Lung Disease, in *Air Pollution and Lung Disease in Adults,* edited by P. Witorsch, and S.V. Spagnolo, pp. 97-127, CRC Press, Boca Raton, 1994.

Schwartz, J., Lung Function and Chronic Exposure to Air Pollution: A Cross-Sectional Analysis of NHANES II, *Environmental Research, 50,* 309-321, 1989.

Ulmer, W.T., G. Reichel, D. Nolte, and M.S. Islam, *Die Lungenfunktion: Physiologie und Pathophysiologie, Methodik,* Fifth Edition, Georg Thieme Verlag, 222 pp., Stuttgart, 1991.

Verbraak, A.F.M., J.M. Bogaard, J.E.W. Beneken, E. Hoorn, and A. Versprille, Serial lung model for simulation and parameter estimation in body plethysmography, *Medical & Biological Engineering & Computing 29,* 309-317, 1991.

Weibel, E.R., *Morphometry of the Human Lung,* Springer-Verlag, 151 pp., Berlin, 1963.