The Atmosphere

Rede uitgesproken door

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bij de aanvaarding van het ambt van hoogleraar
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Für meinen Vater

Mijnheer de rector magnificus, dames en heren bestuurders van de Universiteit en het Leids Universitair Medisch Centrum, geachte collega's, dames en heren studenten, zeer gewaardeerde toehoorders uit het binnen- maar ook uit het buitenland.
Ik heet u namens mezelf, maar ook uit naam van de hele afdeling longziekten van harte welkom bij deze plechtigheid. Deze korte inleiding in het Nederlands is primair bedoeld om u, geachte aanwezigen, ervan te overtuigen dat ik intussen deze taal al redelijk beheers. In principe zou het ook mogelijk zijn u de volgende 45 minuten in het Nederlands toe te spreken, maar met het oog op onze buitenlandse gasten wil ik toch voorstellen deze oratie, voor mij neutraal, dus in het Engels te houden.

Ik heb gezegd (I have spoken) is usually the last words that are spoken at the end of an oratie such as this one.When I was thinking about this day, and I thought about this a lot, it appeared that this expression represents almost something like an anachronism at a situation where a medical center such as the LUMC propagates and proposes a strong 'we' feeling where research groups, divisions, commissions and committees represent and carry the actual mission statement of this institution. At a time where meetings and the culture of holding them seems to be an art of its own, where global communication is the ultimate goal and within a system where, so I have learned, individuals who seem to be sticking out ideally should get leveled back to the general population. So why is it then that under these circumstances a University including a corporate institution such as the LUMC would without hesitation choose to stick with one of those very old traditions giving the opportunity to an individual to express his or her views in a fashion that is formerly absolutely unopposed. I may add that in former times this tradition also included the dispute with the public but that this - very much to my relief - was changed to the present form after incidences of physical abuse were reported. I do believe sticking with this tradition has to do with the fact that an occasion such as this one potentially creates a very specific and also emotional atmosphere which might - everything going well - address the expectations of those who have gathered here that are primarily interested in what happened to an individual they have known for a long time that is family and friends, to colleagues and professional partners that are interested in a vision and view about medicine and science, to the newly found colleagues that would like to know how a new person views his imbedding and corporation with themselves, to the nomination committee and those who are directly involved in the management of the University and the LUMC to hopefully verify that the decision they have made not too long ago hasn't been completely wrong after all, and principally to all those that are just simply curious what will be said, how the future of the department is likely to look like and whether this

individual has the guts, the chuzpe to stand for his convictions also under peer review such as today.

But there may be also another consideration - and that is that even though the whole network of functions in our clinical medicine and science is based on a group effort, it is individuals that add the flavour and are ultimately fundamentally influencing the well or non-well being of a whole group and a department in general.

From these considerations it seemed obvious to me that I should simply be talking today about the atmosphere and this is the title of this oratie. First of all this topic seems such an obvious choice for a respiratory physician since the lung is the organ of atmospheric exchange and it is this atmospheric exchange with its potential impairments that forms the basis of many of the diseases that we in our profeesion are dealing with. Atmospheric pressure is the baseline condition that we need to measure lung function, the atmosphere also carries all those noxious environmental and self inflicted agents that are responsible for our clinical tasks, and it is in the end the increase of atmospheric pressure at the level of the vocal cords that enables us to communicate and speak up.

The atmosphere, however, is also the subject of the research that is performed in a large number of research institutes around the world and also forms to large extend the basis of our own experimental approach. But atmosphere is of course not only the description of the composition of gasses and pressure. Atmosphere - de sfeer- of course also has a broader meaning that for this occasion might serve to illustrate some of the issues that I believe are important for our future tasks and which will accompany us for the next coming years. It is the atmosphere under which subspecialties such as pulmonology are incorporated within internal medicine to form a larger framework of medical care and clinical science. It is the atmosphere that needs to be created and/or maintained to negotiate a sensible and peaceful corporation between basic research and medical needs. But it is of course also the atmosphere for the foreigner, the German foreigner, to move into this country, to work under professional conditions, but also being a social member within this community.

Let me, however, begin with the role of the atmosphere for respiratory medicine in general. Most of the diseases of the lung that we know have ultimately to do with impairment of gasses. Bronchial asthma affecting aproximately 7% of the adult population and traditionally one of the stock paardjes of this department is a disease that is characterized ultimately by narrowing of the airway and thereby impairment of gas exchange. The same applies to chronic obstructive lung disease and emphysema, frequent diseases in the general population esti-

mated to be the fourth leading cause of mortality worldwide by the year 2020 which is also - by other means - responsible for an impairment of exchange of gasses through the loss of lung tissue. The most relevant underlying factor the pathophysiology of this disease lies in the inhalation of air under ambient conditions polluted with tabacco smoke and condensate. And it is the same tabacco smoke and condensate that is also responsible for one of the leading causes of death not only in the Netherlands, lung malignancies such as lung cancer. It is also the atmosphere that carries allergens as major precipitating factors and triggers to the lung being responsible for a great deal of suffering and morbidity in allergic asthma. And finally diseases that are related to a subsensitivity for changes in the atmosphere, specifically carbondioxide, are responsible for some of the rarer and more complex diseases of disturbed respiratory function.

Most of these disorders are frequently occurring, they are responsible for a high degree of morbidity, and are responsible for a great deal of costs to the society and need therefore the attention of a medical community. This department will continue its interest and activity to care for patients with asthma, especially those with severe forms of the disease and for patients with chronic obstructive lung disease and emphysema. Diagnosis and treatment of lung cancer will also continue to be one focus of our clinical tasks and more attention will be given towards the sizeable group of patients that are affected by sleep related breathing disorders. Local increase of atmospheric pressure leads to the generation of sound but we are determined to take this one step further and use ultrasound as a diagnostic tool in our clinical practice. The diagnostic opportunities to use this technique, very much to my surprise hardly developed in Dutch pulmonary medicine, for the routine diagnosis of our patients will broaden our clinical tools and provide additional chances for those who are now in training. Newly recognised endoscopic ultrasound techniques will in my view fundamentally change the clinical management of patients with lung malignancies and will additionally feed the established lines of image analysis at the LUMC from pulmonary medicine.

Pulmonary medicine as a whole theoretically has the distinct advantage over other disciplines that there is no need to argue about the relative importance of lung diseases, they simply are highly relevant. It has, however, to defend the notion that there is a level of expertise and care that needs to be guaranteed and maintained. It is my strong believe that the attention given to respiratory medicine within every Dutch Medical faculty, an attention that is obviously not shared by all countries in the European community, is justified through the frequency and the general relevance of diseases of the lung that are in general associated with increased severity and mortality worldwide. It is necessary to support specialized centers and departments as a significant number of these patients is

probably not optimally treated in the general practice and in general internal medicine. Mortality figures from patients, for example, with asthma make it very likely that for the still intolerable number of individuals dying from this disease, undertreatment and lack of conception of the pathophysiology of these disorders are responsible for a poor outcome. Therefore, it appears simply mandatory for me to be actively involved in hands-on medical care. The function of leading a department such as this one includes the role of an acting physician, as the one that asks uncomfortable questions at times but is also seen internally as one that solves a clinical problem.

The tight relation between atmosphere and lung diseases and the desired context of medical care and basic science in Leiden make it obvious that there is a triangular relation adressing the same object of desire. It has been through very fortunate circumstances that research lines that have been set-up in the past could very comfortably combined with the research interest of the newcomer hopefully creating an even improved research line. Again, atmospheric oxygen through chemical interactions with pollutants in the air is transformed to reactive oxygen products and these reactive substances, including for example ozone may play a major role in the initiation, development and in the pathophysiology of inflammatory disorders of the airway. These changes have been a major research interest area in my clinical home in Grosshansdorf and some of this experience and definitely new ideas will form an aspect of our current and ongoing research.

Allergic inflammation, another major contributor to the development of bronchial asthma is also carried through the airways by the atmosphere. The fundamental research through the Spieksma's here at this place and our ongoing interest in clinical and molecular aspects of allergy illustrate the past experience and will guide us within our future research interests.

But it is not only inhaled air that forms research projects and direct us in our research lines, it is also the exhaled air that has become a major focus of interest for the researchers not only in this institution. Atmospheric components, small molecules and probably also proteins can now be measured in the atmosphere that gets exhaled into the environment from an given individual and may mirror and reflect the changes that are happening under disease condition such as bronchial asthma and other forms of airway inflammation.

But obviously there are factors other than atmospheric ones that may ultimately be responsible for the disease progression and may represent even more important factors determining the clinical outcome of a patient. So why is it than that research lines that do give you a certain choice are directed more to atmospheric changes? Well it may have to do with the fact that having the choice research to

me seems to be more interesting if responsible factors are in principle changeable. That is, you can do something but the prevalence of COPD and bronchial cancer if you would improve the atmosphere you can probably change the impact and the prevalence of allergic sensitization if you understand the mechanisms how these allergens work and think about measures how to avoid them. I know that there are hard core geneticists that would want to debate the role of environmental factors in these research questions and I am far from denying that genes, also for lung diseases, play a role. But rather than assuming that genetic background is the major determinant for disease and is only modulated by environmental and atmospheric factors. I am convinced that for most of the diseases in a larger population scale that we are looking at in respiratory medicine, these diseases are primarily driven by environmental factors and have a, if I may say so, small genetic background. If you allow me, I would like to illustrate this point to you through the model of airway hyperreactivity in humans.

Airway hyperreactivity describes the increase capacity of an airway to contract in response to an exogenous stimulus. While this feature is almost always present in patients with bronchial asthma, it also plays a role in other circumstances such as viral infection, bacterial inflammation and probably also in smokers. While genetic analysis have linked some of the clinical presentation if reactivity to a certain genetic localist I do believe that there is overwhelming evidence that this abnormality is primarily related to environmental factors,. Those of you who are interested in history here is what I find a very nice experiment by two investigators and this is where the story begins. The two investigators were Carl Praussnitz and Heinz Kuestner. One of them Kuestner was the assistant to Praussnitz in Breslau. Kuestner was asthmatic and sensitive to fish. The pivotal experiment that Prausnitz and his assistant performed performed in 1921 included the injektion of Kuestners serum into Praussnitz skin rendering the latter skin-sensitive to the injection of fish allergen. And from these observations, later called the Praussnitz-Kuestner reaction, those researchers postulated that there is in fact a transferable factor at this time called regain that was acquired by the one and could be transferred to the other. So sequentially these experiments became forgotten for many researchers but many years later when IgE was discovered and it became apparent that IgE is a relevant factor for the development for airway reactivity and also the development of bronchial asthma, people further explored the nature and the pathophysiology of this reagent reaction. From these experiments that began in the fifties and the sixties it became clear that hyperreactivity increase sensitivity to allergens as an example could be transferred from one airway in isolation to the other. Many researchers, including us Germany, and now us in Leiden, were interested in the mechanisms of how the sensitization might occur. From our experience over the last years it appears that every single airway from an individual in material taken from oper-

ative resections is primarily susceptible to sensitization under the right conditions. That is, if you would expose this airway or its smooth muscle sitting within the airway to a sensitized environment there would not be a single smooth muscle that could not be rendered hyperreactive independent from the genetic background of its donor, independent of age, and independent of his past medical history. One of the factors that seems to be responsible for this is IgE and, yes, I do agree, that there is a genetic background to produce more of this immunoglobuline. But the evidence points very strongly to environmental factors and by now we know that very targeted interventions with some of those factors including IgE offer a significant new therapeutic modality to treat frequent disorders such as bronchial asthma. In this sense I think we will continue to be interested in diseases where known atmospheric factors play a major role and focus our research interests also towards intervention modalities to interfere with some of those mechanisms known to be responsible for disease. In linking medical necessities in basic research there is, however, another very relevant atmospheric point that needs to be stressed that leads us away a little from the pure physical description of atmospheric pressure and composition. That is the generation and maintenance of a critical dialog between a medic and a basis researcher. It is this dialogue that forms one of the strengths, as I experienced, of this institution that enables medicine to ask right research questions under support and with the creativity of the basic researcher and it enables the basic researchers to ask the right research questions.

Having discussed the relation of medicine and basic research, there comes, however, another atmospheric issue under consideration, which takes us away a little bit from the pure physical description of the composition in pressure. It is the necessity to create and maintain a critical dialogue between those who are responsible for clinical work with those that do basic research. I believe it is one of the strongholds of this institution that it creates an atmosphere where it is in principle possible for both groups to learn from each other. For the medical person to have the creativity and the expertise of the basic researcher to look at an affected patient with his clinical presentation under an analytical perspective, but also for the basic researcher to understand why very small and incremental progress may be rewarding in terms of patient care. It appears, therefore, attractive for an department within internal medicine to aim to educate as many people as possible to acquire clinical experience but also a training in basic science. This MD/PhD philosophy may even become a prerequisite and will ultimately enhance the career perspectives of a given individual. But if we understand and accept that this is based on a critical dialogue between two professional groups - clinicians and basic researchers -, and if we agree that this is indeed the fundament and the core of what the present mission statement of this institution wants, then we have to generate, if at all possible, the same conditions for both

of these groups ranging from career perspectives to rather profane considerations such as material reward. This, in theory could be achieved by two alternative routes: lowering the clinical income to the level of basic research, a modality that appears to be of limited attraction, or finding a compromise that maintains competitiveness for the clinical job market and still motivates those in basic research - the latter seems the better choice.
When I talk about the atmospheric relation between medical and basic scientific staff within an institution there is one aspect where atmosphere also seems to play a major role. Science and international science heavily depends on corporation and cooperativity of individuals. While I do realize, and agree, that you have to formalize this internationalization and that you need to have a structure and the political will to be international, it should not be forgotten that it is an individual decision and most frequently the individual atmosphere between a limited number of individuals that makes international science happen. In that context I personally am very grateful for those researchers who have strtched out their hands across borders and cultures. In this context, I would like to thank my collaborators over many years in the US, especially Alan Leff, who unfortunately cannot be present here today. He is however excused, as he is having his 25th wedding anniversary and for this reason was not really allowed to leave the country. I am grateful to him, not only because I have learned a lot and we have produced science together, I am grateful for him that he worked as a friend and person with me which I think is the basis of international research collaboration. And additionally that he introduced me to the best jiddisch idioms that could not be found in the books. On a more general level, atmospheric conditions are important to create the willingness and to mobilize the energy to seek for partners outside the own environment and research collaborations will only work is there is a personal atmosphere between people. Also researchers should never forget that you usually always see twice in your live.

Under the given focus of scientific excellence and focussing medical care to the exploration of scientific mechanisms and the exploration of rare disease, again for those of you who are interested in historical facts, this institution used to provide medical care free of charge to patients under the historical mission statement that science and teaching are the ultimate goal of this academic institution, a few potential atmospheric disturbances are built-in. It is, for example, under those circumstances not easy to provide a full clinical training for those who are at the early stages of the career. Cooperation with other medical institutions and cooperation within the departments of the division is the ultimate requirement to guarantee a qualitative education. I do realize that the efforts being made provide the principle chance for complete training, but also here it is the individual that has to share some of these considerations and has to invest with creativity into this educational task. This sometimes, even needs a liberal

personal management of so well regulated working hours, but I would encourage hopefully through my own initiative that there are physiological limits to those regulations.

Additionally focussing on academic medicine in the Dutch sense and concentrating on self- defined missions may appear alienating and sometimes even arrogant towards those that are dealing with regular patient care and management. It is one of the great tasks of academic medicine to communicate mission statements in an understandable fashion and transparent to those who provide medical care in the region, in other hospitals and in general practice to create an atmosphere of true cooperativity. I think it goes without saying that there are limits to the concentration on topreferenties and the study of rare disease where patient needs must be met and where medical advise is urgently needed by those in the region. To be seen as the medical experts that we all would like to be requires a common platform that at present seems to have some room for improvement.

But this occasion of today should also be used to address some issues, not only of training for medical specialists, but also for education of medical students. Coming from a different background of medical education, I do believe that medical training for students in this country also through the new curricula provides unique change to have young people interested in medicine and science and in science to support medicine. Teaching of students plays a major role for this department. Since I am convinced that creating a sensitivity for a specialty such as respiratory medicine primarily depends again also on a very individual level on the ability of a teacher to raise interest and the desire to learn about medical aspects and scientific backgrounds of very frequent diseases. In this context, it appears remarkable to me, that not only in Germany, but also in the Netherlands the interests and the capability of a hoogleraar to actually teach appears to play only a small role in the decision to nominate him as the head of a department within a teaching institution.

So what then is the role of a specialized department within the context of internal medicine in the LUMC. This institution hosts almost every subspecialty in medicine, and although from a former new from the outside, lung medicine seems to be of great importance in this country, I was surprised to learn that the institution of chairs in pulmonary medicine happened in the second half of the last century, while lung medicine for a long time was related to infectious disease, especially tuberculosis. Malignancies of the lung, chronic bronchitis and asthma became the basis of a new deformed department that have developed to their own strengths reflecting the frequency and clinical relevance of this medical entity. This department at the LUMC was initially headed by doctor

Swieringa as far as I could find out on a part-time basis before Joop Dijkman took over as head and, therefore, I am only the third person heading this department. Reading through the manuscript of Professor Dijkmans afscheidscollege from November 1997 I am well aware that you have indicated that it was not always without problems. I am not in the position to comment on this but I would certainly like to take this opportunity to pay my respect and thank you dear Joop for the fundament and the structure of this department that I had the chance to take over in October 1998. Even though pulmonary departments in this country have a rather short history, this subspecialty has proved also through the individual achievements of some eminent pulmonologists in this country, the right for independence. If, however, lung physicians in the future would be more self-assured about their own independent identity I would hope for a more relaxed attitude of a subspecialty such as pulmonology to general internal medicine and vice versa. At this point I am not convinced that in the years to come independent professional subgroups within internal medicine serve the necessities of optimal patient care and the advancement of science.

I should not miss the opportunity today, to also address another aspect of atmosphere and the individual. And this is related to the fact that I am very well aware that being nominated as a German foreigner to this institution reflects openness and tolerance on the one hand, but also means responsibility and requires sensitivity from the individual together with modesty at times. One of the most frequent questions I have been asked by my friends and colleagues is related to the fact "how is it then to work in the Netherlands" I might add "as a German". I cannot help to mention it but this has also been on my mind before I made the decision to come here and the situation is probably best reflected by a small anecdote. There was a time shortly before I came here where I was actively considering to move from Grosshansdorf within Germany to the East, to the University of Leipzig. When this was openly discussed amongst family and friends, I was confronted with some sense of insecurity and reservation but the encouragements I got were expressed also in small presents in forms of descriptions and books with titles such as: Beautiful saxony, The History of Leipzig and The prospects of unification. When the tide had changed and the decision was ready to be made to move almost exactly the same distance from the North of Germany to the West, to Leiden, the titles of the book presents were slightly different and the well meant presents collectively described the specific relations between Germany and the Netherlands with titles such as Zwei ungleiche nachbarn and learning to live with the Dutch. And I have to admit at this point that familiar discussions also circled around the atmosphere that was expecting us and whether or not it would be difficult for a professional live, the family, the children. But here again I think it is a very individual and positive attitude and natural curiosity of the researcher met should ultimately be responsible for the

response that you a vogue in a new surrounding. I am aware that I am talking at a location where right behind me, you see it here on the very right next to the podium, Dutch history is illustrated and it obviously includes German-Dutch relations. And I am also very well aware that the Clingendael Institute until quit recently describes an atmospheric problem between these two countries. I think however as an individual born in the year 57 the beginning of the negotiations over the Generalbereinigung at this time under Minister Josef Luns from theNetherlands and Clemens von Brentano from Germany a major political undertaking, it is again a question of personal attitude and openness to enable a process in the heart, which sits very close to the lung, that should have taken place in the heads a long time ago. I hope that my and my families very positive experience will help to further open this university and medical center to more people also from the direct neighboring countries to share the excitement of being here. It remains obscure to me that medical and research relations are still at present happening more frequently between the US and England and the Netherlands compared to the direct neighbour. The 17th century at the University of Leiden has been one of the most prosperous periods in the lung history. We have just celebrated the 425th dies natalis of this university and were remembered that such eminent members as Descartes have foreseen the needs of internationalisation. At this time it was natural and obvious that committees would look outside the own topographical limits for individuals believed to be able to add to the mission statement of their time. At this time things were a little easier since Latin was the only way to enter the data highway and - probably contrary to our believe - the acceptance of academic qualifications and exams was less of a problem than it seems to be even now in the United Europe including the SRC in the Netherlands. So, there probably is still some way to go and also - as usual - to learn from history, an aspect I have been referring to more than once in the proceeding 40 minutes. I do believe that it is individual historical awareness from where one originates to be able to accept a new and not always perfect surrounding.

Again talking about history and coming to the final part of this oratie which is of course amongst the most pleasant ones I would like to follow, quite in contrary to my anachronistic begin, a certain chronology to thank some of you who are today here in the audience.

Meiner Mutter, Dir lieber Mama, will ich dieser Chronologie zufolge natürlich als erste meinen Dank sagen, sozusagen für alles. Dieser Dank geht an zwei Personen aber du bist leider die einzige, die ihn entgegennehmen kann. Zwei Kinder, Physik und Medizin, Humboldt Universität und Leiden, ohne Eure ständige Unterstützung und Liebe für mich nicht vorstellbar.

Liebe Barbara, du hast in Dir typischer Weise gesagt, dass ich Dir nicht danken soll. Darum tue ich´s auch nicht. Jedenfalls nicht jetzt und hier, denn um zu sagen wofür ich Dir, unserem Philip unserer Eva und auch Linda alles danken will, reicht hier keinesfalls die Zeit

Professor Magnussen, lieber Helgo; Die danke ich für eine lange und gute Zeit der Zusammenarbeit. Du bist eines der besten Vorbilder, dass Rahmenbedingungen durch individuellen Einsatz prinzipiell änderbar sind und dass klinische Tätigkeit hervorragende Wissenschaft nicht ausschliesst.

Lieve collega's van de afdeling longziekten. Jullie hebben blijk gegeven van initiatief en een positieve aanpak. Zonder jullie inzet en overtuigingskracht zou ik nooit hier naar Leiden gekomen zijn. Jullie en daarmee bedoel ik Liesbeth en Peter in het bijzonder, hebben met jullie persoonlijke benadering mij naar Leiden gehaald en tot nu heb ik daar zeker geen spijt van gehad.

De positieve uitstraling van jullie als afdeling, heeft er toe bijgedragen te bereiken wat in eerste instantie mijn doel was, een goede sfeer en een gevoel van verbondenheid te creëeren.

Ik wil ook graag mijn dank uitspreken aan mijn collega's en het beheer van divisie 2, omdat ik altijd het gevoel heb gehad welkom te zijn. Ik dank u voor uw professionele en persoonlijke steun.

Tenslotte heb ik de behoefte mijn dank uit te spreken aan Mijnheer de Rector Magnificus en de leden van de Raad van Bestuur van het LUMC, in het bijzonder professor Buruma en professor Vermeer voor het vertrouwen dat u in mij gesteld heeft. Uw open benadering zonder vooroordelen heeft mij goed gedaan. In 1960 werd het onderhandelingsakkoord tussen Duitsland en Nederland uitgereikt aan de koningin met een citaat van Hölderlins Hyperion: So kam ich unter die Deutschen. Ich forderte nicht viel und war gefasst noch weniger zu finden. De tijden zijn gelukkig veranderd en ik hoop van harte samen met u te kunnen bijdragen aan het verder ontwikkelen van de sfeer van internationaliteit. Misschien wordt Leiden, volgens Vincent Icke, nooit Harvard aan den Rijn, maar we zijn met deze dag hopelijk een stuk dichterbij gekomen.

Ik heb gezegd.