International Archives of
Occupational and Environmental Health
Supplement

Peter A.J. Holst

Bird Keeping as a Source of Lung Cancer and Other Human Diseases

A Need for Higher Hygienic Standards

Foreword by P. Zwart

Springer-Verlag
Berlin Heidelberg New York London Paris
Tokyo Hong Kong Barcelona Budapest

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ISBN-13:978-3-540-53555-3 e-ISBN-13:978-3-642-76342-7
DOI: 10.1007/978-3-642-76342-7

Library of Congress Cataloging-in-Publication Data. Holst, Peter A.J., 1943. Bird keeping as a source of lung cancer and other human diseases: a need for higher hygenic standards / Peter A.J. Holst; foreword by P. Zwart. p. cm. "International archives of occupational and environmental health. Supplement" — P. opposite t.p. Includes bibliographical references. Includes index.
ISBN-13:978-3-540-53555-3 1. Birds as carriers of disease. 2. Cage birds. 3. Lungs — Cancer — Etiology. 4. Lungs — Dust diseases — Etiology. I. Title. {DNLM: 1. Animals, Domestic. 2. Bird Fancier's Lung — prevention and control. 3. Communicable Diseases — etiology. 4. Lung Neoplasms — etiology. WF 658 H756b} RA641.B5H65 1991 614.4'34 — dc20 DLC for Library of Congress. 91–4649 CIP.

Typesetting: International Typesetters Inc., Manila, Philippines

19/3130–543210-Printed on acid-free paper

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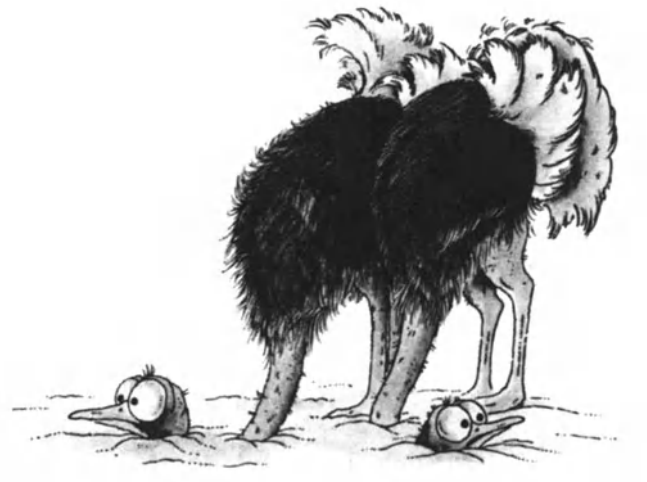

Foreword

Original ideas and observations are rare. They are especially valuable if checked in practice, critically evaluated and supported by material independently collected by others.

It is to the very personal credit of Dr. P.A. J. Holst that he noticed a potential connection between the keeping of birds and the occurrence of lung cancer among members of households where they are kept. He has pursued the idea in his private practice and for over 12 years kept records of every single patient. The data were critically and statistically analysed and supplemented by data and materials collected by lung specialists.

Research in cancer, especially in lung cancer in humans, has involved a large input of science and has contributed considerably to knowledge of the many factors involved.

A new aspect is presented in this book. Avian products, spread in the house in the form of fine dust particles, may be inhaled deeply, cause irritation and contribute to local immune responses in the lungs. It is hypothesized that this sequence of events is independent of other factors and significantly contributes to lung cancer and some other diseases.

It is a pleasure to work with a gifted man who is fascinated by many aspects of human well-being. The author is well aware of the importance of contact between mankind and nature. Living creatures such as dogs, cats, pet and aviary birds play a major role in human well-being. The keeping of birds may, however, as may many other activities, also bring certain health risks. Holst analyses the habits of bird keepers and the consequences of bird keeping on the health of residents of houses where birds are kept. He also suggests measures that may be taken to prevent diseases associated with bird keeping.

This book is a condensed presentation of an important scientific work contributing significantly to the health and well-being of mankind.

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Preface

The main purpose of this book is to present and discuss a number of pieces of evidence suggesting that keeping pet birds is a strong risk factor for lung cancer. The opportunity is taken to give the reader more detailed information about those diseases that can be transmitted from birds to humans — a fairly unknown field in general medicine. Bird keeping is becoming an increasingly popular pastime. However, it is a source of airborne particles that can cause allergic diseases in human, and there are a variety of infectious diseases of pet birds that are known or suspected to be transmitted to human. Environmental tobacco smoke is not the only visible air pollutant. One can see polluted indoor air in the residential homes of non-smokers who keep birds, particularly on a sunny day, because of the scattering of light by fine dust particles. There is often less ventilation in homes with caged pets out of concern for the budgerigar or hamster getting cold. The air can thus be more humid containing more allergens and dust particles. In the early 1970s, I began to be aware that individuals who keep birds as pets tend to have a higher incidence of colds, sore throats, shortness of breath, and coughs and flu-like symptoms than people in households without birds. Furthermore, there also seems to be a disproportionately large number of bird keepers among patients with lung cancer. This was the motive for a general practice survey which I conducted over many years (Holst 1984). This survey looked at the relationship of bird keeping not only to lung cancer but also to death before age 60, and the incidence of other cancers and of a number of other endpoints, including spontaneous abortion. Subsequently, two further studies were carried out: a case-control study of bird keeping and lung cancer (Holst et al. 1988), and a dust measurement study. Some other evidence, based on inter-regional comparisons, is also presented.

The book closes with a number of relevant issues resulting from this research. Budgerigars produce the finest dust particles of all pet birds and keeping and breeding them probably leads to the most problems with indoor air. The strongest association was found between the non-epidermoid type of lung tumours and keeping budgerigars. A possible mechanism by which pollution from birds might lead to lung tumour development is put forward. The importance of bird keeping as a cause of lung cancer relative to other known causes such as smoking and radon is considered, and some recommendations for future research are given.

Peter A. J. Holst

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1.1 Bird Keeping as an Increasingly Popular Pastime

1.1.1 Reasons for Keeping Pet Birds

In the nineteenth century, many species of tropical birds began arriving in Europe in large numbers as a result of the growth of shipping lines and the related increase in overseas commerce. Also the growth of periodicals late in the last century became a medium that encouraged communication among interested bird lovers and breeders, which in turn contributed to the growth of this hobby. The increasing number of people interested in this hobby encouraged trade in birds, which could then be sold at lower prices. Even those with more modest means could devote themselves to bird keeping, something that had previously been the privilege of the affluent. The canary was the bird of choice for the less affluent. Bird associations began to appear at the end of the nineteenth century. Such associations arose as special interest sections of poultry associations, but later became independent. Public shows, which were held several times a year in many European countries, made the hobby increasingly popular. Air cargo has made the importation of large numbers of exotic birds possible.

The urbanization and popularization of these birds have had a major impact on indoor air environments during the present century. Living quarters in many large cities are for the most part not adequate for keeping and caring for dogs and cats. Aquariums and terrariums can, if properly maintained, be very attractive, but they do not afford the same sense of contentment to the inhabitants of the home as do pet birds. Birds appear to be easy to care for, are no bother because they are kept in cages, and do not require any great expense. It is easy to have the birds taken care of during weekends away or longer vacations. The entire life cycle of the bird plays itself out before the keeper's eyes in cages and aviaries. The mating rituals and the caring for and feeding of the young are always fascinating to watch. Their song makes the home a little less empty and quiet. The bird's attention to all its keeper does, its total dependency on the keeper, and its singing when its owner arrives home are all good for the keeper's ego. There is a misconception that those who live alone, or who have just recently started to live alone, are the ones most likely to get a pet to relieve their loneliness. In fact, these people often get rid of their household animals after the last child leaves home. It is, above all, young families that bring in household animals for their children.

Because they are cut off from nature, city dwellers are, in general, insufficiently informed about and have little experience of animals and the problems that can arise as a result of keeping them. Many millions of tropical birds are imported and sold every year, but unfortunately a very high percentage of them die as a result of improper care and rough handling. There was a time when it was popular for schools to keep animals for purposes of education. The idea was to familiarize city-dwelling children with animals, and many young, enthusiastic teachers tried, in this way, to compensate for the poor emotional support that neglected children received at home. Complaints, allergies, odours and distracting noises were dismissed as being exaggerated. It turned out, though, that the animals suffered at the hands of the children, and there were problems with care of the animals during weekends and school vacations. Animals were often given their entire food ration for the weekend on Friday afternoon. If they ate it all by Friday evening, their feeding pattern would be disrupted and they would go hungry until Monday. A song-bird could not survive until then. "Children's zoos" have proved to be better for promoting healthy contact between children and animals (Bosch van Drakestein 1984; Griffioen 1979).

With the above historical perspective as background, it is now easier to answer the question as to why people keep birds and breed them with such fervour. Some of the motives for bird keeping are as follows:

— As a source of "farm fresh" eggs for consumption or sale
— For a sense of contentment, as a living room attraction
— As a bedroom attraction, as "love-birds"
— As companionship for children for educational purposes
— Out of laziness, instead of another kind of pet
— As an object of attention; to boost the ego of its owner; to learn a skill
— As a collector's item; to show off and be seen at shows
— For breeding (and then to give away the offspring as wedding, birthday, or Christmas gifts)
— For gambling in competitions (carrier pigeons), as decoys
— For their beauty, their song, their ability to imitate

Between 75% and 80% of human sensory perception is visual. Birds also have primarily visual contact with their surroundings. The image that the bird forms of its environment is closer to that formed by humans than that formed by other pet animals. Dogs, the most loyal of all pets for many people, rely more on their sense of smell, and their perception of their surroundings is correspondingly much different from that of their owners. Dogs and cats make only rough distinctions between colours. Birds, on the other hand, can distinguish colours very well (Kronberger 1978).

1.1.2 Number of Pet Animals in the Netherlands in 1984

On 1 January 1984, there were about 5.2 million households in the Netherlands containing 7.1 million men and 7.2 million women. Household birds are the most popular pets in the Netherlands, being kept in one out of every three to four households. The bird is the most common pet animal in both young and old households, with dogs next most popular, followed by cats. Rodents are the least popular as pet animals. Careful estimates have been made of the number of household animals in the Netherlands. Figures for the numbers of pets kept of various types in 1984 are shown in Table 1.1.

Table 1.1. Number of pet animals in the Netherlands in 1984

Type of pet	Numbers in 1984 (thousands)
Dogs	1800
Cats	1500
Horses, ponies	30
Household birds	
pigeons	3000
canaries	1600
aviary birds	1500
budgerigars	900
show poultry	500
parrots	100
cockatoos	10
total	7610
Rodents	
rabbits	600
guinea pigs	300
hamsters, rats, mice	50
total	950

1.1.3 Bird Breeders in the Netherlands in 1984

The number of organized bird breeders in the Netherlands has grown dramatically during this century (Robiller 1981). Figures supplied by the Netherlands Society of Bird Lovers (NBvV), the largest organization of bird lovers in the Netherlands, clearly show this (Table 1.2).

The NBvV was formed by the merger of three older groups and holds its annual show in Breda. In 1980, the NBvV sold 1 750 000 leg identification bands, and 25 743 persons showed 236 828 birds at various shows. There are in total 662 local chapters in 580 locations, indicating that some locations have more than one chapter. In the Hague alone there are eight chapters. The NBvV is an umbrella organization with some 47 000 members in 1980–1982. An average of 380 birds

Table 1.2. Growth of the Netherlands Society of Bird Lovers (NBvV)

Year	Chapters	Members[a]
1940	29	1 400
1950	38	4 500
1960	293	15 300
1965	467	28 494
1970	626	39 863
1974	649	40 724
1977	655	44 180
1980	655	46 500
1982	662[b]	47 000
1984	662[c]	45 800
1985	662	42 500

[a] 10% female.
[b] in 580 locations.
[c] 8 in the Hague.

were shown at each show, with a participation rate of 56% of the membership. Approximately 40% of the membership breed birds, but do not show them. The NBvV sponsors some 600 shows annually throughout the country. Subdivision of the 236 828 show birds by species is shown in Table 1.3.

The NBvV membership kept a total of 3 million birds in 1985 (Inquiry 1985). Each member kept an average of 60 birds. Directly after the breeding cycle this increased to a temporary average of 150 birds, but then declined as the young birds died or were sold. The average number of birds kept was 1–25 by 35% of the

Table 1.3. Distribution of birds shown by the NBvV in 1980

Family	Type of bird	Number	%
Canary	Color canaries	116 046	
	Song canaries	5 921	
	Form/posture canaries	21 314	
	Total	143 281	60.6
Parakeet	Grass parakeets(budgerigars)	15 394	
	Large parakeets	15 393	
	Love birds	4 737	
	Total	35 524	15.0
Tropical birds	Tropical birds	26 051	
	Zebra finches	13 026	
	Japanese mews	3 552	
	Total	42 629	18.0
Other birds	Pigeons/quails	4 741	
	European birds	1 180	
	Hybrids	9 473	
	Total	15 394	6.5

members, 25–50 by 33%, 50–75 by 13%, 75–100 by 9% and 100 to more than 200 birds by 10%. Most of the birds were kept indoors. In 1985, 90% of the members of the NBvV were males. Of the members, 9% were younger than 20 years old, 12% between 21 and 30 years old, 30% between 31 and 40 years old, 25% between 41 and 50 years old, 19% between 51 and 64 years old and only 5% over 65 years old. Of the members, 635 were salaried employees, 8% self-employed, 4% students, and 25% no longer part of the workforce. Of this latter category, 10% were retired, 9% on worker's disability, and 6% unemployed. These inquiry results are consistent with my own observations made during the period 1972–1981 in my general practice (see Chap. 2) in that primarily young families kept household birds and that more men were involved with this hobby. Maesen (1972) also reported that homing pigeons were primarily a sport of adult males.

The General Netherlands Society of Bird Keepers (ANBV) in Zutphen is the oldest organization in the Netherlands. It holds annual competitions in Zutphen. Of its members 95% also breed indoors. About 10% of the members also belong to the NBvV.

The General Society of Budgerigar Keepers (ABvP) is located in Doetinchem. Budgerigar keepers more often breed outdoors than do canary breeders, but they also keep many budgerigars indoors.

The Netherlands Society of Show Pigeon Keepers (NBS) was founded in Utrecht in 1923. Its chapters (345) are often organized jointly with rabbit breeders. Their major show, "Avicultura", is held annually during the second week of January in The Hague.

The Netherlands Carrier Pigeon Association (NPO) in Utrecht had 55 000 members in 1982, each keeping an average of 30 carrier pigeons (100 after breeding). The carrier pigeon breeders are also organized as a Netherlands society with a large number of local and neighbourhood chapters. The membership owns a total of some 1–2 million carrier pigeons, depending on the season. The members frequently buy, sell and trade among themselves and with fans of the sport in Belgium. There are almost no commercial carrier pigeon dealers, unless a particular bird dealer happens to be a carrier pigeon keeper himself. Keeping carrier pigeons has become something of an addiction among enthusiasts. The true keeper knows each of his birds and spends most of his free time in the coop. He places bets on the performance of his birds and can win back his investment many times over if his bird finishes first. There is a very well developed system of leg bands and stop clocks. In addition to the above-mentioned societies and associations, there are several others with only a few hundred members each, as for example the Finch Club, the Southern Netherlands Society, and the General Posture Canary Union in Tilburg. Every self-respecting local club of canary breeders holds a show of the birds bred once or twice a year. The shows are usually held in school gymnasiums during school vacations, especially during the autumn break. The large shows are usually held in January. The distribution of the number of organized bird breeders in the provinces, according to the administration of the various bird clubs, is shown in Table 1.4. In my general practice, the ratio of bird breeders among the total number of bird keepers was 1:6. No more than half of

Table 1.4. Organized bird breeders in 1984 per province

Province	Male pop*	Number of members in the different bird leagues Total	NBvV	ANBV	ABvP	NBS	NPO
North Brabant	1 054 281	23 009	10 000	700	160	427	11 722
South Holland	1 539 994	15 612	7 000	400	370	462	7 380
Gelderland	859 840	14 638	6 000	1 150	410	454	6 624
Limburg	540 669	12 426	2 500	1 600	175	174	7 977
Overijssel	519 800	10 096	4 600	1 150	430	397	3 519
North Holland	1 132 305	8 973	4 200	600	120	363	3 690
Utrecht	454 452	6 966	2 800	200	170	196	3 600
Friesland	296 902	5 223	2 200	250	165	320	2 288
Zeeland	176 736	5 046	2 000	100	30	83	2 833
Groningen	278 747	4 952	2 400	250	135	167	2 000
Drenthe	213 472	3 726	2 100	100	130	191	1 205
Netherlands	7 067 198	110 667	45 800	6 500	2 295	3 234	52 838

*Male population as at 1.1.84.

the number of bird breeders in my practice were members of a bird league. The degree of organization of the major bird breeders in the Netherlands is high in relation to participation in breeding competitions. Many of the households that have only briefly attempted breeding, often with one or two (partial) failed breeding trials, do not belong to bird clubs.

1.1.4 Hygiene Among Bird Keepers

The general increase in health standards during this century is the result of technical advances and better housing. Our nineteenth century ancestors fought a daily battle with vermin and dust in their homes. Bed bugs, lice, cockroaches, and various kinds of household mites that infected flour, cheese, and sugar all fared well in those days. It was the vacuum cleaner that changed all this. Around 1910, the well-off began to have their homes vacuumed. The vacuum machine stood outside in the street and long hoses were brought in through the front door. A vacuum cleaner was a luxury item before 1940, and certainly not a mass produced consumer item. Dust was removed by sprinkling tea leaves or wet saw dust on the floor and sweeping. Beating rugs and hanging them out to air was also a method of combatting dust and parasites. The use of vinegar to brighten the colours of clothing probably also helped in minimizing parasites. Mass production of vacuum cleaners began after World War II, and by 1955, 80% of all households owned one (Philips 1984, personal communication). The amount of dust sharply decreased as a result. General welfare in the Netherlands improved so much in the 1960s and the 1970s that most of the damp homes built in pre-war years, housing some three-quarters of the population, were replaced by new dwellings. These homes were better constructed and kept out more dust and moisture. While houses used

to be furnished and decorated with materials made from organic products, such as jute, wool, feathers, down, horse hair, kapok, cotton, rush mats, and other fibrous materials, less expensive synthetic materials, which produce less dust, are now increasingly replacing these. Wooden floors covered by reed mats, which were dust nests, and dust-producing coal furnaces have been replaced by concrete floors and central heating. Better foundations and building materials result in drier homes, thus making it more difficult for parasites to survive. Improved plumbing, 99% of which is now connected to municipal sewer systems, the use of toilet paper, routine hand washing, and the use of washing machines have all contributed to general improvements in personal hygiene. Sewage treatment plants, drinking water purification, and hygienic production of sterile foods (pasteurisation since 1870), have drastically reduced infectious diseases in the population and have greatly reduced childhood mortality. Refrigeration and improved methods of food packaging have left us with only a faint indication of the fauna that our grandparents had to contend with. Mass production of refrigerators began later than that of the vacuum cleaner. In 1965, only 48% of the market had been penetrated, increasing to 87% in 1970. In 1984, this percentage had further increased to 107%, indicating that some households had more than one appliance (Philips 1984, personal communication). The general use of refrigerators and the consumption of more green vegetables and frozen products has practically eliminated the need for canned or pickled food or to keep fat preserves at home. It is not out of the question that these inventions, resulting in the consumption of more germ-free foods and the eating of less salt and animal fats, have contributed to the decline in the frequency of cardiovascular disease. All of these changes have combined over the past 100 years to greatly increase the average life expectancy. In The Hague, the average age of death for men and women has increased by 50 years in one century. The reduction in childhood mortality is one of the most important reasons for this. In summary, the most important advances during the past 100 years have been, in chronological order:

1. Sewage treatment
2. Drinking water purification
3. Food hygiene
4. Hand hygiene
5. Air hygiene

Much remains to be done about the quality of both open and indoor air. The combination of chemical exhaust gases from industry and traffic and the over-production of fertilizer and ammonia from intensive cattle and chicken farming have had an increasingly destructive effect on the natural order in the environment.

The combination of chemical pollution (dust and gaseous particles of tobacco smoke) and biological pollution (keratin microfibrils, allergens, microbes and ammonia) is common in the indoor environment of bird keepers. Increased insulation of residences only makes the living conditions of the bird keepers worse.

The change in the morbidity patterns of people who keep birds as pets in their residence, as found in this study, cannot be explained by the unsanitary living

conditions of bird keepers — they have also benefited from the general hygienic improvements just described. Rather it is the specific consequence of long-term exposure to bioaerosols produced by the suboptimal conditions under which the caged birds are kept. In my experience as a family physician I observed that, even in homes of people with a very high degree of personal hygiene, the presence of caged birds produced a totally different indoor climate. Temperature, degree of humidity and dust content were all higher. Airway conditions are more common among bird keepers, and they have become accustomed to frequent colds, sore throats, shortness of breath and flu-like symptoms.

There are various social reasons for the growth of keeping birds as pets. In the first instance, owning a pet bird in an urban environment does not create the difficulties associated with keeping a dog or cat in such surroundings. People appreciate owing a pet that is easy to look after and which provides a responsive companion in their lives. It is not a coincidence that members of the parrot family, including the budgerigar, are most highly valued by the pet seeker. These birds can become true companions. They have tractable natures and can mimic the human voice and other sounds with accuracy. Contact with a tame bird also appears to have a beneficial effect on stress and in many cases may lead to a detectable fall in blood pressure. These beneficial effects on health, both mental and physical, have to be weighed against the possible health risks from long term exposure, as found in our study. In this respect probably parrots, budgerigars and cockatoos most influence the indoor air quality. Feather dust may prove a direct source of discomfort to bird keepers, typically causing a tight-chested feeling.

1.2 Birds as a Source of Pollution

1.2.1 Introduction

"Caged and aviary birds are bothered by the dust particles they inhale. That's why the ball is in your court. An electronic air purifier can solve these problems". Such is the text of a widely circulated advertisement in bird fanciers' magazines. A device to clean the air of particles that can be inhaled is supposed to improve the condition of the show specimens and also benefit those who care for them. Not only those who care for them but also the birds themselves are exposed to too much dust.

This dust problem has long been recognized, but there is no simple solution. Dust particles suspended in indoor air spread throughout the entire house. The fine dust on the floor floats when disturbed by someone walking across it. When vacuum cleaning, particularly using an older model of cleaner, large quantities of dust are released in the exhaust air. When cleaning cages, aviaries, and fowl coops, the dust burden is so large and so direct that an electronic air purifier of such small capacity as the one advertised is of no use whatsoever. Aerosols are formed from dried bird droppings, cells from the feathers, faeces of bird mites, mould spores

from polluted feed, and horny dust particulates. Some of these particles act as allergens, and both these and various microorganisms can be inhaled.

Such dust pollution in indoor air results in a higher number of positive ions in the air. An excess of positive ions increases the blood serotonin level which produces complaints such as migraine or shortness of breath. Electronic air purifiers and ionization devices produce a stream of negative ions which lower the serotonin level in the blood thereby reducing the number of these complaints (Krueger and Reed 1976). Their action is being studied but they do not clean the air of all dust particles and have no effect on the symptoms of the sick building syndrome (Finnigan et al. 1987; Offermann et al. 1983; Turiel 1985). Their presumed action is to decrease irritability, migraine attacks and complaints of shortness of breath in persons with allergic reaction to house dust who should keep far away from an excess of organic dust particles.

Not so long ago, it was thought that respiratory infections were transmitted by coughing and sneezing fits and that the "spray range" was approximately 1 m. More recently it has become apparent that contaminated droplets measuring 0.5–3 μm can become airborne and that these droplet foci can transmit infections over greater distances. In addition, it now appears that respiratory infections can also be transmitted through suboptimal hand hygiene (Gwaltney 1978). Raising birds in cages and handling contaminated young in the nest afford all sorts of opportunities for contamination through contact (Dekking 1950). Opportunistic cell parasites, such as viruses (e.g. retroviruses) and minute bacteria (e.g. chlamydiae) can easily multiply within cells under favourable conditions. Infections and transmission of viruses or chlamydiae occur among humans as well as animals.

The international trade in imported birds is coupled with high mortality and morbidity in these birds (Belonje 1984; Carter and Currey 1987). In 1975, an estimated 5.5 million tropical birds were imported by Western Europe, North America, and Japan. Mortality during air transport was 2%–5%. Of the original number of birds captured, at least 50% died before export, with up to another 25% dying after import. The most frequent causes of death were parrot disease (i.e. psittacosis), various intestinal infections, tuberculosis, and Newcastle disease (NCD; Belonje 1984). From 1976 several million parrot-like birds were trapped in the wild for the pet trade of rich countries. Mortality in the pet trade remains spectacularly high to this day. Post capture mortality prior to export was regularly around 50%. The wealthy consumer countries of North America and Europe removed previous health restrictions on the imports of parrot-like birds from 1973 to 1976, thereby increasing demand from poorer exporting states which lack the resources to control or prevent the trade. From 1976, the incidence of parrot disease, a dangerous and sometimes fatal disease that humans catch from wild caught birds, increased proportionally to the rise in imports of parrot-like birds, due to an unwary public being uninformed of the consequences of the pet trade.

1.2.2 What Can Go Wrong in Caring for Pet Birds?

The pet bird is fed daily and sheltered from the cold in winter and, in cages and aviaries, has nothing to fear from traffic or predatory animals. It lives longer than its counterpart can in nature. Among great titmice in the wild, about 80% die in the nest and, thus, only 20% survive. The success rate obtained by the conscientious breeder is much higher. The average age of birds kept by a bird breeder is 2–3 years. However, birds are often bred by those with a minimal knowledge of these matters. The bird can easily fall victim to many deficiency diseases because it is no longer free to select its own food. In its predetermined quarters, it falls prey to many infectious diseases as well.

Polluted Drinking Water. When drinking, birds wet the food in their beaks and crops, some of which can find its way into the water container, where decay and incubation may occur. If there are diseased birds in the aviary, they can infect others via the drinking water. As a result of many ornithoses, pigeons, parrots, budgerigars and other sorts of birds can have watery eyes, infected eyelids, and nasal discharge, which can readily infect other birds. Since open containers are used, drinking water that is not changed every day becomes polluted with faeces. Fouling of the water occurs every few minutes.

Fouled Bath Water. Birds instinctively follow their own hygiene regimens and enjoy bathing. As they bathe, the water becomes polluted by faeces that have stuck to the perianal feathers, which then find their way into the drinking water containers. For caged birds and birds in aviaries, it is disastrous for the bathwater to be the daily drinking water.

Deficient Food. Because they are caged, pet birds miss the opportunity to select their own food. They must eat what is provided and this may result in deficiencies. In nature, birds instinctively search from morning to night for the food they need for growth and energy. During the nesting period they are under enormous pressure to catch insects and bring them to their young. In the brooding period, when the young are growing, birds require more protein than in the winter when they are in a rest period. While still young, the chicks require more protein than older birds. During the autumn moulting season, when the birds begin to grow a new winter coat, the birds also need extra protein as a basic building block. When breeding canaries and budgerigars, the composition of the food is extremely important. At many times, birds require extra protein and it must be animal protein. If they do not get enough animal protein they become deficient in certain essential amino acids (e.g. lysine).

Contaminated Food. Particularly in countries where a maritime climate prevails, the increased humidity of the air, particularly on warmer days, can cause the seeds to decay. Moulds can form in seeds with more than 17% moisture. In cases of improper storage, meal mites can also be found in the feed.

Dust Production. Budgerigars and parrots produce an ultrafine, powdery dust consisting of keratin particles, which remains suspended in the air when a bioaerosal is formed. Dropping from budgerigars and canaries are much drier than pigeon droppings. The dust in bird cages is often contaminated with microbes and contains serum proteins secreted into the gut of the birds and antigens from feather mites. Many members of the parrot family and pigeons are contaminated with chlamydiae and can be life-long carriers. Chlamydiae are indifferent to drying and low temperature. The dust can remain contaminated for a long time (Von Sprockhoff 1980).

Bird Droppings. In many cases, the bird cage or aviary is cleaned of bird droppings and seed remnants no more than twice a week. This is not enough. Birds produce a large quantity of droppings every day and, by weight, half consists of microbes that can cause infections in both birds and their owners (Bourne 1975; Gerlach 1977; Graham and Graham 1978; Staib 1984). Infections can spread rapidly through a group of birds. Feed and water containers should be cleaned daily. The sand strewn on the bottom of the cage or aviary should be changed more often than is the custom.

Cages That Are Too Small. Sufficient space is necessary to maintain the physical conditions and to limit conflicts among underlings. Birds that do not have a large cage should be allowed to fly around the room for 1 or 2 h a day. For a parrot, the largest cage that can be purchased is too small for the bird to be able to expand its wings without striking the bars.

Ectoparasites. Failure to use measures to control external parasites such as lice and mites can have serious consequences. Aviaries attract large quantities of lice, mites, ticks, mosquitoes, flies and mice, all of which can carry disease (Eddie 1962; Sexton 1975). Roundworms occur in Australian budgerigars, and tapeworms sometimes occur in parrots.

Fouled Breeding Facilities. Indoor aviaries should particularly be regulated and maintained with knowledge and care. In particular, breeding cages should be clean in order to prevent parasites, since ectoparasites are responsible for many unsuccessful attempts at breeding. During the breeding season, brood boxes are scarcely cleaned. Afterwards they should always be removed and disinfected, i.e. white washed. Air in the breeding cages that is too dry may make it difficult or impossible for birds to emerge from the egg. A relative humidity of 65% is ideal; at lower temperatures this can be maintained by adding moisture to the air. In keeping older birds, on the other hand, drier air is desirable to prevent damp spots that encourage mould spores and mites. A constant temperature of at least 17°C is required for a good breeding season. For this reason indoor aviaries are often heated overnight. Particularly indoors, many unsuccessful breeding experiments occur because of lack of space, lack of daylight, and inadequate ventilation. Many breeders attempt to breed during shorter rather than longer periods, often with lack

of success. There is high mortality among young birds, since the danger of infection is great in this group and the transmission of viruses can occur quite easily. Immediately following hatching, many birds are sold, some of which will certainly be diseased.

Developing Resistance to Antibiotics. The indiscriminate use of antibiotics by dealers and bird fanciers poses a special risk. Antibiotics may be given inappropriately in low concentrations, with a resultant high percentage of resistance (80%–100%). Most popular small caged pets, i.e., birds and rodents, are seldom taken to the veterinarian, the owner generally preferring to experiment with antibiotics such as sulfa drugs and tetracycline which are available without restriction.

Trade and Transport of Birds. Customary bird-keeping practices involve much contagion. Current quarantine regulations are inadequate, contaminated birds being sold daily to the public by traders and hobbyists (Gerlach 1977; Graham and Graham 1978; Hirai et al. 1979, 1983; Panigraphy et al. 1979; Schachter et al. 1978; Schwartz and Fraser 1982; Yamashita and Hirai 1981). Shows provide opportunities for contaminated contact as, frequently, the exhibition room is too small and insufficiently ventilated. Contagion is also spread because bird fanciers, out of their love of collecting birds, show a large number of birds, trade them with one another, or sell them. Whenever pigeons are kept with other birds, *Chlamydia psittaci* infection is likely. In transporting for trade, or in the day trips that carrier pigeons make many times a year to Belgium, France, Spain, or England, the birds are sent in very large baskets, where there is ample opportunity for widespread dissemination of contaminated faeces. The risk of contamination is further magnified because a large percentage of the birds consists of yearlings, which are healthy from the standpoint of selection, but most capable of becoming infected, and, when infected, of excreting the most chlamydiae. Apart from *Chlamydia psittaci* and other bacteria, viruses can also be transmitted via formation of aerosols from dried faeces, contaminated cells from feather follicles, or contaminated food remnants. Keymer (1972) studied 345 birds post mortem and found ornithosis in 6.1% and *Yersinia pseudotuberculosis* in 2.9%. Cultures of the contents of the gut and histological study of the stomach organs were not readily feasible, due to the somewhat advanced stage of decomposition. He estimated the actual percentage of contaminated birds was higher. Salmonella infections were found in 1.4%, and *Mycobacterium avium* in 1.2% of the studied birds.

Herman (1982) warns against the risk of contamination with arboviruses. Birds can also be carriers of disease-bearing insects and together the birds and these insects act as hosts to the arboviruses that cause encephalitis, many epidemics of which occur in summer and autumn in the United States.

Preventive Measures Against Infectious and Allergic Diseases

1. All trade in birds for the pet trade should be limited to captive bred specimens.
2. Pet shops and aviaries where birds linked to cases of disease were obtained should undergo veterinary surveillance.
3. There should be obligatory case reporting of parrot disease and salmonella infection.
4. The source of any infection should be investigated. Suspect birds should be killed. Dead birds should be placed in a box with some ice-bags (definitely not in an envelope!). They should be shipped in a plastic bag to the nearest competent laboratory for necropsy and microbiological assessment.
5. Exposure of noninfected birds to potentially infected birds, or birds of unknown history, should be prevented.
6. Closed drinking water supplies for the birds should be used, with feeders in proportion to the daily intake by the birds.
7. Cages should be cleaned daily and the cage, aviary and the living room properly ventilated.

1.2.3 Contribution of Pet Birds to Biological Pollution

A canary weighs barely 18 g on average and consumes approximately 3.6 g of seed and 5.2 ml of water per day. A grass parakeet (budgerigar) weighs an average of 40 g; it eats approximately 6 g of seed and drinks 1–3 ml of water daily. A grey-and-red tail parrot weighs an average of 450 g, eats approximately 35 g of seed per day, in addition to 40 g of fruit and greens, and drinks approximately 20 ml of water daily. Birds have a high metabolic rate for their low weight. Per kilogram of body weight, the daily consumption of 200 g of food and 288 ml of water by a canary would be equivalent to 12 kg of food and 17 l of water per day for a human weighing 60 kg.

Pet birds and the insides of their cages spread more allergens and microorganisms (bacteria, moulds, and viruses) that can be inhaled inside a house than do either a cat or a dog.

Mould Spores, Bacteria, and Viruses. Bird droppings, after they have dried and during the cleaning of cages and aviaries, can disintegrate into extremely fine dust (Jones et al. 1984). Droppings from budgerigars and canaries are much drier than pigeon droppings (Blackmore 1965).

Microorganisms make up approximately half of the droppings. After drying, the bird droppings are spread as dust particles that can be contaminated, for example, with *Aspergillus fumigatus* spores (3–4 μm), *Cryptococcus neoformans* spores (2–3 μm; Staib 1984), *Chlamydia psittaci* (0.3 μm), *Mycoplasma pneumoniae, Escherichia coli* and *Salmonella typhimurium* (Wagenaar-Schaafsma et al. 1980). Since bird cages are usually kept high up in the room (125 cm), they are at our breathing level and the movements by the bird produce air currents. Food

remnants found on the cage floor are also generally contaminated. The bird ectoparasites that transmit diseases such as flies, ticks, and mosquitos can infect humans with viruses, as has been demonstrated for arboviruses. Humans can also be contaminated with Newcastle disease virus after inhaling the dust particles.

Faecal Particles from Bird Mites. Bird have mites and other ectoparasites. Faecal particles from the feather mites *Falculifer rostratus* and *Cnemidicoptus laevis*, the bloodsucking mites *Dermanyssus gallinae*, and the house mites Pyrogliphidae disintegrate into ultrafine dust particles and produce a very potent allergen that can be inhaled.

Keratin Microfibrils from the Feathers and Horny Scales from the Skin. The finest branches of a feather consist of hard keratin microfibrils (Brush 1978), which, in turn, consist of protein. Since feathers are quite durable, horny scales from the skin of canaries come loose more readily than the keratin microfibrils from the feathers. On the other hand budgerigars and parrots readily produce a powdery substance that consists of bundled keratin microfibrils with the smallest diameter of 1 μm (Marks 1984). Specialized feathers that are growing and being pulverized constantly provide the keratin that is distributed all over the bird as the feathers are preened, this keratin serving as a waterproofing for the feathers. The outer feathers of a healthy parrot have a matt surface. Pigeons have a so-called powder down and powder their feathers.

Inhaled Allergens. Keratin proteins, organic components of bird droppings, throat and nasal discharge, and anal gland products all provide allergens.

Table 1.5 summarizes the best known pollutants in indoor air. Particles smaller than 10 μm can remain suspended in air for long periods of time (suspended particulate matter). In humans, the nasopharynx cleans inhaled air of particles greater than 5 μm. Particles between 1 and 5 μm sediment to a large extent in the bronchi. Particles smaller than 1 μm reach the alveoli, most of which are exhaled. Particles between 1 and 10 μm are generally harmful to the small bronchi. Particles smaller than 3.5 μm are considered the respirable fraction, which is that part of the inhaled fraction that can penetrate to the minute air sacs.

Most of the types of suspended particulate matter in this table have fibrosing properties. Smoking in enclosed spaces, like bird keeping, increases the concentration of particulates. The health standard of particulates (0.26 mg/m^3 air) is based on preventing adverse health effects from exposure to particulates found in outside air. Peak values for three smokers in a room and for the presence of more birds in one living room are 0.5 mg/m^3 air and 0.48 mg/m^3 air, respectively. Dust particulates from bird cages and tobacco smoke are potentially more harmful than the particulates found in outdoor air (i.e. pollen grains, ash, soot, and soil).

Table 1.5. Sizes and indoor air quality standards of some airborne particulates

Airborne particulates	Particle size (largest diameter) [μm]	Smallest diameter [μm]	Health standard[a] [mg/m^3 air]
Wool fibres	500	100	
Synthetic fibres	500	100	
Paper dust	300	20	
Cotton fibres (cellulose)	500	15	
Pollen grains	60	12	
Coal dust	400	10	
Blue, brown asbestos (Hammond et al. 1979)		2	<0.1
White asbestos (chrysotile)		0.02	<0.1
Quartz	10	0.5	0.15
Fibre glass	25	6	
Rock wool, slag wool, glass wool	9	4	
Carbon black	30	5	
Suspended particulate matter (SPM)	10	0.0006	0.26
SPM from bird cages (Jones 1984, van der Wal and van de Belt 1985)	10	0.5	0.26
Most household dust on floor	1000	10	
Cigarette smoke : mainstream	1	0.1	
(Hoffmann et al. 1984) : sidestream	0.1	0.01	
Hygroscopic cigarette smoke particles[b]	3	2	
Three smokers in a room	3	0.01	0.26
Inhaled allergens in indoor air (Reed 1984)	10	0.5	0.1
Inhaled allergens from house dust mites and cats[c]	1.4	0.5	0.1
Bacteria, spores, viruses			0.1
Aspergillus fumigatus spores	3	2	0.1
Cryptococcus neoformans spores[d]	3	2	0.1
Most mould spores	5	1	0.1
Droplet foci (Riley 1959)	3	0.5	
Thermophilic actinomycete spores		0.5	0.1
Legionella pneumophilia bacteria	5	0.4	0.1
Chlamydia psittaci extracellular		0.3	0.1
Bacteria	50	0.1	0.1
Viruses	0.8	0.01	0.1

[a]Daily average.
[b]After remaining in the airways for 2-3 s (Davies 1974).
[c]Approximately 50% of particles (Reed 1984).
[d]From pigeon droppings (Staib 1984).

Preventive Measures Against Inhaled Particles

1. Ventilation standards of pet shops and pet birds' exhibition rooms should be surveyed.
2. Smoking should be prohibited if these standards are insufficient.

Birds As a Source of Respiratory and Intestinal Infections and Allergic Diseases in Humans. In households where birds are kept, and in occupations such as the pet bird trade and the poultry industry with exposure to bird products, infections occur as the result of diminished indoor air and hand hygiene (Altamura 1982;

Andrews et al. 1981). Infectious diseases can develop in humans from contamination with microbes which invade tissue via inhalation, ingestion, from the hands, or through wounds in the skin.

Inhalation of Pathogenic Organisms. Tropical birds bring the greatest risk of infection to humans. Contamination usually occurs from inhalation of an infectious aerosol (Willems et al. 1986). Air circulation helps to prevent a build-up of contaminated air. Parrot disease tends to be observed particularly in the winter, when there is more contact between a bird and its owner indoors, the rate of air circulation is lower (as low as 0.15 m/s), the dust content in the air is higher due to the low relative humidity of the air, and both birds and humans are exposed to greater fluctuations of temperature. Over many years, bird keepers inhale more dust particles, allergens, and microorganisms than those who do not keep birds. When there is less nasal breathing as a result of chronic allergic inflammation of the mucous membrane of the nose, less effective air purification takes place. While it is certainly true that bird keepers exhibit variable immunity (McSharry et al. 1983), in the long run, the clearance of their minute air sacs becomes diminished leading to congestion of the small bronchi, intracellular infections from slightly virulent microbes and a further overburdening of the cellular defences. In the minute air sacs in particular, the macrophages (scavenger cells) bear the bulk of the defensive burden.

Many lung macrophages are destroyed by the microbes and allergens they engulf, causing local granulomatous reactions and thickening and stiffening of the lining of the air sacs of the lungs which leads to progressive breathlessness. Microbes can enter the bloodstream during infections. The valves and the lining of the heart as well as arteries and veins in various places in the body are injured the most (Birkhead and Apostolov 1974; Bromage et al. 1980; Carr Locke 1976; Coll 1967; Darougar et al. 1978; Dick et al. 1977; Hamilton 1975; Jariwalla et al. 1980; Jones et al. 1982b; Kundu and Scott 1979; Laidlow and Mulligan 1975; Lancet 1980; Levisson et al. 1971; Thomas et al. 1977; Vosti and Roffwarg 1961; Ward 1974, 1975; Yow et al. 1959). If *Chlamydia psittaci* enters the bloodstream for a short, period as a result of a sore throat or pneumonia during the 8th week of pregnancy it can cause inflammation of the womb, leading to spontaneous abortion (Beer et al. 1982; Johnson et al. 1985; Page and Smith 1974; Storz et al. 1968a). A so-called flu in a pregnant bird keeper can thus have serious consequences. More epidemiological investigations of the scope of these possible complications are needed (Ward 1978).

Ingestion of Microorganisms. Repeated common colds and bronchitis also affect the alimentary canals, since nasal mucus and sputum are swallowed with the saliva. An empty stomach contains very few bacteria because of the bacteria-killing and growth-inhibiting effect of substances in gastric juice. Only spores, acid-resistant bacteria (tubercle bacilli), and acid-tolerant lactobacilli can withstand the low pH. When driking fluids this defensive factor is by-passed and at meals the pH of the food mixture is insufficiently lowered so that parasites can pass through the stomach. Small amounts of virulent bacteria, such as *Salmonella typhimurium*, in

the food can quickly lead to enteritis. Greater amounts of virulent bacteria or viruses are known to pass the stomach barrier upon repeated ingestion, overcome the colonization resistance and immune secretory system of the intestines, and thus cause enteritis.

Less virulent bacteria, chlamydiae, or viruses lead to less severe types of enteritis, and are much more difficult, if at all possible, to culture from faeces.

Inadequate Hand Hygiene. After handling birds or their cages, the bird keeper should always wash his hands, not only prior to eating or preparing a meal. Pigeon fanciers and breeders of tropical birds spend many evenings near or even in aviaries, bird rooms, bird cellars, dovecotes, or lofts. It is impossible for them to maintain good hand hygiene. They do not even wash their hands thoroughly all the time. This may result in respiratory and intestinal infections. Conjunctivitis in bird keepers can also be caused by decreased hand hygiene through the reduced clearance of the conjunctiva by regular microbial overburdening.

Semen, the vagina, and the external genital tract of both men and women can become contaminated as a result of poor hand hygiene, resulting in an increase of infections (Bowen et al. 1978; Friberg et al. 1985; Storz et al. 1968b). Urethritis and prostatitis can result in males and salpingitis in females. Infections ascending the vagina cause inflammation of the oviducts, resulting in salpingitis and, after repeated episodes, infertility (Sandler 1989). Contamination of the vagina with *Chlamydia psittaci* spores through improper hand hygiene by bird keepers/breeders may cause constriction of the oviducts similar to that caused by *Chlamydia trachomatis* (Jones et al. 1982a).

Preventive Measures Against Infections and Allergic Diseases

1. The public should be educated about the danger of household or occupational exposure to infected pet birds.
2. Birds should not be kept in bedrooms.
3. Absorbent sand in cages should not be used. Birds can live without sand. It is mainly the sand that can turn a cage into a dustbin since absorbent sand can quickly become heavily contaminated, because the droppings dry out and are hard to see.
4. The cage should be cleaned daily.

1.3 Infectious Diseases of Pet Birds That Can Be Transmitted

1.3.1 Introduction

A large number of infectious diseases have been reported to have been transferred from birds to humans (Fiennes 1978; Herman 1982; Storz 1971). Kronberger (1969) found that 22.6% of the birds he studied died of diseases contagious both

to animals and humans. This fact clearly underlines the importance of infectious diseases that can be transmitted from pet birds to man. These diseases are as follows:

— Parrot disease (psittacosis)
— Newcastle conjunctivitis
— Inflammation of the stomach and intestine due to *Salmonella typhimurium*
— Enteritis caused by yersiniae
— Pasteurellosis
— Streptococcus and staphylococcus skin infections
— Erysipeloid
— Mould infections
— Toxoplasmosis
— *Mycoplasma pneumoniae*
— *Mycobacterium avium*
— Arbovirus encephalitis

1.3.2 Parrot Disease (Psittacosis)

Parrot disease is the best studied disease and is caused by *Chlamydia psittaci*. It can be particularly dangerous to humans when contamination occurs as a result of keeping parrots or budgerigars. As has often been observed, more serious forms of this disease can have both an acute fulminating and a devastating course of longer duration; both courses end in death. (Bowman et al. 1973; Byrom et al. 1979; Kuritsky et al. 1984).

Disease Manifestations. Parrot disease is an acute generalized infectious disease with fever, headache and early pneumonic involvement. The diagnostic incidence in general practice is about 0.5 patients per 1000 per year. Human infections may be severe, but are most often mild in character and death is rare. The incubation period is from 4 to 15 days, commonly 10 days. The period of communicability is primarily during the acute illness, especially when the patient has paroxysmal coughing. The disease must be reported to the health authorities.

Mode of Transmission. Infection is usually acquired by inhalation of the agent from desiccated droppings of infected birds in an enclosed space. DeSchrijver (1987) reported an epidemic of ornithosis affecting people who had attended an exhibition of 500 birds in a small room in Zwijndrecht, near Antwerp, Belgium. Of the 1000 visitors, 8% were affected about 2 weeks after their visit. A still higher percentage (17%) of the exposers acquired the disease. One patient died.

Pet birds are the most frequent source of infectious diseases, although laboratory infections have also occurred and transmission from person to person is possible. General diseases of long duration in the form of atypical pneumonia are common, and even local epidemics in which the disease spreads from one individual to another have been reported. Often the acute phase of the disease is

followed by chronic complaints and short periods of recurrence and flu-like symptoms. Nagington (1984) obtained high titres with complement fixation reactions in 10% of the total population of Cambridgeshire from which he concluded that infection with *Chlamydia psittaci* has an endemic character in these areas. The number of infections by *Chlamydia psittaci* is much higher than the number of cases registered by general medical practitioners and clinics.

Immunity. Immunity is slight and of limited duration. Insufficient antibody formation is possibly one explanation for the slight immune response and high percentage of latent infections (Aitken 1981).

Preventive Measures. In the Netherlands all imported birds of the parrot family must undergo a mandatory quarantine period of 6 weeks. However, this is related to the risk of NDV to the fowl (see Sect. 1.3.3) and not to the risk of parrot disease in humans, since NDV is notifiable. While there are import restrictions for several species of parrots and budgerigars to avoid utilisation incompatible with their survival, many other species of parrots and budgerigars are detrimentally affected by the pet trade. Previous health restrictions on imports of parrot-like birds from 1973 to 1976 have been removed. Although the world pet bird trade is concentrated in Belgium, the United Kingdom and the Netherlands, there is no surveillance of pet shops and the public is not educated about the danger of household exposure to infected birds of the parrot family. Apparently healthy parrots and budgerigars, also pigeons and other birds may shed the disease agent intermittently throughout their infection period and sometimes continuously for weeks or months. It is often the case that infected birds are sold to the public.

Virulence and Latency of the Virus-Like Microorganisms. In culture, cells infected with chlamydiae are easily distinguished since they are swollen by the enclosed bodies. In the lungs, *Chlamydia psittaci* may be toxic for, and destroy, the scavenger cells that ingest them. The chlamydiae remain alive within the scavenger cells but are not capable of dividing, possibly because during ingestion the surface receptors are damaged and the capsule can no longer expand. Scavenger cells that are destroyed leave the body with the enclosed chlamydiae mainly through the intestinal tract.

1.3.3 Newcastle Disease Virus Conjunctivitis

NDV causes a fatal disease in fowl. A variety of gallinaceous species as well as sparrows, pheasants, pigeons and parrots can be infected by this virus. NDV is a paramyxovirus and presents a possible risk to breeders and keepers of chickens in particular.

Disease Manifestations. In humans the infection causes limited acute follicular conjunctivitis of one eye in most cases or a slight flu lasting one week.

Mode of Transmission. Contamination in humans arises as a result of direct contact with the infected birds or the virus can be airborne (particularly when spraying a vaccine of the virus). The incubation period is 1 or 2 days. Transmission from person to person is not excluded.

Preventive Measures. Because of the risk of NDV to the fowl in the Netherlands, all imported birds of the parrot family must undergo a mandatory quarantine period of 6 weeks. All birds dying during this period are studied for traces of NDV. In 1972, NDV was found in 16% of parrots presented for dissection to the Health Department's Fowl Division. Among the parrots that survive quarantine, the disease probably occurs rarely. Among infected birds, paralysis with an abnormal position of the head occurs first, followed by bleeding and inflammation of the intestinal tract, affected lungs and a generally poor condition.

1.3.4 Inflammation of the Stomach and Intestine Due to *Salmonella typhimurium*

Disease Manifestations. Kaye et al. (1961) described an intestinal infection by *Salmonella typhimurium* in a 7-month-old child who crawled on the floor directly under a caged budgerigar, thus coming into contact with bird droppings. Large numbers of *Salmonella typhimurium* organisms were isolated from the budgerigar's faeces. The child hat not come into contact with the cage or the budgerigar itself.

Mode of Transmission. Humans can infect themselves orally with Salmonella bacteria. Sporadic cases of infection occur from recontamination within the kitchen after cooking is completed. Members of the parrot family, in particular, and also canaries appear to be carriers of salmonella. Mortality among these birds can reach 50% or more. Birds that have survived the acute infection can remain carriers for a short time or even permanently, and thus provide impetus for new cases of disease again and again. In most cases *Salmonella typhimurium* is propagated.

Preventive Measures. Recognition, control and prevention of salmonella infections among household pets. Infections among chicks, ducklings and turtle doves are particularly common.

1.3.5 Enteritis Caused by Yersiniae

Disease Manifestations. (Pseudo) appendicitis with slight fever due to the invasion of the distal small intestine and intestinal lymph nodes is occasionally the result of intestinal infection by yersiniae.

Mode of Transmission. Humans can contaminate themselves orally with these organisms from the faeces excreted by affected birds. Infections with *Yersinia*

pseudotuberculosis occur regularly in canaries and song-birds. Yersinia has also been isolated from birds. These infections do not occur frequently in parrots. Canaries are often kept in aviaries outdoors so that the chance of contamination through pollution of food on the floor could be greater from mouse faeces. The number of isolated cases is highest in the winter months, perhaps partly because mice are then more likely to go to aviaries to collect bits of food (Borst et al. 1977).

Preventive Measures. Keep mice out of the aviaries. Wash hands before and after the handling of birds.

1.3.6 Pasteurellosis

Disease Manifestations. Infection with *Pasteurella multocida* can lead to local boil formation in humans and inflammation of lymph nodes. Now and then the organism can cause mild infections of the airways.

Mode of Transmission. Whenever pigeons or ornamental birds are bitten by a dog or cat, there is a high risk to the birds of sepsis and death as a result of infection from these bacteria, which occur as normal oral flora in dogs and cats. If other birds peck at birds that have died of pasteurellosis this can lead to new outbreaks of infection in an aviary.

Preventive Measures. Dead birds should be removed quickly and carefully.

1.3.7 Streptococcus and Staphylococcus Skin Infections

Disease Manifestations. Streptococcus and staphylococcus skin infections can lead to the formation of boils. These bacteria are not infrequently resistant to antibiotics if the bird has previously been treated with antibiotics.

Mode of Transmission. The bacteria may be transmitted via the hands. In parrots and budgerigars these bacteria cause abscessing infections, which, when localized orally, lead to a risk of transmission if the owner passes food to the bird with his mouth.

Preventive Measures. Wash hands before and after handling of the birds. It is unwise to pass food to a bird with the mouth.

1.3.8 Erysipeloid

Disease Manifestations. In humans *Erysipelothrix rhusiopathia* can cause local skin infections through small wounds or from pricks with infected needles. The

fingers in particular become involved, as do the backs of the hands, and the infection consists of a few itching patches or purple erythematous plaques, which spread slowly and become white from the centre. There are seldom any generalized symptoms. Endocarditis can occur eventually if the condition is not treated properly.

Mode of Transmission. The bacteria may be transmitted via the hands. Infection of birds with these bacteria is most often sepsis.

Preventive Measures. Washing, especially with small wounds or pricks.

1.3.9 Mould Infections

Disease Manifestations. Aspergillus fumigatus lives and feeds on the dead and putrefying tissues of animals or plants, as do all moulds and infects patients with lowered resistance or a previously existing lung condition. Both direct mould infection and secondary allergic reactions can produce syndromes in humans. Infection of the central nervous system with *Cryptococcus neoformans* usually occurs after the patient has recovered from a recent upper respiratory or lung infection, but it can also occur as a result of stress or lowered resistance due to a previously existing focus in the airways.

Mode of Transmission. Inhalation of spores may lead to transmission of the moulds. Many moulds and yeasts develop optimally in bird droppings; *Cryptococcus neoformans* is particularly well known as a saprophyte in pigeon faeces, even when the birds themselves are not sick. In birds *Aspergillus fumigatus* can cause widespread effects in the lung. The mere isolation of *Aspergillus fumigatus* spores from tracheal smears is not sufficient proof of aspergillosis in a sick bird. The disease first occurs in birds after massive contamination and in connection with lowered resistance. In an environment so full of spores that a bird develops aspergillosis, humans are also at (serious) risk. It is also probable that *Candida albicans* infections occur through airborne bird contacts. Since *Candida albicans* is normally present in the human intestines, this risk is difficult to evaluate.

Preventive Measures. To achieve optimal conditions for the birds, it is necessary to remove the bird droppings and to clean the cage daily. Here again, it is mainly the *sand* that can turn a cage into a dustbin, so it is advisable to line the bottom of the cage with non-woven tissues containing disinfectant. Birds can live without sand. Grit and a cuttle bone can be hung in the cage so that the bird also has easy access to calcium.

1.3.10 Toxoplasmosis

Disease Manifestations. Toxoplasmosis is a disease affecting mammals and birds. Postnatal infections are usually mild and may go undetected. Infections may on occasion, be acute, with fever or inflammation of lymph nodes persisting for several days or weeks. Infection in humans is common, but clinical disease exceptional. Because the mode of transmission of *Toxoplasma gondii* is unclear, and because of the possibility of close contact with humans, it is recommended that all remaining birds in an aviary infected with toxoplasmosis be disposed of.

Mode of Transmission. Toxoplasma gondii is transmitted to humans via undercooked meat, contaminated soil, or by direct contact. In birds, toxoplasmosis leads to the formation of cysts and pseudocysts with foci of infection in the muscles, heart, liver, lungs, intestinal walls, kidneys and brain. Toxoplasmosis is particularly prevalent among canaries. Pneumonia is repeatedly widespread, with a great deal of infection and mortification, and leads to a high death rate in canaries. Tissue preparations of lung infections have shown that pseudocysts occur freely in the airways (Zwart 1986, personal communication). The pseudocysts are released with every sneeze of the bird, and thus the disease can be spread through a group of canaries. These large scale infections occur particularly when the canaries sit only 10-15 cm from one another. The risk of contamination in the keeper is much lower, since the keeper is always at least 50–100 cm away from the birds. Subacute infection of birds occur with eye involvement, such as conjunctivitis, blurred vision, spots in the anterior eye chamber, inflammation of the iris and finally blindness.

Preventive Measures. Prevent exposure of previous noninfected canaries to potentially infected canaries. Because of close contact with humans, it is recommended as noted above that all remaining birds in an aviary infected with toxoplasmosis be disposed of.

1.3.11 *Mycoplasma Pneumoniae*

Birds are a significant reservoir of various mycoplasma strains. A large number of avian types are known for pigeons and poultry. As far as is known these strains do not seem to be a source of contagion for humans. Gerlach (1977) studied 397 pigeons from 50 dovecotes and found avian mycoplasma in 262 pigeons. No mycoplasma could be determined in only five dovecotes. Mycoplasma is slightly pathogenic for pigeons.

1.3.12 *Mycobacterium Avium*

In avian tuberculosis, the tubercles can occur in all organs. Most characteristically, the foci of infection in birds occur in the liver and intestinal tract. The tubercle bacilli are spread via the extremely infectious faeces or from open foci in the lungs. Humans become infected by these tubercle bacilli through the mouth. In about 8% of all cases of tuberculosis in humans, avian tuberculosis is probably the cause (Borst 1973). In children, neck gland infections occur as a result of avian mycobacteria. When prior lung disease is present, such as pneumoconiosis, bronchitis and emphysema, or tubercular sequela, these mycobacteria can also cause further lung problems. As a result of the major decline in human and bovine infections, the significance of avian infection has become greater in relative terms. Recently two patients with lethal disseminated *Mycobacterium avium* complex infections and an impaired immune system were reported, one a 21-year-old female who owned a parrot (Schneider et al. 1988), the other a 55-year-old man with eosinophilia (Krulder and Moffie 1988). Though the clinical picture showed remarkable resemblance to the acquired immune deficiency syndrome, this diagnosis could not be confirmed. The authors assumed that the immunodeficiency was a sequel of the infection with *Mycobacterium avium* complex. In my opinion, this was certainly the case for the 21-year-old woman, in whom the immunodeficiency was the sequel of chronic allergic lung disease and the cause of the dissemination of the *Mycobacterium avium* complex infection (Holst 1988).

1.3.13 Arbovirus Encephalitis

Tropical birds and their insects, mosquitos, and sand flies are reservoirs of Eastern, Western, Venezuela, St. Louis, California, Japanese B, Murray Valley, and tickborne arboviruses that can cause encephalitis in humans (Herman 1982).

1.4 Allergic Diseases That Can Be Caused by Pet Birds

1.4.1 Introduction

The three most serious degrees of chronic non-specific lung disease (CNSLD) occur in almost 10% of the population in the Netherlands (van der Lende 1969; van der Lende and Orie 1975). The cause is attributed to differences in the indoor air hygiene of residences due to chemical (Biersteker and de Graaf 1967) and/or biological pollution (Dijkman 1977). The presence of pets, particularly for the sake of children, is just such a biological factor. Of all pets the bird is the most popular in the Netherlands, and it spreads the most amount of dust. A partial explanation for the enormous number of CNSLD patients in the Netherlands might be found here. More breeding of birds is done than of any other pet; the hobby involves elderly people as well as children, and after the breeding period, the birds are given away to other family members.

Production of antibodies begins in the unborn child around the 11th week of pregnancy. Specific antibodies can be found in umbilical cord blood. Soon after birth the mucous membrane of the airways and alimentary canal must form a barrier against harmful bacteria, toxins, and antigens. Babies under the age of 6 months are not very well protected and, as a result of very early contact with animal skin cells, high antibody production occurs very quickly.

Viral infections can also disturb the immunoregulation of the very young, promoting the formation of antibodies to inhaled allergens. The factors that lead to a constitutional tendency to develop an allergic disease are not known. Familial clustering of lung hyperreactivity, and perhaps lung tumours also, could have both a hereditary and an exogenous familial basis. Incidentally, this same discussion occurred before the tubercle bacillus was identified as the cause of tuberculosis.

Felderhof-Hoytema (1987) carried out a study on 699 healthy school children between the ages of 4 and 16 years in The Hague. Of these children, 39.6% had birds at home. Among the children with birds at home, symptoms of CNSLD were observed in 50.9%, in contrast to 19% of children without birds at home.

Quanjer (1987) reported CNSLD symptoms in around 20% of school children in the age group of 11–19 years.

The various types of allergic diseases that can be caused by pet birds are:

— Allergic Rhinitis and Nasal Polyps
— Allergic Asthma
— Allergic Alveolitis
— Granulomas and Irreversible Lung Fibrosis

1.4.2 Allergic Rhinitis and Nasal Polyps

Disease Manifestations. After being exposed for a period of several weeks to several years to allergens (ultrafine dust from the faecal particles of feather mites *Falculifer rostratus* and *Cnemidicoptes laevis* and from the blood-sucking mites *Dermanyssus gallinae*; cells from feather follicles; horny just particles; proteins from dried bird droppings), many bird keepers develop complaints such as sneezing, coughing, wheezing, itchy eyes and ears, urticaria, inflammation of the eyes and face, eruptions or eczema.

The immune system is still labile in healthy young children, and toddlers readily develop strong allergic and delayed asthmatic reactions. This is the allergic basis for up to 70% of children who seem to always have colds.

Nasal polyps are often found in allergic patients; they occur frequently at a young age, but not during childhood and may occur together with bronchial asthma, which demonstrates that they are an expression of the involvement of the whole respiratory tract. Nasal polyps are often precursors of delayed asthma and occur frequently in conjunction with house dust mite allergy.

Mode of Transmission. Inhalation of house dust and allergens.

1.4.3 Allergic Asthma

Disease Manifestations. Both early and delayed asthmatic reactions are seen as allergic responses to household dust, mould spores, and excreta of mites and birds. (Meyer and Eddie 1960; Muller et al. 1987; Pelikan et al. 1983).

Bar-Sela et al. (1984) studied ten male and six female chicken breeders between the ages of 11 and 47 years who had complained of allergic rhinitis and/or allergic asthma following exposure to bird excreta. The controls were 16 allergic patient, matched by age and sex, who had not been exposed to bird excreta and 12 veterinarians who were free of complaints. According to the results of skin tests, only the group of workers in the bird industry had specific antibodies against Northern bird mite (*Ornithonyssus sylviarum*). Allergic complaints occurred on average after 10 years of exposure to bird excreta.

Lutsky et al. (1984) stated that bird mites are not considered a component of house dust and their potential allergic effects have therefore been studied too little in allergic patients.

Mode of Transmission. Inhalation of mould spores and excretory products of house mites or bird mites.

1.4.4 Allergic Alveolitis

Hendrick et al. (1978) calculated that budgerigar lung was a much more common phenomenon in England than farmer's lung, and that it was the most frequent type of allergic alveolitis. A constantly maintained antigen level in the bronchioli and alveoli, such as that found in bird keepers, leads to allergic alveolitis, which is characterized by a strong reduction in helper/suppressor T-cell ratio in the wash from bronchoalveolar lavage (Keller et al. 1984). Absolute helper T-cell shortages lead to an increased risk of neoplasms.

Disease Manifestations. Inflammation of the walls of the minute air sacs of the lung, the sites of gaseous exchange, is caused by inhaled inorganic dusts such as coal dust, silica and asbestos or by inhaled organic dusts from mouldy hay, straw, dovecotes or the cages of pet birds. Chronic alveolitis progresses slowly to the state of fibrosis, emphysema and bronchiectasis (Lee et al. 1983).

Mode of Transmission. Daily contact with bird antigens is much more intense when a person has one or several birds in his living room than when a person goes briefly to the dovecote to clean it daily, as is usually the case with most pigeon fanciers. Reactions in the lungs of owners of budgerigars and canaries are found much more frequently than in those of pigeon fanciers.

1.4.5 Granulomas and Irreversible Lung Fibrosis

Disease Manifestations. The chronic granulomatous pulmonary inflammatory response observed in patients with allergic alveolitis has suggested a role of cell-mediated immunity. Delayed immune reactions occur, through which stimulated T-cells are produced by antigens, which form a cell infiltrate around the antigens. This type of reaction is characterized by the formation of granulomas in the lungs, and eventually irreversible lung fibrosis (Bütikofer and de Weck 1969; Pepys and Turner-Warwick 1975).

2 Survey of Patients in General Practice

2.1 Introduction

As a general medical practitioner with about 2000 patients in Rijswijk-Steenvoorde, The Hague-Moerwijk and Morgenstond, I began to sense differences in morbidity (particularly from respiratory diseases) between people keeping birds as pets and people who had no pet birds in their houses. As a result I carried out a survey of my practice during a 10-year period looking at the keeping of dogs, cats, birds and rodents. Smoking habits and the social class of patients were also noted. This chapter describes the study methods and some of the main results.

2.2 Methods

Duration of Survey. The main survey period ran from 1972 to 1981 with some analyses incorporating data collected in 1971, 1982 and 1983.

Risk Factors. Data were recorded on sex, age, smoking habits, number of persons per household and occupation of the principal wage earner of the household. In addition, a history of keeping dogs, cats, birds and rodents in each year of the survey was recorded by oral interview during office visits, and was later confirmed by writing to each household member in 1982. The number of pets kept in each year was recorded as well as the locations where they were kept (e.g. the children's bedroom). Appendix B includes a translation of the letter sent to the patients.

Definition of a Smoker. A smoker is defined as a person who has smoked at least 100 cigarettes in his lifetime and still smokes daily.

Definition of Pet Keeper. A person was defined to be a bird keeper if there were caged birds in the home for at least 6 consecutive months. The same definition was used for other pet ownership. Information about the extent of bird keeping and other pet ownership in the whole practice population from 1972 to 1981 is given in Tables 2.2–2.6.

Endpoints. The following occurrences during the study period were used for analysis: death under 60 years of age; newly diagnosed malignant tumour; nasal polyps that were newly diagnosed and removed; spontaneous abortion (as a form of intra-uterine death); immature parturition; perinatal death; infertility. The diagnoses were all confirmed by relevant specialists.

Relationship of Mortality and Morbidity to Pet Keeping. Results of analyses comparing the keeping of pets to mortality and morbidity are given in Tables 2.7–2.15. The period of exposure to bird keeping considered varied according to the endpoints studied (see Table 2.1).

The period of 5–14 years' exposure prior to diagnosis was used in the case of cancer for two reasons. Firstly, it takes at least 5 years (25–30 cell divisions) before a tumour in epithelial cells becomes detectable by X-ray examination. Secondly, the latency period for lung cancer, which is usually about 30 years for cigarette smoking alone, can be considerably reduced where there is combination of cigarette smoking and lung infections to about 10 years (Polednak 1974).

The third year prior to death in cases of death before age 60 years and before the onset of subacute diseases such as nasal polyps was used as the period of exposure considered on the somewhat arbitrary basis that if pet keeping had given rise to chronic and sometimes fatal diseases there could have been more intensive contact with pets over a period of several years. People with more intensive pet contact own their pets mostly for longer periods. The third year before was also chosen because it is closer to diagnosis than the 5–14 years before diagnosis which is used in the case of cancer. In the four cases of death during the first year of life (Table 2.8) the year prior to birth was used.

Exposure during the year before pathological miscarriage was used because the latency period for possible effects of infectious diseases is short. In the case of childlessness or infertility after some years of marriage, use of this exposure

Table 2.1. Period of exposure to pet keeping by endpoints studied

Endpoints	Period of exposure	
	Patients	Rest of general practice population
Cancer	5-14 years before diagnosis	1972-1981
Death before age 60	During the third year before death	1981
Removed nasal polyps	During the third year before removal	1981
Live birth, childlessness, infertility, or pathological miscarriage	During the year before occurrence	1981

definition was more arbitrary, but not crucial since most people, especially married couples, who have pets keep them for several years.

Information outside the period 1972–1981 was not available for the whole of the general practice population, only for those patients with the various endpoints studied. For this reason, exposure from 1972 to 1981 was used when making comparisons with cancer patients and exposure during 1981 when making other comparisons. Since there was a general tendency for pet keeping to become more common over the study period (see Table 2.5), the resulting comparisons should be somewhat conservative.

Statistical Methods. The methods used and the reasons for using them are described in detail in Appendix A. Briefly, the observed incidence of an endpoint among a subset of the population (e.g. bird keepers) was compared with that expected among the total general practice population after adjustment for age (at diagnosis or at time of survey, as appropriate). Adjustment was normally in 10-year age groups but age groups were combined where numbers at risk were low. Two-tailed p values were calculated based on standard methodology for stratified contingency tables. In the case of malignant tumours the observed incidence was also compared with an expected value based on national clinical incidence. Additional analyses, stratified according to age (in 10-year periods), sex, social status (upper, middle, lower) and smoking habits in 1972 (never smoked, ever smoked), were also carried out for certain endpoints. When correlating the distribution of one risk factor with the distribution of another risk factor (e.g. the percentage of smokers among bird keepers) percentages were standardized by 10-year age groups.

2.3 Results

2.3.1 Distribution of Risk Factors Among the General Practice Population

Table 2.2 gives the distribution of the general practice population by age, sex, smoking and bird keeping in 1981. Of the 944 men, 34% kept birds and 40% smoked; of the 983 women, 32% kept birds and 27% smoked. In both sexes, bird keeping was rather more common in those aged under 50 than in older people. The average age of bird keepers was 32.8 in men and 33.8 in women, somewhat younger than the average age of those who did not keep birds 38.2 year in men and 40.8 years in women. Smoking was most common in men aged over 20 years and in women aged 20–59 years. Little relationship was seen between smoking and bird keeping; the percentage of smokers among bird keepers was close to that of smokers among the whole general practice population.

Table 2.3 shows the distribution of ownership of dogs, cats, rodents and of any pet (including birds). Because of ownership of two or more types of pet, the numbers keeping any pet do not coincide with the sum of the numbers keeping

Table 2.2. Distribution of general practice by age, sex, smoking and bird keeping in 1981

	Age group (years)								
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70+	Total
Male									
Total number	101	134	178	140	103	123	129	36	944
% in age group	11	14	19	15	11	13	14	4	100
Bird keepers	39	54	66	50	38	37	30	5	319
% by age group	39	40	37	36	37	30	23	14	34
Smokers	0	22	83	72	51	70	58	17	373
% by age group	0	16	47	51	50	57	45	47	40
Smokers and bird keepers	0	9	31	31	19	25	15	2	132
% by age group	0	7	17	22	18	20	12	6	14
% of bird keepers who smoke by age group	0	17	47	62	50	68	50	40	43[a]
Female									
Total number	113	105	174	134	94	168	135	60	983
% in age group	11	11	18	14	10	17	14	6	100
Bird keepers	46	40	66	47	34	43	30	9	315
% by age group	41	38	38	35	36	26	22	15	32
Smokers	0	23	67	57	33	54	29	3	266
% by age group	0	22	39	43	35	32	21	5	27
Smokers and bird keepers	0	5	22	18	11	13	7	0	76
% by age group	0	5	13	13	12	8	5	0	8
% of bird keepers who smoke by age group	0	13	33	38	32	30	23	0	24[a]

[a]Standardized to the overall age distribution for each sex.

each of the four types. Among both sexes, dog keepers (24% of men and 22% of women) were next most common after bird keepers, with cat keepers next (15% of men and 14% of women) and rodent keepers (7% of each sex) least common. Compared with bird keepers, cat keepers and particularly rodent keepers were younger, with dog keepers about the same average age.

Table 2.4 compares age-standardized percentages of smokers among people who keep birds, dogs, cats, rodents or no pets. Although there was a clear tendency for dog keepers and, in males, cat keepers, to be more often smokers than average, no such tendency was seen for bird keepers.

Table 2.5 shows some increase over the study period in the percentage of the practice who kept birds and cats, with little evidence of a trend for dogs and rodents. National data also show an increase in animal ownership over his period.

The family practitioner is in a good position to classify households in his practice by social class since he is familiar with the (latest) occupation and life

Table 2.3. Distribution of general practice by pet keeping in 1981

	Age group (years)								
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70+	Total
Men									
Dog keepers	23	46	43	26	30	25	27	3	223
% by age group	23	34	24	19	29	20	21	8	24
Cat keepers	18	30	24	27	22	14	6	2	143
% by age group	18	22	13	19	21	11	5	6	15
Rodent keepers	13	12	14	9	9	7	1	0	65
% by age group	13	9	8	6	9	6	1	0	7
Bird keepers	39	54	66	50	38	37	30	5	319
% by age group	39	40	37	36	37	30	23	14	34
Keepers of any pet	62	99	107	85	68	83	49	10	563
% by age group	61	74	60	61	66	67	38	28	60
Keepers of no pet	39	35	71	55	35	40	80	26	381
% by age group	39	26	40	39	34	33	62	72	40
Women									
Dog keepers	26	26	46	31	28	33	22	4	216
% by age group	23	25	26	23	30	20	16	7	22
Cat keepers	25	12	33	26	17	18	9	2	142
% by age group	22	11	19	19	18	11	7	3	14
Rodent keepers	12	18	13	12	9	6	0	0	70
% by age group	11	17	7	9	10	4	0	0	7
Bird keepers	46	40	66	47	34	43	30	9	315
% by age group	41	38	38	35	36	26	22	15	32
Keepers of any pet	76	73	106	82	63	77	46	12	535
% by age group	67	70	61	61	67	46	34	20	54
Keepers of no pet	37	32	68	52	31	91	89	48	448
% by age group	33	30	39	39	33	54	66	80	46

Table 2.4. Age-standardized percentages of smokers by pet keeping in 1981[a]

Sex	Bird keeper	Dog keeper	Cat keeper	Rodent keeper	Any pets	No pets	Whole population
Male	48	56	57	50	47	40	44
Female	27	38	32	22	32	29	31

[a]Standardized to the sex-specific age distribution of those aged 10 years or over.

Table 2.5. Change in percentage of pet keepers from 1972 to 1981[a]

Year	Bird keeper	Dog keeper	Cat keeper	Rodent keeper	Any pets	No pets
1972	26	21	10	6	50	50
1976	27	22	12	9	52	48
1981	33	22	15	7	56	44

[a]Results are for sexes combined.

Table 2.6. Number of pet keepers by social class in 1981[a]

	Bird keeper	Dog keeper	Cat keeper	Rodent keeper	Any Pets	No pets	Total	% of all
Upper class								
Scientific and professional occupations	1	8	4	4	16	15	31	2
Upper level employees	46	37	13	16	84	142	226	11
Total	47	45	17	20	100	157	257	13
As %	18	18	7	8	39	61	100	
Middle class								
Independent business people in agriculture	36	11	11	14	56	36	92	5
Independent business people in industry or services	26	12	5	0	34	37	71	4
Mid-level employees	157	90	105	36	274	214	488	25
Total	219	113	121	50	364	287	651	33
As %	34	17	19	8	56	44	100	
Lower class								
Lower-level employees	163	111	74	43	259	168	427	21
Skilled/semi-skilled workers	84	44	33	25	134	37	171	9
Agricultural workers	10	6	3	2	10	1	11	1
Unskilled workers	45	28	15	4	83	23	106	5
Total	302	189	125	74	486	229	715	36
As %	42	26	17	10	68	32	100	
Unemployed/retired								
Total	90	94	33	0	163	204	367	18
As %	25	26	9	0	44	56	100	
All social classes								
Total	658	441	296	144	1113	877	1990	100
As %	33	22	15	7	56	44	100	

[a]Results are for sexes combined.

style (residential environment, estimated income) of the principal wage earner in each household. In order to do this, he can make use of the list of classification of occupations (CBS 1971) and on this basis, divide the population into upper, middle and lower classes. As shown in Table 2.6, 13% of the practice could be classified as upper class, 33% as middle class and 36% as lower class; the remaining 18% were either unemployed or retired. There is a clear increase in the percentage of pet keepers with decreasing social class: for keepers of any pets the figures were 39%, 56% and 68% for upper, middle and lower class, respectively; for bird keepers a similar trend is seen, 18%, 34% and 42% respectively. Of the 11 agricultural workers, 10 (91%) kept birds.

The percentage of bird keepers in 1981 was inversely related to the average age in households where birds were kept. For households with average age 10–19 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years and over 70 years the percentages where birds were kept were 77%, 60%, 50%, 45%, 41%, 30% and 27%, respectively. Of the total 804 households, birds were kept in 392. In 71 (18%) of these, birds were bred. In households where birds were bred, they were more frequently kept in the bedroom (55%) than in households where they were kept but not bred (34%). This suggests that though bird breeders have more intensive contact with birds than other bird keepers they show no increased awareness of hygiene.

2.3.2 Mortality Before Age 60

During the survey period 28 deaths occurred before age 60 years, of which 19 were in men and 9 in women. As shown in Table 2.7, there was no significant increase in death rates among those who kept dogs, cats or rodents, but there was a significant increase, in males and in both sexes, among those who kept birds.

Table 2.8 gives a detailed breakdown of the causes of death according to the keeping of birds. It was interesting to note that there were ten deaths in patients who had intensive contact with birds.

Table 2.7. Deaths (excluding suicides and accidents) occurring before age 60 years by pet keeping during the third year before death

	Males			Females			Combined		
Exposure	O	E	*P*	O	E	*P*	O	E	*P*
Bird keeping	13	6.6	<0.01	4	2.7	N.S.	17	9.3	<0.01
Dog keeping	5	4.7	N.S.	4	2.0	N.S.	9	6.8	N.S.
Cat keeping	1	3.2	N.S.	2	1.3	N.S.	3	4.5	N.S.
Rodent keeping	1	1.6	N.S.	1	0.5	N.S.	2	2.1	N.S.
No pets	5	6.6	N.S.	2	4.1	N.S.	7	10.7	N.S.

O, observed deaths among exposed; *E*, expected deaths adjusted for age in 10-year age groups; *p*, two-tailed *p* value; N.S., $p > 0.1$.

Table 2.8. Causes of death before age 60 by bird keeping during the third year before death[a]

Cause of death[b]	Bird keepers (sex; age)	Not bird keepers (sex; age)
Premature birth/hyaline membrane disease	1 (Male; 1 day)	0
Meningitis	0	1 (Male; 11 days)
Premature birth	1 (Male; 5 days)[c]	0
Congenital transposition	1 (Male; 1 year)	0
Ewing's sarcoma	1 (Male; 14 years)[c]	0
Sudden death with aortic valve stenosis	1 (Male; 32 years)[c]	0
Pneumonia	0	1 (Male; 39 years)
Chronic bronchial asthma	1 (Female; 31 years)[c]	0
Rheumatic carditis	0	1 (Female; 38 years)
Cardiomyopathy/mitral valve insufficiency	1 (Male; 41 years)	0
Breast cancer	1 (Female; 54 years)	2 (Female; 43 and 52 years)
Bronchial carcinoma	3 (Males; 44, 48 and 55 years)[c]	0
Ethmoid sinus carcinoma	1 (Male; 47 years)[c]	0
Acute heart death	1 (Male; 48 years)	0
Cervix cancer	0	1 (Female; 46 years)
Myocardial infarction	1 (Male; 52 years)	2 (Males; 55 and 59 years)
Stroke	1 (Female; 59 years)	2 (Male; 52 years)
Dissecting aoartic aneurysm	1 (Male; 55 years)[c]	0
Ovarian carcinoma	1 (Female; 55 years)[c]	0
Corpus uteri sarcoma	0	1 (Female; 59 years)
Oesophageal varices	0	1 (Female; 59 years)
Total deaths observed	17	11

[a]Or, in the case of four deaths during the first year of life, the year prior to birth.
[b]Causes of death are given in approximate order of age.
[c]Intensive contact: more birds were present in these households over a greater number of years.

2.3.3 Malignant Tumour Incidence

There were 79 newly diagnosed malignant tumours in the study population, of which 41 occurred in men and 38 in women. All but five of the tumours were in men and women aged 30 or more. Table 2.9 summarizes the incidence by sex, type of tumour and bird keeping, while Table 2.10 compares observed and expected incidences according to the type of pet kept. People who kept no pets had a significantly reduced incidence ($p < 0.001$) of malignant tumours compared with those who kept pets. The largest excess tumour rate was in keepers of birds where, for the sexes combined, 33 cases were seen as against 18.3 expected ($p < 0.001$). Keepers of other pets also showed an increased incidence of malignant tumours, with significant excesses seen in the case of cats in women ($p < 0.05$) and rodents in men and sexes combined ($p < 0.01$). Since there were relatively few malignant tumours among cat and rodent keepers,

Table 2.9. Newly diagnosed malignant tumours among men and women by bird keeping during the period 5-14 years prior to diagnosis

Malignant tumour		Number of patients			
		Bird keepers		Not bird keepers	
ICD Code (8th rev. 1967)	Name	Male	Female	Male	Female
149	Submandibular gland	1	0	0	0
151	Stomach	0	0	2	0
153	Colon	2	2	2	1
154	Rectum	2	3	0	1
155	Liver	1	0	0	0
157	Pancreas	0	0	1	1
160	Ethmoid sinus	1	0	0	0
162	Lung	7	0	5	0
170	Ewing's sarcoma	1[a]	0	0	0
171	Neurofibroasarcoma	0	0	1[a]	0
172	Malignant melanoma	1	0	0	0
173	Basal cell carcinoma	2	2	1	3
174	Breast	N.A.	2	N.A.	10
180	Cervix	N.A.	3[a]	N.A.	4
182	Uterus	N.A.	0	N.A.	2
183	Ovary	N.A.	1	N.A.	1
185	Prostate	0	N.A.	3	N.A.
188	Bladder	1	0	1	0
190	Retinoblastoma	1[a]	0	0	0
193	Thyroid gland	0	1[a]	0	0
200	Tonsil	1	0	0	0
201	Hodgkin's disease	0	0	1	1
203	Kahler's disease	1	0	0	0
204	Leukaemia	1	0	1	0
140-209	Total	23	14	18	24
	Total aged over 30 years	21	12	17	24
Population aged over 30 years in 1981		160	163	371	428

N.A., not applicable
[a]One tumour in man or woman aged less than 30 years.

Table 2.10. Newly diagnosed malignant tumours occurring from age 30 on by pet keeping during the period 5-14 years prior to diagnosis

	Males			Females			Combined		
Exposure	O	E	*P*	O	E	*P*	O	E	*P*
Bird keeping	21	9.4	<0.001	12	8.9	N.S.	33	18.3	<0.001
Dog keeping	11	7.1	N.S.	6	6.4	N.S.	17	13.5	N.S.
Cat keeping	4	3.5	N.S.	7	3.0	<0.05	11	6.5	<0.1
Rodent keeping	5	1.2	<0.01	2	1.1	N.S.	7	2.3	<0.01
No pets	12	20.0	<0.001	16	21.2	<0.1	28	41.1	<0.001

O, observed deaths among exposed; *E*, expected deaths adjusted for age in 10-year age groups; *P*, two-tailed *p* value; N.S., $P > 0.1$.

and since a number of these also kept birds, it was not possible in this study to be sure whether these represented independent associations.

The incidence of newly diagnosed malignant tumours among bird keepers in all age groups was also compared with national clinical incidence data and found to be much higher — 37 cases observed versus 19.9 expected. Six specific types of malignant tumours occurred often enough to justify further analysis. Results for bird keeping are summarized in Table 2.11 and are discussed in the sections below, where reference is also made to some similar analyses carried out in relation to other types of pet keeper.

Colon. A total of seven malignant tumours were seen, four in men and three in women. Of these, four occurred in bird keepers as against 1.6 expected, an excess which approached statistical significance ($0.05 < p < 0.1$). Although an excess was also evident in dog keepers ($O = 3$, $E = 0.8$, $p < 0.05$), two of the three dog keepers with colon cancer also kept birds.

Rectum. A total of six malignant tumours were seen, two in men and four in women. Of these, five tumours were in bird keepers as against only 1.3 expected, a highly significant excess ($p < 0.005$). No relationship to keeping of dogs, cats or rodents was seen.

Lung. A total of 12 malignant tumours were seen, all in men. Of these, 7 occurred in bird keepers as against 3.2 expected, an excess which was statistically significant ($p < 0.05$). No significant excess was seen in keepers of dogs ($O = 3$, $E = 2.5$), cats ($O = 2$, $E = 1.3$) or rodents ($O = 2$, $E = 0.5$) though numbers were rather low for a sensitive test. As expected, an increased incidence of malignant lung tumours was seen in smokers ($O = 11$, $E = 5{,}9$, $p < 0.01$).

Table 2.11. Specific types of malignant tumours occurring from age 30 on by bird keeping during the period 5-14 years prior to diagnosis

	Males			Females			Combined		
Tumour type	O	E	*P*	O	E	*P*	O	E	*P*
Colon	2	1.0	N.S.	2	0.5	N.S.	4	1.6	<0.1
Rectum	2	0.4	<0.1	3	0.9	=0.05	5	1.3	<0.005
Lung	7	3.2	<0.05	None seen					
Basal cell carcinoma	2	0.8	N.S.	2	0.9	N.S.	4	1.7	N.S.
Breast	None seen			2	3.1	N.S.			
Cervix	N.A.	N.A.	N.A.	3	2.3	N.S.			

O, deserved deaths among exposed; *E*, expected deaths adjusted for age in 10-year age groups; *P*, two tailed *p* value; N.S., $p > a1$; N.A., not applicable.

Basal Cell Carcinomas. There were eight cases, three in men. There were more cases in bird keepers than expected (0 = 4, E = 1.7), but this did not represent a statistically significant excess. No relationship was seen in relation to the keeping of other pets.

Breast. Of 12 malignant tumours, only 2 were in bird keepers as against 3.1 expected. This deficiency was not statistically significant, nor did risk relate to the keeping of other pets.

Cervix. Of seven malignant tumours, three were in bird keepers as against 2.3 expected. This excess was not statistically significant. Again, other pets showed no relationship to risk.

2.3.4 Nasal Polyps

There were 16 patients, 15 of whom were men, in whom a nasal polyp was diagnosed and subsequently removed during the study period. Table 2.12 compares the observed incidence with the age standardized expected incidence for the sexes combined according to type of pet kept. Some of the 16 patients kept more than one type of pet. The results were very striking, with a very highly significant ($p < 0.001$) increased incidence in bird keepers, who accounted for 13 of the 16 patients, and no indication at all that keeping other pets increased incidence of nasal polyps.

Table 2.12. Removed nasal polyps by pet keeping during the third year before removal[a]

Exposure	Observed[a]	Expected	*P*
Bird keeping	13	5.31	<0.001
Dog keeping	2	4.00	N.S.
Cat keeping	0	2.42	N.S.
Rodent keeping	1	1.04	N.S.
No pets	3	6.32	N.S.

[a]In a few cases the condition recurred. If the same person had multiple polyps removed, only the first is considered in the analysis.

2.3.5 Problems of Pregnancy

From 1971 to 1983, 253 children were born in this study population (Holst and Brand 1986), including five sets of twins. In the same period, there were 40 pathological miscarriages, 35 of which were spontaneous abortions, 3 immature parturitions and 2 perinatal deaths. There were also 21 provoked abortions. Any

termination of a pregnancy prior to the end of the 16th week, calculated from the 1st day of the last menstrual period, was considered an abortion. Terminations between the 16th and 28th weeks of pregnancy were considered to be immature parturition. Children who died in the first week after birth, irrespective of birth weight, body length or duration of pregnancy, were considered to be perinatal deaths (Hoogendoorn 1986).

Table 2.13 summarizes the results of analyses showing the relationship of smoking and the keeping of birds, dogs, cats and rodents to the change of a pathological miscarriage. In contrast to the expectation that the most substantial

Table 2.13. Live births and pathological miscarriages from 1971 to 1983 in relation to smoking and pet keeping during the year before

			Pathological miscarriages					
Subgroup	Age	Total Pregnancies[a]	SA	IP	PN	Total	Expected	p^b
All	10-19	11	2	2	0	4	4.0	
	20-29	200	24	1	2	27	27.0	
	30+	77	9	0	0	9	9.0	
	Total	288	35	3	2	40	40.0	
Smokers	10-19	8	1	1	0	2	2.9	
	20-29	95	16	0	1	17	12.8	
	30+	24	5	0	0	5	2.8	
	Total	127	22	1	1	24	18.5	<0.1
Bird keepers	10-19	6	0	2	0	2	2.2	
	20-29	74	15	1	2	18	10.0	
	30+	27	6	0	0	6	3.2	
	Total	107	21	3	2	26	15.3	<0.001
Dog keepers	10-19	2	1	0	0	1	0.7	
	20-29	45	4	0	1	5	6.1	
	30+	11	1	0	0	1	1.3	
	Total	58	6	0	1	7	8.1	N.S.
Cat keepers	10-19	2	2	0	0	2	0.7	
	20-29	32	6	0	0	6	4.3	
	30+	11	0	0	0	0	1.3	
	Total	45	8	0	0	8	6.3	N.S.
Rodent keepers	10-19	1	0	0	0	0	0.4	
	20-29	12	0	0	0	0	1.6	
	30+	2	0	0	0	0	0.2	
	Total	15	0	0	0	0	2.2	N.S.
No pets	10-19	1	0	0	0	0	0.4	
	20-29	79	7	0	0	7	10.7	
	30+	36	3	0	0	3	4.2	
	Total	116	10	0	0	10	15.2	<0.1

SA, spontaneous abortions; IP, immature parturitions; PN, perinatal deaths.
[a]Excluding provoked abortions; i.e. live births plus pathological miscarriages.
[b]Two-tailed p-value from χ^2 test stratified for age.

increase in miscarriage would be in cat keepers, due to the risk of toxoplasmosis, bird keepers were the only group of pet keepers who showed a clear increase in risk of pathological miscarriage. A total of 26 cases were seen in bird keepers as against only 15.3 expected ($p < 0.001$). There was also some suggestion of an increase among smokers, where 24 cases were seen as against 18.5 expected ($0.05 < p < 0.1$).

In our study as a whole there were 309 pregnancies (in which five twin births occurred). The percentage of spontaneous abortions, 11.1%, was similar to the 11.4% reported in the obstetrics study in 1958 of the Dutch College of General Practitioners (NHG) and to the 12.5% calculated by Ligtenberg (1966) for the 1960 NHG abortion study.

2.3.6 Infertility

From 1971 to 1983 there were in all 65 married couples in the survey population with wanted or unwanted childlessness after at least 4 years of marriage. None of the women were 50 years old by 1977 and neither of the partners had been sterilised. Of these couples, 22 were tested for infertility by gynaecologists during these years. Table 2.14 gives results of analyses relating childlessness and the taking of infertility tests to the keeping of pets. No relationship was seen as regards dogs, cats or rodents, but an increase was seen for bird keepers, both for childlessness ($0 = 31$, $E = 24.0$, $p < 0.1$) and, particularly, for infertility ($0 = 18$, $E = 8.1$, $p < 0.001$). Despite the fact that only 37% of women in this age group kept birds, 18 of the 22 infertile patients (82%) kept birds in their households and in eight cases (36%) at least one of the couple had bred birds. The budgerigar was the most popular. Of these 18 bird-keeping couples, 9 kept budgerigars, 7 kept canaries, 2 kept pigeons and 3 kept other birds. Details of these couples are given in Appendix C.

Table 2.14. Childlessness after at least 4 years of marriage and diagnosis of infertility by relevant specialists in relation to pet keeping during the year before diagnosis

			Childless			Infertility tests		
Exposure	Age	Total female population	O	E	*P*	O	E	*P*
All	20-29	174	35	35.0		10.	10.0	
	30-49	228	30	30.0		12	12.0	
	Total	402	65	65.0		22	22.0	
Bird keeping	20-29	66	17	13.3		8	3.8	
	30-49	81	14	10.8		10	4.3	
	Total	147	31	24.0	<0.1	18	8.1	<0.001
Dog keeping	20-29	46	8	9.3		2	2.6	
	30-49	59	11	7.8		4	3.1	
	Total	105	19	17.1	N.S.	6	5.7	N.S.
Cat keeping	20-29	33	8	6.6		1	1.9	
	30-49	43	6	5.7		2	2.2	
	Total	76	14	12.3	N.S.	3	4.2	N.S.
Rodent keeping	20-29	13	6	2.6		1	0.7	
	30-49	21	2	2.8		1	1.1	
	Total	34	8	5.4	N.S.	2	1.9	N.S.
No pets	20-29	68	8	13.7		0	3.9	
	30-49	83	7	10.8		2	4.3	
	Total	151	15	24.4	<0.05	2	8.2	<0.01

O, observed deaths among exposed; *E*, expected deaths adjusted for age in 10-year age groups; *p*, two-tailed *p* value; N.S., $p > 0.1$.

2.3.7 Further Statistical Tests

The analyses for which the results have been cited so far adjust only for age. Some further analyses were carried out in which the relationship of bird keeping to various endpoints was carried out adjusted additionally for social status in three categories (upper, middle, lower) and smoking habit in two categories (never smoked, ever smoked). These analyses were standardized for age in 1972, again in 10-year age groups, and were based on a comparison of bird keeping during the period 5–14 years before diagnoses among the patients and during the period 1972–1981 among the general practice population as a whole. Results of these analyses are presented in Table 2.15. They confirm the independence of the relationship of bird keeping to lung cancer.

Table 2.15. Results of further statistical tests

Diagnosis	Sex	Age	Odds Ratio	95% confidence interval	Significance
Lung cancer	Male	30+	6.3	1.4-29.0	$p = 0.02$
Other cancer	Male	30+	2.0	0.8- 5.0	$p = 0.1$
All cancer	Female	30+	1.4	0.7- 3.0	N.S.

p, two-tailed p value; N.S., $p > 0.1$.

2.4 Discussion

The marked increase in risk of *rectal cancer* among bird keepers may be an important finding. Long-term inhalation, expectoration and swallowing of contaminated dust particles affects the alimentary canal as well as the respiratory tract. About 1–5 million macrophages per hour leave the alveoli with their contents and the majority are swallowed.

An intact intestinal wall and quick passage through the intestines do not provide absolute protection from intestinal infection. Many less severe intestinal infections are self-limiting diseases. Less virulent bacteria, chlamydiae, or viruses lead to less severe types of enteritis and are much more difficult, if at all possible, to culture from faeces. The bacterial count in the digestive tract increases distally: the duodenum contains 1000-100 000 bacteria/ml of intestinal contents, the jejunum and proximal ileum, 100 million/ml, and the distal part of the ileum and colon, 10–100 billion/ml or more. Repeated enteritis is said to burden the mucosa of the rectum to the greatest degree, since this is where the most stasis occurs and the greatest number of potentially pathogenic microbes are present. Damaged lung macrophages and their contents reach the colon and rectum by secondary ingestion. Chlamydiae for instance are toxic to macrophages and leucocytes because of the lipopolysaccharides in their capsules and they survive in the cells of the immune system. Thus chlamydiae destroy many lung macrophages during phagocytosis and reach the mucosa of the rectum in dead macrophages. Infection with chlamydiae or other microorganisms could lead to persistent intraepithelial infections here. Bird keepers have a higher incidence rate of enteritis and both the number of bird keepers and the incidence rate of rectal cancer are highest in the lower social classes. All these arguments can be considered when examining the possible relationship between bird keeping and the higher incidence rate of rectal cancer.

A clear finding in our study was the strong and highly significant relationship between bird keeping and the occurrence of *nasal polyps* (Table 2.12). Nasal polyps often occur together with bronchial asthma and are thus indicative of a condition affecting the entire respiratory tract. The polyps often precede the asthma. There is evidence from other studies of a connection between the presence of pet birds and CNSLD. Felderhof-Hoytema (1987) carried out a study on 699

children between the ages of 4 and 16 years in Loosduinen, the Hague. Of these children, 39.6% had birds at home. Among the children with birds at home, symptoms of CNSLD were observed in 50.9%, in contrast to 19% found in children without birds at home. Quanjer (1987) reported a percentage of around 20% for CNSLD symptoms in children in the age group 11–19 years.

Our study also found a clear increase in the incidence of *spontaneous abortion* and *infertility*. As discussed in Chap. 1, short-term entry by *Chlamydia psittaci* into the bloodstream as a result of a sore throat or pneumonia during the 8th week of pregnancy can cause inflammation of the womb, leading to spontaneous abortion. A so-called flu in a pregnant bird keeper can thus have serious consequences. As a result of decreased hand hygiene, semen, the vagina and the internal genitals of men and women can become contaminated, resulting in an increase of infections. Infections ascending the vagina can cause inflammation of the oviducts resulting in infertility. It is possible that contamination of the vagina with for instance *Chlamydia psittaci* spores as a result of improper hand hygiene by bird keepers/breeders can cause constriction of the oviducts, such as that caused by *Chlamydia trachomatis*. An increased risk of spontaneous abortion and infertility in bird keepers has not been described elsewhere in the literature so far. There is some mention of *Chlamydia psittaci* infections causing sporadic complications (Cech et al. 1960; Wong et al. 1985; Sandler 1989). Maesen reported in 1972 that in his group of patients with pigeon fancier's lung 10 of 17 patients complained of impotence. Likewise, a patient with budgerigar lung and symptoms of encephalitis, as reported by Schipperijn in 1976, complained of impotence. These complaints of impotence might possibly have been the result of short-term hematogenic infections of their internal genitals with *Chlamydia psittaci*.

Our findings for cancer of the rectum, for nasal polyps and for spontaneous abortion and infertility require independent confirmation, but so far we have not yet been able to conduct further studies. We have, however, been able to carry out additional studies confirming the increased incidence of *lung cancer* in relation to bird keeping in our general practice survey. Detailed discussion of this issue is deferred until Chap. 6, by which time all the relevant evidence will have been described.

3 Hospital Case-Control Study of Lung Cancer and Bird Keeping

3.1 Introduction

As has already been clearly demonstrated, keeping birds as pets in the home contributes greatly to indoor air pollution (Bourne 1975). As described in the previous chapter, we found an association between keeping pet birds and lung cancer in a general practice survey conducted in the Hague between 1972 and 1981. In order to follow up this finding, it was decided to conduct a case-control study to provide an independent test of the hypothesis. This study and its results are described in this chapter.

3.2 Methods

Location. The case-control study began in April 1985 in four hospitals in the Hague: Bronovo, Leyenburg, Red Cross and West End. This city, located in the Western part of the Netherlands, has about 450 000 inhabitants.

Selection of Cases. Only patients with primary malignant neoplasm of the trachea, bronchus or lung (ICD 162) who were aged under 65 years, had lived in the Netherlands since 1965 and were registered with one general practice in the Hague during the study period were selected as cases for the study. Patients who were too ill to fill in a questionnaire were excluded from the study.

There are several reasons why only patients under 65 years old were chosen. Firstly, it was felt that the influence of variables other than smoking would be easier to see in younger patients who have not had so much time to accumulate the effects of smoking over large numbers of pack years. Secondly, older patients would have more difficulty filling in questionnaires. Thirdly, selection from younger patients would be more likely to occur because the elderly drop out of a family practitioner's care when they are placed in senior citizen residences and nursing homes. Finally, classification into social groups is based on the occupation of the principal wage earner and this would be increasingly unreliable in the case of persons over 65 years old.

Classification of Tumours. Tumours were classified according to World Health Organisation criteria by the pathologists as epidermoid carcinoma (I), small cell carcinoma (II), adenocarcinoma including bronchioloalveolar carcinoma (III) and large cell carcinoma (IV).

Selection of Controls. Two control subjects matched for age and sex were randomly selected for each patient from the same general practice list by a procedure described in Appendix B.

Questionnaire. Nine chest specialists and 48 general practioners handed out questionnaires to patients and control subjects respectively. The patients and control subjects completed the questionnaires by themselves. The standardized questionnaire (see Appendix B) asked about occupation, smoking habits, bird keeping and diet.

Occupation. The occupation of the wage earner was taken as the indicator of the social status of the household. Based on the International Standard Classification of Occupations the participants were divided into those with an upper, middle, or lower social status, as described in Appendix B.

Smoking. Questions about smoking habits included kind of tobacco, whether cigarettes, cigars or a pipe were smoked and amount and duration of smoking. A patient in the study was considered to be a smoker if he or she had ever smoked in the period up to and including the 5th year before cancer was diagnosed or, in the case of a control, the date of diagnosis of the patient.

Bird Keeping. Information was collected on how long birds were kept and the type of birds. A patient or control was considered to be a bird keeper if he or she had kept caged birds in the home for longer than 6 consecutive months in the period 5 to 14 years before lung cancer was diagnosed or, in the case of a control, the same period before the date of diagnosis of the patient. Reasons for the choice of this period have been discussed already in Sect. 2.2.

Diet. Information on diet was collected by asking questions about how often fruit and vegetables containing β-carotene or vitamin C had been regularly eaten since 1975 and about the consumption of alcohol. The intake of β-carotene and vitamin C was calculated based on average portion size by multiplying the intake of foods by their nutrient content (see Appendix B).

Statistical Methods. Before the study started it was decided to perform an interim analysis after 1 January 1987 if the number of patients had reached 50. Statistical methods used were as described in Appendix A. These include the use of logistic regression analysis for assessing odds ratios because of the stratified structure of the case-control study (SUGI 1983). Different multivariate models were used, some of which included interaction terms. The models were compared using log likelihoods.

3.3 Results

Between 1 April 1985 and 1 January 1987 there were 76 patients under 65 years in the four hospitals with cancer of the lung. Of these, 13 were excluded by the chest specialists because they were considered to be too ill to take part, four having cerebral metastases and nine being terminally ill. Therefore, 63 patients were eligible for entry into the study. Of these 14 did not participate, 3 because they were being treated by non-participating specialists and 11 because holiday periods and changing personnel prevented them from participating. These 14 patients were classified as missing. The remaining 49 patients (79% of those eligible) participated. Two controls refused to participate and were replaced by two others selected by the same methods.

The distribution of the patients and of the excluded and missing subjects is shown in Table 3.1. The proportion of the originally identified patients actually taking part in the study varies markedly according to the cell type of the cancer, being much higher for small cell cancers (21 of 22 = 95%) and for large cell cancers (9 of 12 = 75%) than for epidermoid cancers (14 of 29 = 48%) and adenocarcinoma/alveolar cancers (5 of 13 = 38%).

Some demographic characteristics of the patients and controls are shown in Table 3.2. The average age of the 49 patients at diagnosis was 56.9 years. The average age of the 37 male patients (57.9 years) was greater than the average age of the 12 female patients (53.9 years). The average age of the control subjects was 57 years. Patients and control subjects did not differ appreciably in social class: 78% of the patients belonged to the lower social class compared with 67% of the control subjects.

Information about smoking habits and dietary variables is given in Tables 3.3 and 3.4. Of the patients, 95% were smokers as against 84% of the controls, with the average number of cigarette-years of smoking for patients significantly ($p < 0.001$) greater than that for controls. The patients had a significantly ($p < 0.05$)

Table 3.1. Tumour pathology for 76 incident lung cancer patients under 65 years of age

	Carcinoma type									
	Epidermoid		Small cell		Adenocarcinoma/ alveolar		Large cell		Total	
Category of patient	*n*	%	*n*	%	n	%	*n*	%	n	%
In study	14	29	21	43	5	10	9	18	49	100
Excluded [a]	8	62	0	0	3	23	2	15	13	100
Missing [b]	7	50	1	7	5	36	1	7	14	100
Total	29	38	22	29	13	17	12	16	76	100

[a] Due to cerebral metastases or terminal phase of the disease.
[b] Did not participate for various reasons — see methods.

Table 3.2. Demographic characteristics of lung cancer patients and controls

Characteristic	Level	Patients		Controls	
		n	%	*n*	%
Sex	Male	37	76	74	76
	Female	12	24	24	24
Age (years)	35-39	1	2	2	2
	40-44	3	6	6	6
	45-49	6	12	12	12
	50-54	5	10	10	10
	55-59	14	29	28	29
	60-65	20	41	40	41
Social status	Low	38	78	66	67
	High	11	22	32	33
Total		49	100	98	100

Table 3.3. Smoking habits of lung cancer patients and controls

Smoking habit			Patients	Controls
Up to 5 years before diagnosis, all patients and controls	Never	[*n* (%)]	1(2)	16(16)
	1-15 cigarettes/day	[*n* (%)]	8(16)	29(30)
	>15 cigarettes/day	[*n* (%)]	40(82)	53(54)
	Heavy/light smokers	[ratio]	5.0	1.8
	Pack-years of smokers[a]	[mean]	37.1	30.9
Ever smoked up to 5 years before diagnosis, excluding those who never smoked or who stopped smoking longer than 15 years before diagnosis	1-15 cigarettes/day	[*n* (%)]	7(15)	18(28)
	>15 cigarettes/day	[*n* (%)]	40(85)	46(72)
	Heavy/light smokers	[ratio]	5.7	2.6
	Pack-years of smokers	[mean]	37.3	35.7

[a]One pack-year is one pack of cigarettes per day for 1 year.

Table 3.4. Smoking and dietary variables among lung cancer patients and controls

	Patients		Controls	
	Mean	S.E.	Mean	S.E.
Smoking (cigarette-years[a])	651.0	48.00	448.00	38.70
Vitamin C (mg/day)	64.8	7.90	84.70	5.10
β-carotene (mg/day)	2.8	0.23	2.73	0.15
Alcohol (measures/wk)	12.0	1.80	10.00	1.10

S.E., standard error.
[a]One cigarette-year is one cigarette a day for one year.

lower vitamin C intake than the controls, but no significant difference between patients and controls was observed for β-carotene intake and alcohol consumption.

It is notable that the one patient who did not smoke kept birds. Nine of the ten patients aged under 50 years were bird keepers compared with 11 of the 20 controls aged under 50 years.

Table 3.5 gives details of the number of patients and controls keeping birds of particular species and overall. Overall, 67% of patients kept birds in the period 5–14 years before diagnosis as against 33% of controls. The increased frequency of keeping birds by patient was evident for all three types of bird considered: pigeons, canaries and birds of the parrot family. The percentage of patients keeping budgerigars (45%) was higher than for any other type of bird and higher than the percentage of controls keeping budgerigars (20%).

Table 3.6 shows the percentage of bird owners for both patients and controls from 1951 to 1986. The percentage of bird keepers among patients was higher than that among controls in all of these years except one where it was the same. This implies that the association is not due to the chosen time interval and the definition of bird keepers. The difference in exposure for both groups was the greatest in the period 1965–1975, 10–20 years prior to the diagnosis of lung tumours.

Cigarette smoking was strongly related to lung cancer. The crude odds ratio for smokers compared to non-smokers amounted to 10.0. The crude odds ratio for keeping birds 5–14 years before diagnosis of lung cancer was 5.1. Vitamin C intake was significantly inversely related to lung cancer. The crude odds ratio for persons with a low vitamin C intake (≤ 50 mg/day) compared to those with a high vitamin C intake (> 50 mg/day) was 0.23 (Table 3.7).

Multiple conditional logistic regression analyses showed no significant interactions of bird keeping with sex or age, so the risk of lung cancer incidence was

Table 3.5 Lung cancer patients and controls keeping birds in the period 5-14 years before diagnosis on the lung tumor

Species	Patients[a]										Controls[a]	
	Epidermoid		Small cell		Adeno-carcinoma/ alveolar		Large cell		Total			
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Budgerigors/parrots	4	29	10	48	4	80	4	44	22	45	22	20
Canaries	5	36	7	33	1	20	3	33	16	33	22	22
Pigeon	1	7	2	10	0	0	2	22	5	10	7	7
Any birds	9	64	14	67	4	80	6	67	33	67	34	35
No birds	5	36	7	33	1	20	3	33	16	33	64	65
Total subjects	14	100	21	100	5	100	9	100	49	100	98	100

[a]Some patients or controls kept more than one species.

Table 3.6. Lung cancer patients and controls keeping birds from 1951 to 1986 among the 49 patients and 98 controls

Year	Patients		Controls	
	n	(%)	*n*	(%)
1952	12	25	20	20
1954	13	27	19	19
1956	16	33	20	20
1958	12	25	22	22
1960	13	27	26	27
1962	14	29	24	25
1964	15	31	20	20
1966	17	35	21	21
1968	18	37	23	23
1970	21	43	24	25
1972	21	43	26	27
1974	16	33	26	27
1976	13	27	25	26
1978	15	31	27	28
1980	19	39	29	30
1982	22	45	30	31
1984	20	41	32	33
1986	20	41	30	31

Table 3.7. Crude and adjusted odds ratios for the different risk factors for lung cancer

	Odds ratios		
Risk factor	Crude	Adjusted	(95% confidence interval)
Bird keeping (yes vs no)	5.1	6.7	(2.2-20)
Smoking (yes vs no)	10.0	10.0	(1.2-83)
Vitamin C intake (> 50 mg/day vs ≤ 50)	0.23	0.23	(0.1-0.6)

modelled as a function of bird keeping; smoking; vitamin C, β-carotene and alcohol intake; and social class. A backward regression analysis showed that social class and alcohol intake were not significantly related to the risk of lung cancer and that deleting these two factors from the model did not influence the coefficients of the remaining factors in any appreciable way. In the final model the risk of lung cancer was related to bird keeping, smoking and intake of vitamin C (Table 3.7). This analysis showed that these three risks factors were independently related to lung cancer. Bird keepers had a 6.7 times greater risk of lung cancer compared to persons who did not keep birds. The adjusted odds ratios for smoking and low vitamin C intake did not differ from the crude odds ratios.

3.4 Discussion

The lowest percentage of missing patients was among those with small cell tumours because these patients returned several times to hospital for chemotherapy and were seen more frequently by their chest specialists. The 14 patients who were eligible to participate in the study but did not do so (defined as missing) were less likely to have small cell tumours than those who participated, and their absence may have affected the relation between bird keeping and lung cancer observed here. To assess whether there was bias, an analysis was performed which assumed that in the most extreme case each missed patient would have been classified as a non-bird keeper, while their (fictitious) controls were randomly assigned to be a bird keeper or a non-bird keeper proportionally to the distribution of the other control subjects. This of course greatly reduced the estimated odds ratio (to 2.8), but this estimate was still significant at the 1% level. Even in this extreme case our results cannot be explained by chance alone. It is unlikely that the reason for a patient being missing is related to the exposure and therefore the estimated odds ratio will probably not be severely biased.

The estimated odds ratio may be influenced by the chosen time interval of exposure, although this was the same as chosen in the general practice survey (Holst and Brand 1986). We therefore considered three other 10-year periods (Table 3.8).

Table 3.8. Odds ratios for 10-year exposure periods

Years before diagnosis	Odds ratio (95% confidence interval)	
4-13	6.1	(2.2-17)
6-15	4.8	(1.9-12)
7-16	2.4	(1.1-6)

The slight change in the definition of a bird keeper influenced the point estimate heavily, although the odds ratio remained significantly different from one at the 5% level in all patients. These different odds ratios suggest that the actual point estimate is unstable due to variability in the data.

Another explanation may be that bird keeping affects the risk of fast growing tumours most. In that case one should expect to see a decreasing odds ratio when the time interval moves backwards from the date of diagnosis. Further investigations are needed to confirm this hypothesis.

Overall the results of this study lend support to the belief that bird keeping may be an important contributing factor in the aetiology of lung cancer and indicate the need for much more scientific attention. This hypothesis is further discussed in Chap. 6, after additional evidence has been presented in Chaps. 4 and 5.

4 Dust Measurement Study

4.1 Introduction

The dust measurement study was designed to test a possible relationship between suspended particulate matter concentrations, particle size and the keeping of birds.

4.2 Methods

With the cooperation of the administration of the bird breeders association of The Hague, we searched for two bird-keeping households with comparable living conditions. In a limited study it is quite important for the areas measured to be as comparable as possible. Two households with approximately the same living conditions were to be selected as controls. Such locations could not be found in Rijswijk, but were found in a new apartment building in Zoetermeer, where many young families reside (Table 4.1).

Measurements were carried out in four almost identical apartments (two households with pet birds, two without) on the second floor of the new Meerzicht

Table 4.1. Characteristics of the apartments investigated

Apartment	Living room dimensions	Number of family members	Bird room dimensions	No. of birds	Other pets
1.	7.10 × 4.00 m h = 2.80	3	4.00 × 2.50 m h = 2.80	Living room 1, bird room 29	1 cat
2.	8.00 × 4.00 m h = 2.56	3	4.00 × 2.00 m h = 2.56	Bird room 125	1 dog
3.	7.10 × 4.00 m h = 2.80	3	N.A.	None	1 dog
4.	8.00 × 4.00 m h = 2.56	3	N.A.	None	2 dogs

h, height of room; N.A., not applicable.

development in Zoetermeer between 14 and 17 January 1985. The apartments had similar furnishings (no rush mats, for example) with many synthetic materials; all had central heating. Measurements were taken in the living rooms and — in households where birds were kept also — in the rooms where the birds were kept for 6 h continuously between 10:00 am and 4:00 pm. In order that the measurements in the various apartments might be comparable, the influence of such dust sources as smoking, house cleaning activities, ventilation, humidifiers, and cooking was practically eliminated by keeping to a preestablished protocol. During the 24 h prior to the measurements being taken, there was no vacuuming and air humidifiers and purifiers were turned off. On the day of the testing, there was no smoking or cooking in the apartments and the windows were kept closed. During the testing, there were preferably no more than two persons in the rooms under study.

The air samples were collected at breathing level (125 cm) in the middle of the rooms. The following measurements were taken:

Respirable dust concentration was measured using the following procedure: the concentration of particles smaller than approximately 5μm, was measured using the β-particle monitor (Frieseke-Hoepfner apparatus, type FH-62–1 and FH-62–12). The apparatus consisted of a β-ray emitting source and a ray detector, between which a transportable band of fibreglass filter membrane allowed the passage of air. β-radiation that flowed across the band was continually measured and registered on a recorder. The dust concentration was derived from the decrease in β-radiation caused by the buildup of a layer of dust on the filter and from the air volume sucked through. The aspirator pump was fitted with a cyclone, so that only particles smaller than 5 μm could pass through and be measured.

Total dust concentration was determined with a membrane pump (Du Pont Constant Flow Sampler, Model P2500), in which air passed through a filter holder containing a glass filter. The filter was weighed before and after sampling under standardized conditions, the dust concentration being calculated from the weight gain of the filter and the quantity of air passing through. Particles up to around 30 μm were measured in this manner.

The numerical particle concentration was determined with the aid of an HIAC-Royco particle apparatus, which makes measurements on the basis of the diffusion of light by the particles. The particles were counted by various particle size categories: 0.3–0.5 μm, 0.5–1.5 μm, 1.5–3.0 μm, 3–5 μm, 5–10 μm and larger than 10 μm. The apparatus was also equipped with a printer which recorded the number of particles averaged over a given period (in this case, 3 min every quarter of an hour) in each size classification. The numerical particle concentrations were derived from the number of counted particles and the air volume passing through (Van der Wal 1981; WHO offset publication 1984).

4.3 Results

The respirable and total dust concentrations averaged over a period of 6 h are reported in Table 4.2. During the investigation, the cage in the living room of apartment 1 was moved to another location and cleaned; the effect of cleaning the cage on the respirable dust concentration (particles smaller than 5 μm) was not noticeable. The results of the average numerical particle concentrations are shown in Table 4.3. The sudden increase in particle concentration in apartment 4 after 3:50 pm in all particle size categories is possibly explained by the return home of the son of this household at this time. He was exuberantly greeted by the two dogs (a Bouvier and a young shepherd). The dogs remained quite unruly during this period. Even though this excess motion was not in conformity with the protocol, it was interesting to see how it led to a dust explosion. The total dust concentration

Table 4.2. Respirable and total dust concentrations

		Dust concentrations μg/m^3 air		
Apartment/Bird keeping	Room	Respirable	Total	Date
1/Birds	Living room	40	180	14/1/85
	Bird room	40	100	14/1/85
2/Birds	Living room	200	360	17/1/85
	Bird room	90	480	17/1/85
3/No birds	Living room	60	60	15/1/85
4/No birds	Living room	100	180	16/1/85

Table 4.3. Particle concentrations

		Number of particles per dm^3 of air				
Apartment/Bird keeping	Room	0.3-0.5 μm	0.5-1.5 μm	1.5-3 μm	3-5 μm	5.10 μm
1/Birds	Living room	80 000	40 000	4 000	220	135
2/Birds	Living room	75 000	120 000	7 000	160	130
	Bird room[a]	80 000	130 000	6 000	390	360
3/No birds	Living room	140 000	100 000	13 000	80	85
4/No birds	Living room					
before 3.50 pm		90 000	40 000	7 500	25	25
after 3.50 pm		120 000	140 000	40 000	175	150

[a]measurement period about 1 h.

in apartment 4 was also influenced by this. There appeared to be hardly any systematic differences in the dust concentrations that could penetrate into the alveoli (smaller than 3 μm — the respirable fraction) between households with and without birds. However, the difference was very obvious for the total fraction that could be inhaled. The total dust concentration was highest in apartment 2, where a large number of birds were kept. In apartment 1, the influence of the birds on the total dust concentration was less evident. The results of the numerical particle concentration counts showed that the higher concentrations occurred in the larger classes of 3–5 μm and 5–10 μm. This was especially noticeable in apartment 2. No influence was noticeable for concentrations of smaller particles of 0.3–3 μm.

The average temperature and relative humidity of the apartments is shown in Table 4.4. The temperatures and relative humidities were comparable in the residences during the measurement intervals. In all cases the lowest temperature was between 21° and 23°C and the relative humidity between 19% and 28%. These low values are due to the weather that week being cold with a strong frost.

Wind direction, wind velocity, outdoor temperature and outdoor relative humidity are shown in Table 4.5. These values were taken from the daily weather reports broadcast on KNMI in Den Bilt and were measured at the Rotterdam weather station at 1:00 pm. The barometric levels for the 4 days of the measurement period were 1025, 1026, 1025 and 1018 mb.

Table 4.4. Average temperature and relative humidity (RH) in the apartments between 10.00 am and 4.00 pm

	14 Jan		15 Jan		16 Jan		17 Jan	
Apartment/Bird keeping	temp °C	RH %	temp °C	RH %	temp °C	RH %	temp °C	RH %
1/Birds	23	28	22	24	24	24-40	23	30
2/Birds	25	19	23	18	23	19	21	24
3/No birds	22	23	22	22	21	22	23	23
4/No birds	22	18	21	17	22	19	22	19

Table 4.5. Meteorological data at the time of the study

	14 Jan	15 Jan	16 Jan	17 Jan
wind direction	WSW	ENE	S-SSW	variable
wind velocity m/s	0.5	4.5	2	1
temperature (°C)	–7.1	–9.8	–7.3	–6.3
relative humidity (%)	85	73	79	83

4.4 Discussion

A clear relationship between the concentration of suspended particles of 3 μm diameter or more and the presence of birds in the home was found in this limited experimental study. Bird keeping can lead to continuous inhalation of excess suspended particulate matter. The presence of birds indoors gives a long-term exposure to larger dust particles of 3 μm or more.

5 Other Evidence on Bird Keeping and Lung Cancer

There are regional differences in the Netherlands in male lung cancer mortality (Table 5.1) that cannot be explained by the differences in the age distribution of the population (Hoogendoorn 1983). Unfortunately, regional information about smoking habits is not available. The rural province of North Brabant had, in 1984, the highest age-standardized lung cancer mortality. This province contains three towns among the eight largest municipalities with the highest lung cancer mortality in the Netherlands. Tilburg and Maastricht had the highest standardized lung cancer mortality among the eight largest municipalities for the years 1969–1978 (CBS 1980). Tilburg also had the highest mortality in 1984. Most of the bird clubs and most of the organized bird keepers are traditionally found in North Brabant. The number of organized bird breeders of the Netherlands society of bird lovers grew dramatically from 1400 in 1940 to 45 800 in 1984. The incidence of lung

Table 5.1. Lung cancer mortality (per 100 000 per year) in men in different Dutch provinces and large municipalities

		Lung cancer mortality	
Province	Municipality	1969-1978	1984
North-Brabant		91	114
	Tilburg	117	131
	Eindhoven	98	121
	Breda	98	117
Utrecht		89	109
Limburg		93	104
	Maastricht	103	92
Overijssel		75	104
North-Holland		95	104
	Haarlem	101	114
	Amsterdam	100	104
South-Holland		92	103
	Rotterdam	102	123
	Leiden	99	102
Gelderland		77	102
Groningen		67	90
Friesland		62	89
Drenthe		60	88
Zeeland		60	86

cancer was quite low in the Netherlands until 1950. In 1950, 1179 men and 167 women died from this disease. By 1983, the numbers had increased to 7104 men and 800 women. Standardized for age, the mortality per 100 000 men increased from 27 to 120 between 1950 and 1988 (Table 5.2) and per 100 000 women from 3.3 to 10.6 over the same period. Since 1975, the percentage of male smokers over 35 years of age has declined from 70% to under 50% (Baan 1986; see Table 5.3). A slight decline in smokers has also occurred among women since 1975. In the period 1975–1983, taking into account the aging of the population, the number of newly diagnosed cases in women of cancer of the trachea, bronchus and lung has increased by 73% and mortality by 58%. In men, the number of actual newly diagnosed cases increased by 18% and mortality by 8% (CBS 1986).

Overall 60%–80% of the trade in tropical birds is concentrated in Belgium, the Netherlands, England and West Germany. Most of the organized bird lovers are in these countries and most of the shows are held there. Considerably fewer household birds are kept in the USA than in the Netherlands. In 1980, there were 25.6 million household birds per 230 million inhabitants (1:10) in the USA as compared with 7.5 million household birds per 13.6 million inhabitants (1:2) in the Netherlands (Marks 1984). Belgium, the Netherlands and the United Kingdom have for years had the highest standardized lung cancer death rates of the world (World Health Statistics Annual 1984–1987). Lung cancer mortality in the USA was always lower than in these three countries, even though the number of smokers

Table 5.2. Age-standardized lung cancer death rates of Dutch men from 1950 (per 100 000 per year)

Year	Rate
1950	27
1958	40
1960	49
1963	57
1970	75
1980	95
1988	120

Table 5.3. Smoking habits of Dutch men of 20 years and older

Year	Percentage of smokers	Tobacco sales (100 g/head)
1958	90	41
1965	80	
1970	76	43
1975	67	
1980	55	36
1985	44	

was not smaller (Table 5.4). Bird breeding is preeminently a male hobby in these countries. The popularisation and urbanisation of domestic and tropical birds species during the twentieth century, discussed in Sect. 1.1, may have contributed to the enhanced male lung cancer mortality rates in the Netherlands, Belgium and the United Kingdom.

Lower lung cancer mortality has been observed for various higher lying areas (Rawson 1980). In the US mountain region, lung cancer mortality for the period 1950–1969 was lower than in the rest of the USA. In Wyoming, lung cancer mortality in this period for males was 27/100 000 and cigarette consumption was 3200 per capita of the population. Despite the high cigarette consumption, there was less lung cancer and less colon and rectum cancer here than in the entire USA (Mason and Mackay 1974). This area is dry in summer as well as winter, situated about 1500 m high, and has major temperature fluctuations between the day and night-time (sometimes 30°C). The outdoor air in this area is clean, and also the indoor air contains less bioaerosols, consisting of dust particles, allergens and microbes. House dust mites are practically nonexistent because of the low night-time temperatures and low relative humidity (Spieksma et al. 1971; Vervloet et al. 1982). The indigenous population of Alaska that lives above the Arctic circle also has less lung cancer (Lanier et al. 1980). Because of the low humidity and low temperatures of the indoor and outdoor air, less microbiological active dust particles are also found here. In contrast to this, Finland has a high lung cancer mortality rate compared with other northern countries such as Sweden and Norway. Less (tropical) birds are kept in this low lying country. Up to 35% of the working population of Finland in 1980 was employed in the agricultural and poultry industries. The inhalation of bioaerosols by workers in these industries occurs on a major scale and a possible association with lung cancer should be investigated further.

Table 5.4. Age-standardized lung cancer mortality (per 100 000 per year) in men in different countries in 1984 in relation to per adult consumption of manufactured/hand-rolled cigarettes in 1970

Country	Cigarette consumption per adult[a]	Lung cancer mortality
Italy	84	77
Norway	88	43
France	92	65
Finland	93	87
Netherlands	108	117
Belgium	119	119
Western Germany	125	73
Japan	141	43
United Kingdom	153	100
USA	184	84

[a]In packs of 20 per year.

6 Discussion of the Relationship Between Bird Keeping and Lung Cancer

6.1 Introduction

Data from both the general practice survey and the case-control study show bird keeping to be a risk factor for lung cancer which is independent of smoking. This hazard, which appears to be related to long-term exposure to dust particles of 3–10 μm in size, is not mentioned in the literature and will be discussed in detail in this section. A possible mechanism by which bird keeping may cause lung cancer is described in Sect. 6.2. Then, in Sect. 6.3, evidence relating to the other main causes of lung cancer — smoking, occupation, and nutrition — is summarized and these causes are compared with the importance of bird keeping. Finally, in Sect. 6.4, the main conclusions are summarized and a number of recommendations for further research are outlined.

6.2 Mechanisms by Which Bird Keeping May Cause Lung Cancer

6.2.1 Bioaerosol-Related Allergic and Infectious Diseases

People suffer discomfort and display medical symptoms because they live in overcrowded conditions. New workers in poorly ventilated air-conditioned offices often find that previous conditions such as allergies or other types of hypersensitivity become aggravated. In some cases, such as dust-related allergies, a poor indoor climate itself can actually cause the illness. Public debate and the media have highlighted such issues as radon, formaldehyde, fungus and rot, asbestos, air ions, dry air, office illness, self-copying paper, visual display units, etc. Those health aspects which have come into prominence relate particularly to matters such as hypersensitivity.

Cleaning processes such as sweeping, vacuuming and dusting normally remove the larger particles, but can often increase the airborne concentration of the smaller particles (Green 1984). Cooking, broiling, grilling, gas and oil burning, coal and wood fires, and smoking also generate large amounts of airborne particulates, vapours, and gases. If the windows are closed these can only accumulate in the internal environment. Over the life of the building, more dirt enters with the supply and return air. Good filters reduce the rate of this accumulation, but no

perfect filter exists. Even ultra-efficient HEPA filters used in hospital operating rooms allow fine particles through. Frequently more spores are found behind the filter than in front of them. Many of these fine particles coalesce, sticking to each other by adhesion or hygroscopic or electrostatic attraction, so that larger particles form with time. Fungi are able to grow in air-conditioning filters. Fungal spores are numerous if the relative humidity is high, as is normally the case in autumn and spring. In addition to the spores, free allergens have also been detected. In air-conditioned rooms the detached allergens cause symptoms similar to humidifier fever caused by sensitization to thermophilic actinomycetes growing in humidifiers. It seems that not only actinomycetes, but also fungi in humidifiers and in air-conditioning filters can cause air-conditioning disease, which is generally an allergic disease caused by sensitization to fungi allergens dispersed by air-conditioning systems (Ashton et al. 1981). Infectious diseases known to be caused by indoor air problems associated with poor indoor air quality include Pontiac fever, humidifier fever, legionellosis and pneumonia. Dirt and dusts in the ventilation ductwork may be allergenic. Most of the dusts are, by definition, household dusts notorious for causing allergies in many people. The dirt encourages germs, which can cause infections to breed (Robertson 1988).

The pollutant most often blamed for the symptoms of sick building syndrome is the visible air pollutant environmental tobacco smoke (ETS). Smoking restriction have been enforced by management as well as government as an excuse to avoid dealing with the overriding air quality issue. Sick building syndrome results primarily from energy conservation efforts to seal buildings. Such efforts have reduced the natural infiltration of fresh air that previously existed in many buildings, exacerbating the often previously undiscovered problem of a poorly designed or maintained air-conditioning system. In addition to tightening buildings and sealing windows, building managers have shut down air-conditioning systems at nights and weekends in an effort to lower energy costs. When the air-conditioning is shut down in humid climates, condensation builds up and settles inside the ductwork. If dirt is present in damp ductwork, spores and microbes can flourish, only to be spread throughout the building once the air-conditioning system is turned on the next morning. Mites, which need a relative humidity of more than 40%, thrive in certain buildings where the ventilation is insufficient. Studies have shown that these tiny creatures are often the culprit in cases of asthma and dust-related allergy. To save more energy, automatic temperature controllers are used to cycle fans on and off during the day. Vibrations from the start-up of these fans can cause dirt and microbes trapped inside ductwork to be dislodged and carried into occupied areas.

The presence of high concentrations of tobacco smoke indicates a much more serious problem than the tobacco smoke itself. Poor ventilation is the primary cause of poor indoor air. Many of the invisible and odourless pollutants are potentially far more dangerous than environmental tobacco smoke. It is significant that where high concentrations of ETS are found, an excess of fungi and bacteria in the air-conditioning systems are often found. These microorganisms are usually the primary cause of adverse health effects (Robertson 1988). ETS is not the only

visible air pollutant in residential homes. Especially when the sun shone, I saw polluted indoor air in the homes of bird keepers because of the scattering of the light by fine dust particulates. I have observed that there is often less ventilation in homes with caged pets out of concern for the bird or hamster getting cold. The air may thus be more humid and contain more allergens and dust particles. It is an ecological mistake to transport parrots or tropical song-birds out of their natural habitat into our climate, place them in cages, and then provide them and us with extra warmth and humidity. The higher relative humidity of the air and extra heat encourage growth of moulds and mites. Keeping pet birds in the home results in increased dust concentrations in the indoor air (Holst and van der Wal 1985). This dust contains antigens produced by the mites and may also contain microbes, including *Chlamydia psittaci* spores, which can remain infectious for weeks, even when dry. Air is not a natural habitat for microorganisms and they only exist there as accidental contaminants. Pathogenic microorganisms are transmitted through the air on two types of particle; the residues of evaporated exhalation droplets (droplet nuclei), and the much larger dust particles. These types of particle are very different with respect to their source, settling behaviour, significance in causing disease, and the methods which must be used to assess and control them. Some of these differences are summarized in Table 6.1.

In households where birds are kept, dust levels are considerably elevated. As described in Chap. 4, concentrations of inhalable dust particles in the 3–10 μm range were higher in households that kept birds than in households without birds. Suspended particulate matter levels of 40–200 $\mu m/m^3$ in size were however similar in all the households, regardless of bird keeping. These findings agree with those reported in the literature. Jones et al. (1984) studied the dust spread by 30-day-old chickens and found levels of 3.5–20 μm, with only 35% of particles smaller than 10 μm and capable of being inhaled. Marks (1984) found that the smallest particle size from the finest budgerigar dust was 1 μm. Inhaled dust particles of 3–10 μm, which for the most part sediment in the bronchi and bronchioli, may increase the deposition on a site predisposed for bronchial carcinoma in a bird keeper. Microbes and inhaled allergens may produce microinfections and allergic reactions.

Table 6.1. Characteristics of airborne particles

	Droplet nuclei	Dust particles
Source or particles in air	Evaporation of droplets expelled from the respiratory tract by sneezing, coughing and talking (in decreasing order of effectiveness)	Movements causing the shedding of particles from skin and clothing. Air turbulence causing the shedding of particles from mouldy places or redistributing previously settled dust
Particle size and smallest diameter	3–0.5 μm (Riley 1959)	Most household dust > 10 μm; allergens 10 - 0.5 μm; allergens from house dust mites, cats, bird mites 3–0.5 μm; powdery dust from budgerigars 10–1 μm
Settling behaviour	Particles <10 μm remain suspended indefinitely as a result of minor air turbulence (average settling velocity in still air 0.002 m/s^{-1})	Particles > 10 μm settle rapidly to the ground (average settling velocity, 0.007 m/s^{-1}) j redistribution by major air turbulence. Particles <10 μm remain suspended in the air
Organisms per particle	Rarely more than one	Usually many
Significance in causing disease	Particles around 2 μm sediment in the bronchi, particles <1 μm in the small air sacs	Particles > 10 μm are deposited on external surfaces and in upper respiratory tract. Particles around 2 μm sediment in the bronchi. Particles <1 μm, sediment in the small air sacs
Epidemiological characteristics	Responsible for most pulmonary infections, propagated epidemics (disease transmitted serially from person to person)	Epidemics associated with specific places as reservoirs of infection

6.2.2 Biological Factors Spread by Birds and Their Possible Relationship to Tumour Development

Interesting epidemiological data which suggest common causal factors in the development of cancer in animals and humans (possibly as a result of transmission of viruses) have come from China. A high incidence of oesophageal cancer in both humans and chickens has been reported in Northern China (Priester 1975). There are areas in China where carcinomas of the nose and throat are common in humans, and where clusters of pigs with the same disease have been found. In addition, there are indications in Southern China of a connection between the frequent occurrence of cancer of the liver in ducks and of carcinoma of the liver in humans.

Most types of tumour, both in animals and humans become manifest in later life. The so-called cancer age in certain animals (chickens, pigs) is not reached by the majority of individual animals in the Western world. In China, where small pets generally reach an old age the pattern is different. Small pets share a number of environmental factors in common with humans and could have a signal function (Misdorp 1981). In particular, caged animals soil themselves in the confined space in which they live and consequently their surroundings.

Tumours are not rare in birds. As early as 1929, Reitsma reported a number of tumours in birds and Ratcliff reported in 1933 that the very popular budgerigar *Melopsittacus undulatus* had the highest percentage of malignant tumours. The percentage of malignant tumours found in budgerigars in later routine dissection studies was even higher than the 16% first reported by Ratcliff (Beach 1974; Blackmore 1966; Gardner et al. 1981; Neumann and Kummerfeld 1983; Petrak and Gilmore 1982; Schlumberger 1957). In a survey, Beach found tumours in 24.2% of budgerigars, the incidence being considerably higher in caged birds (33.4%) than in aviary birds (13.7%). Among all the classes of birds, budgerigars and parrots birds develop the highest number of cancers.

This situation is still unchanged (Petrak and Gilmore 1982). The percentage of cancers in these birds is also higher than that observed in mammals. In the case of budgerigars, carcinomas of the kidney, testis and ovaries, and cancers of the muscle and bone have been found (Gardner et al. 1981; Petrak and Gilmore 1982; Neumann and Kummerfeld 1983). The factors below may be related to the development of tumours.

Avian Retroviruses (Type C). Canaries, decorative birds, parrots, budgerigars, and pigeons can develop the leucosis complex, although the incidence is much lower than in fowl where avian retroviruses cause the disease. Birds are contaminated via the egg (vertical transmission). These RNA tumour viruses are not very resistant in vitro, and infections through direct contact (horizontal transmission) may occur in large indoor aviaries or by infected insects.

In chickens, retroviruses have been found both in normal and tumour tissue. It was therefore important to determine whether retroviruses were present in the tumours occurring in budgerigars. Gardner et al. (1981) performed electron microscopic studies of 38 malignant and 6 benign tumours from budgerigars ranging in age from 1–17 years (average 4 years) to see if retroviruses were present. In 23 cases, the malignant tumours were found to be carcinomas of the kidneys, testes, ovaries, liver and bone and, in 15 cases, fibrosarcomas. The benign tumours were subcutaneous lipomas and xanthomas. No retroviruses were found in the malignant tumours but perhaps more refined techniques might make it possible to find some retrovirus activity in the malignant tumours of budgerigars. For the time being, it appears that only leucosis and sarcoma in chickens are caused by retroviruses. In the series of tumours studied by Gardner, there were a good number of fibrosarcomas and two liver carcinomas, but no leucosis complex. In humans, contamination by these retroviruses has not been proved, but there are strong indications that leukaemia may be connected with retrovirus C.

Marek's Disease Virus. Tumours in pet birds are also caused by Marek's disease virus, a herpes virus which may also cause latent infections, in which no further virus is produced. In this non-productive condition, nuclear transformation occurs after some time and tumours are formed in all types of tissue, except the skeleton. Marek's disease virus is one of the few DNA viruses that cause cancer spontaneously in the host animal. The virus is highly cell binding and occurs in the infectious form only in epithelial cells of feather follicles. These virus-contaminated epithelial cells are gradually shed and spread as dust particles. Sharma (1973) studied 200 persons with exposure to Marek's disease virus. Of these, only 8% had positive immunofluorescence (IF) tests. Neutralizing antibodies could not be found. The conclusion of this limited study was that Marek's disease virus poses no health risk to humans.

Chlamydia Infections. In the literature listed in Index Medicus, hardly any articles can be found under the heading "chlamydia infections/neoplasms". Cancerlit, which deals with articles from 1970 onwards, was also searched but only passing mention was made of the possibility that chlamydia infection might play a role in the formation of tumours. No article was found on a possible connection between bronchial carcinoma and *Chlamydia psittaci* infections. Rainey (1954) described 11 patients whose lymphogranuloma inguinale developed into carcinoma of the anus and the rectum. Markowa and Marek (1967) reported that, following bone injections of purified suspensions of *Chlamydia psittaci*, the surrounding muscle tissue in a number of test animals developed rapidly growing tumours. Animal experiments of this type are of little value, however, since they deal unnaturally with contamination. Infection with these microbes runs a totally different course in humans.

Fortuny (1973) responded by letter to an editorial appearing in the Lancet (1973) on sporadically recurring retinoblastomas of one eye. He described nine children aged 2–7 years (average 3 years) with this tumour, diagnosed in 1960–1965 in a region where there is a high prevalence of vaginal chlamydia infections. Four of the nine children with retinoblastoma of one eye came from an area with endemic trachoma. He suggested there was a potential link between non-hereditary tumours and perinatal infections of the eye with malignant transformation of the neuroepithelium of the retina. Paavonen (1979) and Schachter et al. (1982) studied hundreds of women with cervical tumours and found a significant association between cervical carcinoma and positive serology for *Chlamydia trachomatis*. No differences were found between patients and controls for herpes type II virus and cytomegalovirus. These findings do not prove an aetiological connection between chlamydiae and cervical carcinoma, since the positive serology may merely reflect frequent and changing sexual contacts and diminished sexual hygiene. *Chlamydia trachomatis* is related to *Chlamydia psittaci*, but is a totally different disease in humans. If chlamydiae cause tumours, it seems likely both species can do so since they are both obligatory cell parasites and can produce latent and persistent intracellular infections.

Antigens As Serum Proteins, Keratin Microfibrils, and Bird Mite Antigens. Bird keeping leads to continuous inhalation of bird proteins and bird mite antigens. Birds are the only animals with feathers, which consist of keratin in the form of microfibrils with the smallest diameter of 1 μm. Keratin is very resistant to wear, insoluble in most solvents and resistant to enzymatic breakdown (Brush 1978). The smallest keratin particles may not be as capable of damaging the cell wall of bronchial cells as asbestos fibres, but the chance of intracellular infection with simultaneous microbiological pollution is greater. The diameter rather than the length of the keratin fibres determines where they sediment in the airways (Timbrell et al. 1971). As long as the inert dust particles are captured in the airways, the risk of damage is small. The limiting membrane surrounding the alveoli protects the interstitium against dust penetration. This limiting membrane is not present around the respiratory bronchioli, so that damage to the interstitial lung tissue can occur there. The mucociliary system cannot handle a dust load of more than 50 mg/day and keratin enters the interstitium.

6.2.3 Local Immune Deficiency Syndrome

In a review paper, Holt and Keast (1977) concluded that enhanced prevalence rates of respiratory infections and neoplastic diseases resulting from chronic exposure to air pollutants, in particular cigarette smoke, were found to be associated with impaired immunological control mechanisms.

Reynolds et al. (1988) reported a temporary increase in T-lymphocytes in the bronchoalveolar lavage fluid of pigeon breeder groups compared to normals ($p = 0.0001$). All pigeon breeders had undergone indirect challenge with antigens in their own lofts within 24 h from the start of the study. In patients with allergic alveolitis, the long-term antigen activity from exposure to bird excreta causes an increase in T8 suppressor lymphocytes and a decrease in the T4 helper/T8 suppressor lymphocyte ratio (Bosch et al. 1986; Costabel et al. 1984). Long-term exposure to bird antigens will progress to pulmonary fibrosis (DuWayne Schmidt et al. 1988). The T4 helper/T8 suppressor lymphocyte ratio is also lowered in patients with pulmonary fibrosis (Reynolds et al. 1988).

An increase in the number of lung macrophages (scavenger cells) was found in smokers, together with a decline in lymphocyte numbers and a concomitant reduction in antibody production (Warr et al. 1976). Also, bird keepers who smoked appear to have lower antibody levels than non-smoking bird keepers (Boyd et al. 1985). Because of the hypersecretion, there is greater drainage of the alveolar spaces in smokers than in non-smokers. Consequently, in the bird keeper who smokes, the antigen activity is shifted from the minute air sacs to the bronchi. The antigens reach the minute air sacs in smaller quantities and the immune reactions occur more readily in the smaller bronchi (McSharry et al. 1985; Warren 1977). In the long run, keeping pet birds causes decreased antibody production and lowered T4 helper lymphocyte counts and may be an independent contributing risk factor for bronchial obstructive syndrome. Both smoking and bird keeping

produce dysfunction of the lung macrophages followed by local deficiency in humoral (McSharry et al. 1985) and cellular immunity (Bosch et al. 1986; Daniele et al. 1985). The consequence is lesser protection of the bronchial epithelium against continuous immunogenic and particulate material in the bronchial fluid layer and subsequently lung cancer. It can thus be understood why most lung tumours are found at a distance from the places in the smaller bronchioli where gaseous and dust particles sediment. Bird keepers, with their enhanced prevalence rates of allergic process and infections in the lung, have a higher relative risk for lung cancer independent of smoking. This supports the hypothesis that a local immune deficiency syndrome is a precursor rather than a consequence (Weiss 1987) of the lung neoplasms related to allergens.

6.3 Causes of Lung Cancer and Their Relative Importance

6.3.1 Smoking

Cigarette smoking is the most important risk factor for the development of lung cancer. More than 50 retrospective studies and eight major prospective studies have demonstrated the high relative risk of bronchial carcinoma in smokers compared with non-smokers. The risk for smokers appears to be ten times greater than that of non-smokers and the risk for heavy smokers is greater than that for lighter smokers. The strength of the association, the dose-response relationship, and the reduced incidence in ex-smokers compared with continuing smokers all argue strongly in favour of causality (Surgeon General 1982).

World-wide differences in lung cancer mortality cannot be explained by cigarette smoking alone. The lung cancer mortality in Japan is a quarter of the lung cancer mortality in Western European countries. The percentage of smokers in Japan and the Netherlands is almost the same (Keys 1980), but the lung cancer mortality in men in the Netherlands is five times higher (Table 5.4). In the United States, where cigarette-making machines were first in full swing, lung cancer mortality is significantly lower. This underlines a need for examination of other factors. Smokers are at higher risk in Belgium, the United Kingdom (Passey 1962) and the Netherlands. Lung cancer mortality in the USA has always been lower than in these three countries which have for years had the highest lung cancer mortality rates of the world, even though there were no fewer smokers in the USA (World Health Statistics Annual 1984–1987; Beese 1972). A number of different studies have shown that lung cancer mortality cannot be attributed to smoking alone. It has been claimed that in the USA the risk of lung cancer in non-smokers has increased (Enstrom 1979), though this has been disputed (Doll and Peto 1981; Garfinkel 1981). While a dose-response relationship suggests a valid connection, it is not all inclusive, since even among the heaviest smokers there are a large number who do not develop lung cancer. While the latency period for lung carcinoma is long, the risk for lung cancer quickly decreases when a person stops

smoking, even for someone with a large number of pack-years. However this risk never returns to that for a non-smoker. We excluded from the patients and controls in our study in the Hague those smokers who stopped smoking more than 15 years ago. The number of pack-years of the remaining smokers was similar (see Table 3.3) for patients and controls. There were more heavy smokers among the patients than among the controls. One out of six heavy smokers develops lung cancer and most of the lung cancer patients came from this group of heavy smokers. It is possible these lung cancer patients form a subpopulation in which an interaction has occurred with other risk factors for bronchial carcinoma. Perhaps the study of low risks will provide an answer to this question. Is it a coincidence that the only two lung cancer patients in our study who had not smoked in the past 15 years prior to diagnosis were in fact bird keepers during this period?

The calculated population-attributable risk percentage increases from 92% for smoking alone to 98.4% for the double risk of smoking and bird keeping in this study population (Walker 1981).

Cigarette smoke is a dense aerosol of chemical combustion gases with a particulate phase and a gas or vapour phase. The particulate phase consists of particles ranging in diameter from 0.1 to 1 μm. The deposition of particles of 0.5–1 μm in the airways is only 10%–15%; the remainder is exhaled again. The deposition of particles of 2 μm in the lungs is 40%, three to four times greater than that of the 1 μm particles, but such large particles are relatively rare in tobacco smoke. The size of the particles determines the site of sedimentation; particles around 2 μm sediment in the bronchi while particles smaller than 1 μm sediment in the minute air sacs. Most cigarette smoke particles are smaller than 1 μm and cannot sediment in the bronchi to any extent. Cigarette smoke contains water particles of 0.2–0.5 μm in size that may become as large as 1–3 μm and be deposited quite readily in the bronchi. The smallest particles in cigarette smoke of around 0.02 μm cannot increase enough in size through water vapour uptake to sediment in the bronchial mucous membrane (Davies 1974). Smokers who inhale smoke for 2–3 s and keep it in their bronchi by exhaling slowly have a greater degree of deposition of particles of 1–3 μm in their bronchi. The process of absorption of water vapour by the hygroscopic particles in cigarette smoke is recognizable by the fact that the smoker expels white smoke instead of the blue smoke that is the original colour of the tobacco combustion gases. The smallest particles in cigarette smoke of around 0.02 μm cannot increase enough in size through water vapour uptake to sediment in the bronchial mucous membrane (Davies 1974). Irritation of the respiratory tract mucous membrane as a result of smoking leads to increased mucous production. In the long run, the heavy smoker's first cigarette of the morning does not produce enough irritation to cough up all the mucus that has collected during the night. A drainage problem arises in the minute air sacs involving stasis and a diminution of the diameter of the smaller bronchi. Stasis increases the risk of infection and allergic processes if inhaled microorganisms and antigens can reach these areas. Some smokers cough and bring up mucus. Some develop a severe bronchial obstructive syndrome, in which coughing is completed with shortness of breath and wheezing in the chest. In addition to the

accumulation of mucus, these patients have bronchial spasms and oedema of the bronchial mucous membrane due to the increased sensitivity of the mucous membrane and muscles of the bronchial wall, and to allergic processes in the bronchial wall. Smokers who develop dyspnoea, coughs and wheezing in the chest are individuals who develop the most lung tumours (van der Wal 1964; van der Wal et al. 1966). This gives good reason to be aware of the subgroup of bird keepers among smokers. Bird keepers have an increased risk of infection with local damage to the tissue and allergic processes with local immune disorders in the lung tissue. Hyperreactivity of the airways may also be present from early youth on.

6.3.2 Occupation

Since lung cancer incidence is not fully explained by cigarette smoking, attention has been focussed on other factors that may affect risk. A number of occupational factors are known or are suspected to be related to lung cancer, evidence for some of which is summarized below:

Asbestos. Lung cancer mortality for heavy-smoking asbestos workers is almost 90 times higher than for persons who do not smoke and do not work with asbestos. After working for less than 9 months in a factory processing brown asbestos fibres (Amosite, 2 μm), risk of bronchial carcinoma (keratinized squamous cell carcinoma) was doubled with the latency period shortened to 10–20 years (Hammond et al. 1979).

Radon. For workers in uranium mines, an increased risk of bronchial carcinoma (mostly small cell undifferentiated bronchial carcinoma) has been found with an average latency period of 9.4 years (Lundin et al. 1979). Lundin found a proportionately much lower increased risk for non-smoking uranium miners than for smoking uranium miners. He concluded from this that smoker's bronchitis makes the lung more susceptible to tumours which develop under the influence of radon gas. Radon is a gaseous radioactive element which is formed from the decay of uranium. Precipitation of fine dust particles, which occurs in the mines (rock dust 1–10 μm), is responsible for the high dose of radiation that the bronchial epithelium receives from the continuous breathing of radon dust particles.

Another source of radon is the radium in building materials and/or the ground beneath. This radon problem is severe in Sweden where there is an abundance of radium in bedrock. Radium is also present in many building materials, particularly in alum shale-based blue-grey concrete, manufactured between 1927 and 1975, but few building materials contain so much radium that they release large quantities of radon. Radon is possibly not as dangerous as is generally claimed. The population of areas where the ground contains large quantities of radon have to be exposed to large doses of radiation throughout time in order to be at risk. The province of Skaraborg, near Göteborg in Sweden, is such an area. If radon is

extremely dangerous, the population of Skaraborg ought to display a high frequency of lung cancer, but they do not!

Polycyclic Aromatic Hydrocarbons. Workers who have worked on the top of coke ovens for 5 years or more and have breathed polycyclic aromatic hydrocarbons (boiling point 200–250°) over the duration, have similarly been found to have an increased relative risk and excess mortality for bronchial carcinoma (Lloyd 1971; Doll et al. 1972). The latency period equals 20–30 years. Polycyclic aromatic hydrocarbons are probably also responsible for bronchial carcinoma of roofers and workers in the tar and asphalt industry.

6.3.3 Nutrition

World-wide differences in lung cancer mortality may also be influenced by world-wide differences in eating habits. The diet of industrialized countries with Western life-styles, characterized by high fat consumption with much animal protein and commercially processed food, is very different from that of rice-eating and other populations without Western life-styles.

One nutritional component that may influence the development of lung cancer is vitamin A. Vitamin A deficiency causes metaplasia and keratosis of all squamous epithelia in the body, with the result that sebaceous glands, hair follicles and tear glands dry up. Keratomalacia, not found in populations with Western life-styles, is the most obvious consequence of vitamin A deficiency. Between 50 000 and 100 000 children become blind from this yearly, as a result of drying and ulceration of the corneas. Animal experiments have demonstrated vitamin A administration prevents carcinoma formation in experimental animals and tissue culture. Vitamin A deficiency in hamsters caused heavier penetration of benzopyrene into tracheal cells and binding of the carcinogen with nuclear DNA. High doses of vitamin A provided protection (Sporn 1977). The marked increase in lung cancer mortality in the Netherlands cannot be attributed to vitamin A deficiency since this is a rare occurrence because of the addition of this vitamin to margarine. At the beginning of this century, fresh vegetables were only available during the summer months and plenty of cod liver oil was administrated as soon as an "r" appeared in the month. In 1935, the margarine and butter in the Netherlands was enriched (for three cents more per package) with vitamin A so that it had the same vitamin A content as the fresh butter available only in summer. Since the Margarine Act of 17 December 1950, 20 IU/g vitamin A has been added to each package. Thus, it seems highly unlikely that a vitamin A deficiency could play a major role. The Dutch consume a huge amount of dairy products, fresh vegetables, organ meats, and vitamin preparations so there could not have been a vitamin A deficiency in adults over the past 30 years, which is precisely the period in which lung cancer frequency has increased. No protection against lung cancer by higher vitamin A consumption has been noticed according to the trend of the lung cancer mortality figures over the past 30 years (cf. Chap. 5). Standardized for

age, the mortality per 100 000 men increased from 27 to 120 and per 100 000 women from 3.3 to 10.6 between 1950 and 1988.

Das et al. (1983) carried out a case-control study on newly diagnosed lung cancer patients in the Tan Tock Seng Hospital in Singapore. The controls were matched by age group, sex, and ethnic group. The authors found no significant serum vitamin A differences between patients and controls. The serum vitamin A, however, was not strongly correlated with the vitamin A content of the food. In a review article, Peto et al. (1981) concluded that serum vitamin A does not itself provide protection, but that β-carotene offers some protective action during later stages of carcinogenesis. β-carotene is the most important of the provitamin A carotenoids. It is found mainly in dark green and orange vegetables. In food, 6 μg β-carotene is equivalent to 1 μg vitamin A, but only one-third of the β-carotene is absorbed in the small intestine and only half of this is converted by the liver into vitamin A.

In 1975, Bjelke calculated a combined vitamin A and β-carotene index, based on the consumption of meat, poultry, fruit, and vegetables of a group of 8278 males aged 45–74 years who were followed by post for 5 years. Of these, 19 men developed squamous cell, large cell or small cell carcinoma, with the risk 4.6 times higher for those with a low vitamin A index than for those with a high index. Adjustment for social group was not performed in this study. The same Nordic group (Kvale et al. 1983) later reported results from 11.5 years of follow-up. Based on 65 cases of squamous cell or small cell carcinoma, there was a strong negative relationship between risk and the combined vitamin A and β-carotene index, which persisted after standardizing for social group, smoking habits and age. Hirayama (1979) carried out a prospective study of over 100 000 men in Japan from 1966 to 1976, during which 611 lung cancer deaths occurred. In all social groups, men with a daily consumption of green and yellow vegetables had an age-standardized lung cancer risk that was 1.2-1.8 times lower in all social groups. It was striking that the lowest indication (1.2 times higher risk) of a possible protective effect from consumption of green and yellow vegetables occurred in the lowest social group, which had the highest number of lung cancer cases. In a 19-year follow-up of 1954 men, Shekelle et al. (1981) found a strong inverse relationship between β-carotene intake to development of lung cancer. In a study reported by Menkes et al. (1986), serum was collected for 25 802 persons in 1974. β-carotene was later determined for 99 persons who later developed lung cancer and for 196 controls matched for age, sex, race, smoking habits and month of blood analysis. Risk of squamous cell lung cancer was 4.3 times higher in the group with the lowest β-carotene levels. This study also did not correct for social group. In the Zutphen Study (Kromhout 1987), 35 out of 870 males died from lung cancer between 1960 and 1980. In addition to β-carotene, vitamin C was also inversely related to lung cancer mortality. β-carotene and vitamin C are strongly correlated with each other since they occur in the same foodstuffs, i.e. vegetables and fruit. The epidemiological studies carried out so far indicate that β-carotene in particular is inversely related to lung cancer. This is supported by an experimental study which showed that β-carotene captures reactive oxygen metabolites (superoxide anions, hydro-

gen peroxide and hydroxyl radicals). Lung macrophages produce these oxygen metabolites and with them destroy foreign dust particles that have penetrated into the lung. An overproduction of these metabolites also causes oxidation and damage to the lipids in the cell wall (Peto et al. 1981). It has not been proven, however, that this oxidative damage to the cell wall actually plays a role in the process of respiratory carcinogenesis. In our case-control study in the Hague, vitamin C intake was significantly inversely related to lung cancer. The crude odds ratio of persons with a low vitamin C intake (≤50 mg/day) compared to those with a high vitamin C intake (50 mg/day) was 0.23. β-carotene intake was not significantly related to lung cancer in our study (Table 3.4).

Alcohol and beer consumption have also been connected with bronchial carcinoma (Hinds et al. 1984; Potter and McMichael 1984). The odds ratio found, however, was not significant after correction for smoking. Most of the supporting evidence has come from the results of some animal studies (Potter and McMichael 1984). In our case-control study, smoking and alcohol or beer consumption clearly show a common association. Alcohol and beer consumption were not significantly related to lung cancer after correction for smoking.

6.3.4 Pet Birds

Although smoking is a strong risk factor for lung cancer, it by no means fully explains geographic patterns in incidence (Fraumeni 1975; Blot and Fraumeni 1976; Hammond and Garfinkel 1980). While some occupational exposures such as asbestos and uranium are strong risk factors, they only affect a small proportion of the total population, and in the studies performed occupation or general air pollution are not considered to provide a complete explanation. Nor has it been claimed that radon or dietary factors, such as β-carotene, tell the whole story. Although there is much work still to be done in quantifying exposure to these factors and the role they play in lung cancer, it seems eminently possible that there may be still other factors which play an important role in determining the national or regional level of lung cancer mortality. Could bird keeping be such a factor?

The general practice survey and the case-control study supply sufficient evidence that exposure to bird excreta in fact results in risks to health. Coupled with evidence from other studies that bird keepers have an increased prevalence of infections and allergic processes in the airways, the finding that they have an increased risk of lung cancer independent of smoking supports the biological hypothesis of a local immune deficiency syndrome (Sect. 6.2.3) caused by the long-term exposure to bioaerosol-related allergic and infectious disease of the airways.

The data from the general practice survey and the case-control study not only show that bird keeping is a strong risk factor, but also that it cannot be explained by differences in smoking habits between those who keep birds and those who do not. Table 6.2 shows how the percentage of disease attributable to a factor increases according to the frequency of the factor in the population and to the

Table 6.2. Percentage of disease attributable to a factor according to (i) frequency of the factor in the population and (ii) relative risk in relation to the factor

	Relative risk					
Frequency of factor	2	4	6	8	10	12
10%	9	23	33	41	47	52
35%	26	51	64	71	76	79
70%	41	68	78	83	86	89
95%	49	74	83	87	90	91

relative risk in relation to the factor. Our research indicates that, for the Hague, a relative risk of about 6 and a frequency of about 35% would be appropriate, which yields a percentage of disease attributable to bird keeping of 64%. In other words, if no one kept birds, it seems that only 36% as much lung cancer would have occurred, i.e. total lung cancers would be almost three times lower.

Assuming 70% of smokers and a relative risk of 10 for smoking, one can calculate the percentage attributable to smoking as 86%, with total lung cancers about seven times lower if everyone had the risk level of someone who has never smoked. From these data, while smoking is a more important determinant of risk than bird keeping, it is clear that bird keeping is still a major factor, especially when as prevalent as it is in the Netherlands, and may help to explain why Dutch men have such high lung cancer rates.

In attempting to extrapolate to other countries with different frequencies of smoking and bird keeping, it is important to bear in mind a number of factors. Firstly, it is not to be expected that the effects of smoking and bird keeping will necessarily be the same in all countries. The types of cigarettes and other smoking materials used vary from country to country as do the types of birds and the circumstances in which they are kept. Secondly, our studies have provided very little data on the possible risks of bird keeping among those who do not smoke. The case-control study only provided data on one lung cancer patient who had never smoked and one who had given up more than 15 years ago. While bird keeping may multiply the risk of lung cancer to a similar degree in smokers and non-smokers, it is a possibility, which requires further investigation, that bird keeping may be more (or less) of a risk in smokers.

6.4 Conclusions and Recommendations for Further Research

The quality of the indoor air we breathe is a major determinant of health. We breathe in some 15 000 litres of air each day, of which at least 7500 litres are breathed indoors. In the 13 years that I have been a general practitioner, I have

visited at least 5000 different homes and have personally observed noticeable differences in indoor air quality in the course of my experience. ETS, a visible air pollutant, is the pollutant most often blamed for poor indoor air. Especially when the sun was shining, I also saw polluted indoor air in the homes of bird keepers because of the scattering of fine dust particulates by the light. I have noticed that there is often poor ventilation in homes with caged pets. This often arose out of fear lest the caged pet got cold. The air is also more humid and contains more dust particles and more allergens. Bird keepers are subject to long-term exposure to more dust particles, allergens, keratin microfibrils, and microbes than those who do not keep birds. Particularly young households keep birds and rodents and caged animals in the home create risks for expectant mothers, infants and young children. We found that keeping birds as pets in the home during pregnancy multiplied the risk of spontaneous abortion by four. Exposure to birds as pets in the home gives young children a substantial risk of developing asthma and CNSLD. These health risks may be reduced by improved cage hygiene and hand hygiene among bird keepers. More medical and veterinary attention to the bird keeping hobby and to sick birds as being reservoirs of bioaerosol-related allergic and infectious diseases is needed.

A possible connection between the keeping of pet birds in the home and the transmission of viruses or bacteria which are implicated in the causation of lung cancer cannot be demonstrated in a way which fulfils Koch's postulates. For instance, isolation of the *Chlamydia* organism from transformed cells is not conclusive evidence that the organism caused the transformation. Furthermore, many healthy people are carriers of *chlamydiae* without showing any symptoms of disease. Demonstration of a connection by epidemiological methods is the most appropriate way of trying to determine the possible relationship between a tumour and a risk factor. Animal experiments can then be carried out to determine which component of the risk factor has the strongest connection with the tumour.

In our study, lung cancer risk was increased six-fold in those who had kept birds as pets for about 10 years previously. This finding, coupled with the fact that one household in three or four keeps birds, implies that more than 50% of the total lung cancer rate can be attributed to keeping pet birds. It is notable that for many years both the percentage of bird keepers and the lung cancer death rate of the Dutch male population have been among the highest in the world. For years Belgium, the Netherlands and the United Kingdom have had the highest standardized lung cancer mortality in the world. It is noteworthy that 60%-80% of the trade in tropical birds is concentrated in Belgium, the Netherlands and the United Kingdom. Most of the organized bird keepers are in these countries and most of the shows are held there. Regional differences in the Netherlands in lung cancer mortality cannot be explained by the differences in the age distribution of the population (Hoogendoorn 1983). In 1984, the rural province of North Brabant had the highest age-standardized lung cancer mortality. Most of the bird clubs of the organized bird keepers are traditionally found in this province. In the United States, lung cancer death rates have always been lower, even though there were no fewer smokers in the past. In 1980 in the United States there were 25.6 million

birds in households per 230 million inhabitants as compared to 7.5 million birds in households per 13.6 million inhabitants in the Netherlands. The United States Department of Agriculture (USDA 1988) estimated approximately 15% of the US households had birds. The finding in our study of a sixfold increase in lung cancer risk among bird keepers coupled with the fact that 15% of the households kept pet birds in the USA in the previous 10 years could imply that up to 40% of the total lung cancer rate in the USA can be attributed to keeping pet birds.

A number of additional lines of research are required. To confirm our findings, further epidemiological studies should be conducted, which should be large enough to give more detailed information on the risk of lung cancer in women and in non-smokers. A study of the percentage of bird keepers among patients newly diagnosed as having particular diseases over a limited period of time will give similar estimates of risk to those from a study based on a well-defined group of bird keepers (a cohort). The first type of study which we conducted is more efficient and will give results more quickly than the second type. It is very important to use a standard definition of bird keeping in any new epidemiological studies and to describe the periods during which the bird keeping is studied.

Definition of a Bird Keeper. A person is defined as a bird keeper if there have been caged birds in his or her home for at least 6 consecutive months.

Periods to Be Studied for the Keeping of Birds as Pets in the Household. For cancer patients 5–14 years before diagnosis of the cancer, for asthma and chronic non-specific lung disease 0–10 years before first diagnosis and for spontaneous abortion 0–1 years before the diagnosis.

Warnings. Those starting a study of the risk factor of keeping birds as pets in the home among their patients will have to cope with at least three myths.

— The first myth is that pets are good for everything and everyone.
— The second myth is that cigarette smoking is the sole cause of lung cancer.
— The third myth is that of the wife of a bird breeder who supports her husband and thinks he can better spend his evenings near the dovecotes or aviaries because she at least knows where he is.

Data should be collected in different countries on the proportion of the population keeping birds, and an attempt should be made to determine the extent to which variation in this factor might contribute to variation in national lung cancer rates. Singapore Chinese are a population with high female lung cancer rates (McLennan et al. 1977). It would be interesting to examine if bird keeping and the care of birds is a female hobby in this population.

Experimental studies should also be conducted. Firstly, tests in laboratory animals should be conducted to see whether allergic reactions and/or non-specific infections in the airways can be caused by bird dust, characterized by the level of known allergens. This dust contains keratin particulates of the feathers, bird excreta, moulds and other microorganisms, i.e. *Chalmydia psittaci* spores. Then

one should study if these reactions are similar to those found in the airways of bird keepers. This preliminary work would be a pilot study for a long-term animal study. Hamsters should probably be the species of choice because the long-term study will involve carcinogenic chemical substances such as benzo(a)pyrene or a nitrosamine, and an experimental lung cancer model of hamsters is already available (Feron 1975). These experiments may provide more evidence that bird dust is a causal factor in the development of lung cancer.

Appendix A
Interpreting Data From Epidemiological Studies

In an epidemiological study, the data showing the relationship of a risk factor, such as bird keeping, to a disease, such as lung cancer, are often laid out in the form of a 2×2 table as follows:

		Exposure		
		Yes	No	Total
Disease	Yes	a	b	n_1
	No	c	d	n_0
	Total	m_1	m_0	N

For a prospective or a cross-sectional study, the relative risk (R) of disease for exposed and non-exposed individuals can be expressed by the formula:

$$R = (a/m_1)/(b/m_0) = am_0/bm_1 = a(b + d)/b(a + c)$$

For a case-control study, where the disease is seldom encountered, $b + d$ is well approximated by d, and $a + c$ is well approximated by c so that the formula:

$$R = ad/bc$$

may validly be used. R may be rewritten as

$$R = (a/b)/(c/d)$$

so that the relative risk may be calculated from the relative frequency of exposure to non-exposure for the patients and the relative frequency of exposure to non-exposure for the controls. Clearly for the estimate to be valid the selected controls must be representative, as regards exposure, of the population at large.

A simple estimation of relative risk from a single 2×2 table for the whole population provides only a preliminary indication of risk. Correction is necessary for all other risk factors, which may be unevenly distributed among both exposure groups. Failure to make a correction may result in the situation where the relative risk found in the first instance shows a completely distorted picture. This phenomenon is called confounding. Thus, if it was the case that average male bird keepers smoke considerably more than those who do not keep birds, an association between bird keeping and lung cancer might be seen in a simple 2×2 analysis even if bird keeping actually had no effect at all.

We used two different methods of correcting relative risk estimates for confounding factors. The first method is based on stratification. The population are divided into subgroups, or strata, based on the factor(s) to be corrected for. Thus strata might be 10-year age groups or be based on smoking habits, e.g. never smoked, ex-smoker; current 1–20 cigarettes a day, current > 20 cigarettes a day. They may also represent combinations of age groups and smoking habits to simultaneously correct for both factors.

If there are k strata and the data for a 2×2 table within a specific stratum, i, are defined using the same notation as above but with a subscript i, then an estimate of relative risk adjusted for the confounding factor is given by:

$$R = \frac{\sum_{i=1}^{k} (a_i d_i)/N_i}{\sum_{i=1}^{k} (b_i c_i)/N_i}$$

To test for significance, the procedure is as follows. First, within a stratum, calculate:

O_1 = observed $= a_i$

E_1 = expected $= m_i n_i / N_i$

$\text{var}E_i$ = variance of expected $= \dfrac{n0_i\, n1_i\, m0_i\, m1_i}{N_i{}^2 (N_i - 1)}$

Secondly, accumulate over strata to form:

$$0 = \sum_{i=1}^{k} 0_i,\ E = \sum_{i=1}^{k} E_i,\ V = \sum_{i=1}^{k} VarE_i$$

Finally, calculate a statistic asymptotically distributed as a χ^2 statistic:

$$\chi^2 = (|O\text{-}E| - \tfrac{1}{2})^2/V$$

Confidence limits for the relative risk can be calculated from the formula:

$$\log_e R_{upper} = (1 + Z/\chi)\log R$$
$$\log_e R_{lower} = (1 - Z/\chi)\log R$$

where χ is calculated omitting the continuity correction of $\frac{1}{2}$, and Z is the normal deviate corresponding to the desired confidence limit.

The second method used to correct relative risks for confounding factors is based on multiple conditional logistic regression analysis. This is described in Breslow and Day (1980), where more details are also given on the first method and the relative advantages and disadvantages of the two methods.

Appendix B
Some Investigative Methods

B.1 Introduction

This appendix gives some fuller details about the way that the general practice survey and the case-control study were conducted. Included are the following: the classification by social group used in both studies (B.2), the method of selection of controls used in the case-control study (B.3), an English translation of the letter sent in 1982 to all families in the general practice (B.4), the method of calculating β-carotene and vitamin C used in the case-control study (B.5), and an English translation of the questionnaire used in the case-control study of lung cancer patients (B.6). Furthermore, an example is presented of a questionnaire used in a case-control study of patients with miscarriage or stillbirth (B.7).

B.2 Classification by Social Group

The social status of the principal wage earner in each household was determined using the systematic occupational classification of the CBS (1971), which is based on the International Standard Classification of Occupations (I.S.C.O 1968) of the International Labor Organization of the United Nations. The following groups were used:

Upper social group	1. Scientific and professional occupations
	5. Upper level employees
Middle social group	2. Independent business person in agriculture
	3. Independent business person in commerce, industry or services
	6. Mid-level employees
Lower social group	7. Lower level employees
	8. Skilled/semi-skilled workers
	9. Agricultural workers
	10. Unskilled workers
	4. Unemployed

From some analyses, social groups 1,2,3,5 and 6 were combined into a higher social group and compared with groups 4,7,8,9 and 10 combined into a lower social group.

B.3 Selection of Controls

In order to select controls for the case-control study, 200 page numbers were selected at random from the telephone books of The Hague, Rijswijk, Voorburg and Wassenaar. The three-letter keys for family names found on the top of these pages were used to produce random letter combinations. The letter combinations were then used to select 200 controls in the alphabetically arranged card file system. The patients were numbered from 1 to 100, and the controls from 301 to 500, as follows:

1. Number patients as 1,2,3, etc.
2. Take the first letter combination from the table assigned to a patient's number.
3. Select the first five patients from the card file system whose names come alphabetically after this letter combination and who:
   — do not have the same diagnosis (controls)
   — were born within 2 years (+ or -) of the patient
   — are of the same sex as the patient
4. Select the control who is the closest to the patient in terms of age.
5. Repeat this process for the second letter combination of the patient's number.

B.4 Letter Sent to Families in General Practice Survey

Household Animal History Survey

PAJ Holst, General Practitioner
Franklin D. Rooseveltlaan 15
2285 CB Rijswijk

March, 1982

To the Family:

As you know, in connection with an investigation, I have been collecting information for some time on household animals that are kept indoors and that you come in daily contact with.
I may have questioned you about this before, but in order for me to ensure good results, I would like to ask you for some detailed information.
Please note: Most animals pose no threats to you as household pets and you can continue to enjoy them as you always have.
Some animals may spread disease more readily than others, however, and this is what I propose to investigate.
Please review the information below, which was obtained from you, and correct or amplify it as necessary.

The study concentrates on the period from 1971 to 1982.

For example:
1 cat from 1974 to 1982

.. dogs	.. to ..	.. dogs	.. to ..
.. cats	.. to ..	.. cats	.. to ..
.. rodents	.. to ..	.. rodents	.. to ..
.. parrots	.. to ..	.. parrots	.. to ..
.. budgerigars	.. to ..	.. budgerigars	.. to ..
.. canaries	.. to ..	.. canaries	.. to ..
.. pigeons	.. to ..	.. pigeons	.. to ..

.. other birds (pleases specify):

I would like to thank you in advance for your assistance. Please complete the form carefully and return it as soon as possible to me or my secretary.

B.5 Calculation of Intake of β-Carotene and Vitamin C

In the case c-control study, the intake of β-carotene and vitamin C was calculated as illustrated in Tables B.1 and B.2, respectively.

Table B.1 Calculation of β-Carotene intake

	β-Carotene (mg/100 g)	Assumed portion size (g)	Estimated β-carotene (mg/day) according to frequency of intake			
			Times/month		Times/week	
			<1	1-3	1	> 1
Endive	1.20	200	0.04	0.17	0.34	0.69
Kale	0.05	200	0.00	0.01	0.01	0.03
Spinach	5.00	200	0.18	0.71	1.43	2.86
Green cabbage	1.00	200	0.04	0.14	0.29	0.57
Purslane	1.70	200	0.06	0.24	0.49	0.97
Broccoli	2.50	200	0.09	0.36	0.71	1.43
Carrots	6.00	200	0.21	0.86	1.71	3.43
			Pieces/week			Pieces/day
			<1	1-2	3-6	1	≥2
Orange	0.20	110	0.02	0.05	0.14	0.22	0.44
Mandarin	0.12	55	0.00	0.01	0.04	0.07	0.13
Apple	0.10	160	0.02	0.04	0.11	0.18	0.36
Tomato	0.60	70	0.03	0.09	0.27	0.42	0.84
Pear	0.00	140	0.00	0.00	0.00	0.00	0.00
Banana	0.20	130	0.02	0.06	0.17	0.26	0.52
			Glasses/week			Glasses/day
			<1	1–2	3–6	1	≥2
Orange juice	0.06	150	0.01	0.02	0.06	0.09	0.18
Tomato juice	0.60	150	0.06	0.19	0.58	0.90	1.80
Apple juice	0.00	150	0.00	0.00	0.00	0.00	0.00
Other juice	0.00	150	0.00	0.00	0.00	0.00	0.00

Table B.2. Calculation of vitamin C intake

	Vitamin C (mg/100 g)	Assumed portion size (g)	Estimated vitamin C according to frequency of intake (mg/day)			
			Times/month		Times/week	
			<1	1–3	1	>1
Endive	1	200	0	0	0	1
Kale	43	200	2	6	12	25
Spinach	8	200	0	1	9	5
Green cabbage	30	200	1	4	9	17
Purslane	4	200	0	1	1	2
Broccoli	34	200	1	5	10	19
Carrots	3	200	0	0	1	2
			Pieces/week			Pieces/day
			<1	1–2	3–6	1	≥2
Orange	50	110	4	12	35	55	110
Mandarin	30	55	1	4	11	17	33
Apple	10	160	1	4	11	17	33
Tomato	15	70	1	2	7	11	21
Pear	4	140	0	1	4	6	11
Banana	10	130	1	3	8	13	26
			Glasses/week			Glasses/day
			<1	1–2	3–6	1	≥2
Orange juice	20	150	2	6	23	30	60
Tomato juice	15	150	2	5	17	23	45
Apple juice	0	150	0	0	0	0	0
Other juice	0	150	0	0	0	0	0

B.6 Questionnaire

An English translation of the questionnaire used in the case-control study is shown below. It was developed with the help of a statistician and includes 20 questions on known and suspected indoor risk factors for lung cancer, such as active smoking, passive smoking, bird keeping, social class, intake of vitamin A and β-carotene in food, and consumption of alcoholic beverages. The numbers to be computerized, from 101 to 324, each represent one or more card column positions (e.g. 227 means column 27 on the second 80-column card for that subject).

Instructions for Completing the Form

There are two types of questions in this form.

1. Some questions require information to be filled in. You are requested to complete these, as for example dates. The question will indicate clearly if filling in answer is required.
2. Other questions will ask you to place a tick next to the appropriate answer. All possible answers will be given, but you are to select only one appropriate answer. Some questions will allow more than one answer. In such cases, the question will contain information on how to do this!

Questionnaire

Investigation numbers: (patients 0–100 controls 300–500)		101–103 104–109
1. What is your date of birth? (fill in)	year ..... month ..... day	
2. Are you male or female? (tick as appropriate)	male female	110
3. Are you employed at present?	no yes	111
If yes, what is your present occupation? (fill in)	.....	
If no, what was your last occupation?	.....	
Until what year were you employed in your last job? (fill in)	.....	
Please indicate your current status. (tick as appropriate)	retired unemployed other	112
If other, please describe what your current situation is? (fill in)	.....	
4. Have you smoked at least 100 cigarettes in your lifetime? (tick as appropriate)	no yes	113
If you have answered *no* to question 4, you may skip questions 5,6, and 7 and go directly to question 8.		
5. How old were you when you began to smoke cigarettes regularly?	..... years old	114, 115

6. Thinking back over the entire period you have smoked, how many cigarettes have you smoked on average per day? (fill in number)	..... cigarettes per day	116, 117
7. Do you currently smoke cigarettes? (tick as appropriate)	no yes	118
If you answered *yes* to the above question, how many cigarettes do you smoke on average per day (fill in number)	..... cigarettes per day	119, 120
If you answered *no*, how old were you when you stopped smoking?	..... years old	121, 122
8. Have you regularly smoked cigars? (tick as appropriate)	no yes	123
If you have answered *no*, you can skip the rest of this question and go to question 9.		
For how many years have you smoked cigars? (fill in years)	..... years	124, 125
How many cigars have you smoked? (fill in number)	..... cigars per day	126, 127

9. Have you regularly smoked a pipe? (tick as appropriate)	no	
	yes	128
If you have answered *no*, you can skip the rest of this question and go to question 10.		
How many years have you smoked a pipe?	..... years	129, 130
How much you have smoked? (fill in amount)	..... pipes per day/week	131, 132
(tick as appropriate)	..... per day	
	..... per week	133
10. Does anyone in your household or workplace smoke in your presence? (tick as appropriate)	no	
	yes	134
If *yes*, how many cigarettes per day? (fill in number)	..... cigarettes per day	135, 136
11. Were there any caged birds in your parental home for a period of more than 6 consecutive months? (tick as appropriate)	no	
	yes	137
If you have answered *no*, you may skip the rest of this question and go to question 12.		
For what period were birds kept in your parental home? (fill in years)	from 19... to 19...	138–141
Please indicate the number of different types of birds kept in your parental home. (If a particular type was not present, leave the space blank) (fill in number) there were	... parrots	
	... budgerigars	142, 143
	... canaries	144, 145
	... pigeons	146, 147
	... other birds such as	148, 149
	... chickens	150, 151

12. Did you ever keep birds in or around (e.g. in garden or shed) your house in a cage or aviary after leaving your parental home? (tick as appropriate)	no yes		152
If you answered *no* to the above question, you can skip the rest of this question and go to question 13.			
What was the period during which you kept birds in and around your house? (fill in years)	from 19...	to 19...	153–156
Please indicate the number of different types of birds in your home. (if a particular type was not present, leave the space blank) (fill in number) there were	... parrots ... budgerigars ... canaries ... pigeons ... other birds such as .... chickens		 157, 158 159, 160 161, 162 163, 164 165, 166
13. Do you currently keep caged or aviary birds around your house? (tich as appropriate)	no yes		167
If you have answered *no* to this question, you can skip the rest of this question and go to question 14.			
In what year did you first start to keep birds in your household. (fill in year)	from 19...		168, 169
Please indicate the number of different types of birds in your hosehold. (if a particular type is not present, leave the space blank) (fill in number) there are	... parrots ... budgerigars ... canaries ... pigeons ... other birds such as .... chickens		 170, 171 172, 173 174, 175 176, 177 178, 179

14. Please carefully indicate how many caged or aviary birds you have owned in the past 10 years.

Have you kept birds in your home at any time from 1975 to 1985? (tick as appropriate)	no yes	180

If you have answered *no*, you can skip the rest of this question.

For example, let us suppose that you owned a parrot from 1975 to 1979, and in 1977 you also started keeping pigeons, and in 1983 your daughter kept a budgerigar in her bedroom. You would then indicate the information as follows:

	'75	'76	'77	'78	'79	'80	'81	'82	'83	'84	'85
parrots	X	X	X	X	X						
budgerigars									X		
canaries											
pigeons			X	X	X	X	X	X	X	X	X
other birds											
chickens											

Now please complete the following chart with your own information:

	'75	'76	'77	'78	'79	'80	'81	'82	'83	'84	'85
parrots											
budgerigars											
canaries											
pigeons											
other birds											
chickens											

204–258

15. Have you ever kept caged birds in your bedroom? (tick as appropriate)	no yes	259
If you answered *yes* to the above, in what years did you do so?	before 1975 in or after 1975	260

16. Have you ever bred birds yourself?		
(tick as appropriate)	no	
	yes	261
If you answered *yes* to the above, in what years did you breed birds?	before 1975	
	in or after 1975	262
17. Have you frequently visited friends, neighbours or family members who owned birds and where you sat in the room where the birds were kept for any length of time?		
(tick as appropriate)	no	
	yes	263

If you answered *yes*, would you please write a brief description of these situations?
(type of bird, how long were you there on average for each visit, etc.)

.....
.....

18. Do you work, or have you ever worked in a pet store or as a caretaker of caged birds.		
(tick as appropriate)	no	
	yes	264
Have you ever worked on a poultry farm?		
(tick as appropriate)	no	
	yes	265
Have you ever worked in greenhouse horticulture with (chicken) manure?	no	
(tick as appropriate)	yes	266
Have you regularly cleaned bird cages or do so at present?	no	
(tick as appropriate)	yes	267

19. Have you changed any of your dietary habits during the past year? (tick as appropriate)	no yes	268

If you have answered *no* to the question, you can skip the rest of this question.

Did you do so with the intention to lose weight? (tick as appropriate)	no yes	269
Did loss of appetite have anything to do with eating less? (tick as appropriate)	no yes	270
Do you actually eat more? (tick as appropriate)	no yes	271

Would you please described in more detail why you changed your dietary habits:

.....

.....

20. We would like to know which of the following foods you eat and how often. Would you pleace place a tick under the frequency with which you have regularly eaten each type of food since 1975:

Vegetables	seldom or never	less than once a month	1-3 times a month	once a week	more than once a week	
Endives						304
Kale						305
Spinach						306
Green cabbage						307
Purslane						308
Broccoli						309
Carrots						310

Fruits	seldom or never	less than 1 piece a week	1-2 pieces a week	3-6 pieces a week	1 piece a day	2 or more pieces a day	
Orange							311
Mandarin							312
Apple							313
Tomato							314
Pear							315
Banana							316

Fruit juices	seldom or never	less than 1 glass a week	1-2 glasses a week	3-6 glasses a week	1 glass a day	2 or more glasses a day	
Orange							317
Tomato							318
Apple							319
Other Such as							320

Alcoholic beverages	seldom or never	1-6 glasses a week	1-2 glasses a day	3-4 glasses a day	5 or more glasses a day	
Beer						321
Wine						322
Hard liquor (gin, cognac)						323
Other Such as						324

B.7 Questionnaire Used in a Case-control Study of Patients with Miscarriage or Stillbirth

Investigation number

Patient No :.... ....
Control No: 101-103

If patient: Date of miscarriage (fill in) Weeks of gestation OR Date of stillbirth Weeks of gestation If control: Date of delivery Weeks of gestation	 year ..... month ..... day .... year ..... month ..... day .... year ..... month ..... day		 104-109 110,111 112-117 118,119 120-125 126,127
1. Your age when you stopped full-time education	..... years		128,129
2. Your occupation:			130,131
3. Do you have a partner? (tick as appropriate)		no yes	132
4. If yes, what is his occupation:			133,134
5. How many times have you been pregnant?	.....		135,136
6. How many miscarriages have you had?	.....		137,138
7. How many stillbirths have you had?	.....		139,140
8. How many terminations have you had? (tick as appropriate)		none one more	141
9. How many live births?	.....		142,143
10. Have you smoked within the last 12 months? (tick as appropriate)		no yes	144

11. If yes, how many cigarettes per day? (tick as appropriate)		less than 5 5-10 more than 10	145
12. During the last 12 months, have you kept birds: (tick as appropriate)	in your house?	no yes	146
	in an aviary attached to your house?	no yes	147
If you have kept birds, please specify which type of bird: (delete as appropriate)	Parrots, budgerigars, parakeets, canaries, pigeons, chickens, other		148
	Other (please specify):		149
13. Have you ever lived in a house where birds were kept? (tick as appropriate)		no yes	150
If yes, please specify, which birds:			151
During which period (fill in years)	..... to .... to		152, 153
14. Have you worked with birds during the last 12 months? (tick as appropriate)	pet shop on a farm in a veterinary practice other (please specify):	no yes	154 155
15. Have you ever worked with farm animals in the last 12 months? (tick as appropriate)		no yes	156
If yes, please specify which animal:			157

Appendix C
Case Histories of the 22 Couples with Infertility Tests in the General Practice Survey

Couple 1 (lower social group) was examined from 1971 to 1975 after 4 years of marriage. The woman had right oophorectomy for Stein-Leventhal syndrome. One child was born in 1975 after the couple had been married for 8 years (gravida I, para I). This couple had always had birds in their home from the date of marriage. They kept a parrot from 1967 to 1976 in their living room/bedroom. They also kept a dog from 1971 to 1976.

Couple 2 (higher social group) was examined from 1971 to 1976 after 3 years of marriage. The woman had a tubal correction in 1974. Children were born in 1976 and 1980 (gravida II, para II). This household kept a budgerigar from 1970 to 1979.

Couple 3 (lower social group) had infertility tests from 1971 to 1973. The man had atrophy of the right testicle and a varicocele of the left testicle. One child was born in 1974 (gravida I, para I). When the man was young, he was a bird breeder and he had an aviary with nine pairs of tropical birds. As a wedding gift from their family this couple got a show pigeon. This household kept a budgerigar from 1969 to 1977.

Couple 4 (lower social group) was examined from 1975 after 3 years of marriage. The man had an epididymitis in 1972 and an optic neuritis in 1966 in his medical history. No children were born (gravida 0, para 0). The man had always had exposure to budgerigars in his parental home. This couple kept a canary from 1971 to 1982. They also kept a cat from 1979 to 1982.

Couple 5 (higher social class) had infertility tests from 1971 after 9 years of marriage. The woman had had a spontaneous abortion three times and no children were born (gravida III: 1962, 1965, 1974; para 0). From their date of marriage in 1962 they had always kept and bred birds. They had an aviary with 20 birds in their bedroom from 1962 to 1965. They kept a canary in their living room/bedroom from 1962 to 1982. The woman had always had exposure to many budgerigars in her parental home. The couple also kept a dog from 1962 to 1982.

Couple 6 (lower social group) was examined from 1971 to 1979 after 3 years of marriage. The man had oligoteratospermia. In 1976 the man had an aspecific lung infiltrate and from this time onwards a temporal epilepsy. In 1983 a non-Hodgkin's

lymphoma was diagnosed. The man died aged 38 years in 1984. No children were born (gravida 0). Before marriage the man had an aviary with a parrot and budgerigars and a dovecote. After marriage, the couple kept and bred about 15 pairs of canaries on their top floor permanently.

Couple 7 (lower social group) had infertility tests from 1977 after 4 years of marriage. No children were born (gravida 0). The gynaecologist found no abnormalities. The couple kept a budgerigar from 1974 to 1981, five zebra finches from 1976 to 1978 and a cockatoo and a dwarf parrot in 1981 and 1982. They also kept a dog from 1974 to 1982 and two hamsters from 1974 to 1981.

Couple 8 (higher social group) had infertility tests from 1982 on after 4 years of marriage. The man had epididymitis in 1976 in his medical history and the gynaecologist found oligospermia. No children were born (gravida 0). Before marriage, the man had worked regularly in a pet store with birds (cages). After marriage, the couple kept four tropical birds in an aviary in their bedroom and one budgerigar in their living room from 1975 to 1982.

Couple 9 (lower social group) was examined from 1974 to 1980 after 3 years of marriage. The man had a small varicocele and oligoteratospermia as well as severe asthma since having had pneumonia in 1958. The woman was pregnant by artificial insemination by donor (AID) and one child was born in 1980 (gravida I, AID; para I). They never kept birds in their house. They kept a rabbit from 1972 to 1975.

Couple 10 (lower social group) was examined from 1975 to 1980 after 6 years of marriage. The man had ejaculatory impotence. In April 1980 the man suddenly died while jogging in the dunes. Post-mortem examination showed aortic valve stenosis with calcification and signs of endocarditis. No children were born (gravida 0). The man kept and bred birds in his youth and had an aviary in his bedroom over his folding bed with many pairs of tropical birds. His father died from lung cancer at the age of 50 years. After the couple married, they kept a parrot from 1972 to 1982, a Japanese nightingale from 1976 to 1978, two budgerigars from 1973 to 1975 and a mozambique from 1978 to 1982. They also kept a cat from 1972 to 1973.

Couple 11 (higher social group) was examined from 1974 to 1982 after 1 year of marriage. The woman had a tubal adhesiolysis in 1977. No children were born (gravida 0). The couple kept two tropical birds from 1972 to 1979.

Couple 12 (higher social group) was examined from 1976 to 1982 after 5 years of marriage. The woman had cystic endometriosis. Once she had salpingitis and was examined for chlamydia. The IgG was positive at 1:64 and the IgM was 0. No children were born (gravida 0). The couple kept a parrot from 1967 to 1974 and two budgerigars from 1972 to 1982. They also kept a dog from 1973 to 1982.

Couple 13 (higher social group) was examined from 1974 to 1980 after 3 years of marriage. The woman had a hypophyseal adenoma. In her medical history, she had a spontaneous abortion in 1971. One child was born in 1980 (gravida II, para I). They kept a budgerigar from 1971 to 1982.

Couple 14 (higher social group) was examined from 1975 to 1980 after 4 years of marriage. The man had aspermia from (mumps?) orchitis. No children were born (gravida 0). The couple never kept pets in their house during their marriage.

Couple 15 (lower social group) was examined from 1969 to 1975 after 7 years of marriage. The woman twice had a pregnancy outside the womb in 1970 after tubal insufflation. No children were born (gravida II, para 0). The couple kept and bred show pigeons from 1958 to 1971, canaries from 1974 to 1977 and parrots from 1977 to 1983. They also owned two dogs and four cats from 1972 to 1982.

Couple 16 (lower social group) was examined from 1971 to 1975 after 5 years of marriage. No children were born (gravida 0). The couple never kept pets in their house during their marriage.

Couple 17 (lower social group) was examined from 1981 to 1983 after 5 years of marriage. The man had small limp testes, without spermatogenesis. No children were born (gravida 0). During their marriage, the couple kept no birds in their house. In his parental home, the man had kept and bred tropical birds in the kitchen from 1957 to 1976. For several years, he cleaned the aviary three to four times per week. The couple kept two cats from 1976 to 1982.

Couple 18 (higher social group) was examined from 1980 to 1982 after 2 years of marriage. The woman was 29 years old and had primary infertility. The man had had healthy children with his first wife. No children were born after 1978 (gravida 0). The woman kept a canary from 1976 to 1983.

Couple 19 (lower social group) was examined from 1966 to 1975 after 1 year of marriage and a first stillbirth. The woman had three stillbirths with severe congenital deformities in 1966 to 1967 (gravida II, para III, all stillbirths). From the beginning of their marriage in 1965 up to 1972 when they lived in lodgings, they kept and bred canaries in an aviary. Before marriage the woman had kept a canary in her parental house and the man bred canaries.

Couple 20 (lower social group) was examined from 1978 to 1979 for secondary infertility after 10 years of marriage. The couple wanted to have further children. The woman had had two spontaneous abortions in 1967 to 1977. After the infertility tests, two children were born in 1979 and 1981. In total four children were born (gravida VI; para IV, 1969, 1970, 1979 and 1981). The couple kept a budgerigar from 1973 to 1982.

Couple 21 (lower social group) was examined from 1982 for secondary infertility after 7 years of marriage. The couple wanted to have further children. One child was born in 1978 (gravida II, para I). In 1981 the woman had a spontaneous abortion with secondary amenorrhoea. During the infertility tests a benign ovarian cyst was found. The man kept and bred pigeons and canaries in his parental home. The couple kept a canary from 1977 to 1982 in their living room/bedroom.

Couple 22 (lower social group) was examined from 1982 for secondary infertility after 8 years of marriage. The couple wanted to have further children. Two children were born in 1977 and 1979 (gravida II, para II). The woman had secondary amenorrhoea in 1982. The couple kept two canaries and five zebra finches in their bedroom from 1977 to 1983. They also kept a dog from 1969 to 1982.

Appendix D
Steps to Prevent the Formation of Bioaerosols from Pet Birds

In order to improve the indoor air quality in the spaces where people keep birds as pets a number of steps can be taken. These are summarized below.

Prevent Mould Developing. In countries with a maritime climate, the relative humidity is higher and bird seed can quickly decay on warmer days. Mould may begin to form when the relative humidity exceeds 17%. Improper storage of food can cause infestation by mites. The feeder should only contain enough seeds for the bird to consume in one day. Leftover seeds spoil quickly and develop mould. The size of the feeder should be in proportion to the bird's daily intake. A canary weighs only 18 g on average, and eats about 3.6 g seed and drinks about 5.2 ml water per day. A budgerigar weighs an average of 40 g. It eats about 6 g seed and drinks 1–3 ml water per day. A grey and red tailed parrot weighs an average of 450 g. It eats about 35 g seed plus about 40 g fruits and vegetables per day and drinks about 20 ml water per day. Some older designs of cages incorporate a false wire floor above the dirt tray. This should be removed, primarily because the bird could trap its foot or leg in the mesh, but also because it hampers cleaning. Droppings tend to adhere to the wire, rather than falling through onto the dirt tray beneath. This means that the bird keeper will need to remove and wash the grid every day to ensure it remains clean. Good hygiene is vital for a caged bird, since it may drop food onto the floor and then descend to pick it up. Clearly, the bird will be at serious risk if the floor covering is very dirty or mouldy.

Clean the Bottom of the Cage Daily. Food remnants and droppings dry quickly. There is an old English saying: "My mouth tastes like the bottom of a parrot's cage." The droppings turn to dust after drying. It is mainly sand that can turn a cage into a dustbin. Loose sand can quickly become contaminated because the droppings dry out and are hard to see. Most new cages have a sliding tray that slots into the base. In practice, although these trays usually fit flush with the floor of the base unit, debris tends to accumulate around the sides. It is necessary to open the door to clean the interior thoroughly. Furthermore, parrots and budgerigars produce ultrafine powdery dust composed of keratin particles, which can be suspended in the air after being deposited on the bottom of the cage by air currents and the flutter of the birds. Suspended dust particulates from the bird cage are often contaminated.

Cleaning a cage, if done properly, takes time and requires contact with unsanitary material. These facts make it very easy to find reasons to put off the job. It then becomes a job that at best only gets done once every 2 weeks. A variety of materials can be used to cover the floor of the cage. These floor coverings should be neither toxic nor likely to turn mouldy when wet. The possibility of mould developing is a good reason for not using hay or straw as a lining material in a bird cage. All birds will chew the floor covering of their cage and so are liable to be affected by harmful chemicals in this way. Do not use coloured sheets or a newspaper, as these could contain toxic substances. Loose sand tends to prove messy, can end up being scattered into the room, is not particularly absorbent and may cause irritation. The fine so-called shell (or quartz) sand is too sharp for many species of aviary birds. Through regular mechanical irritation, the birds develop intestinal bleeding and inflammation. By pecking at the food residues on the bottom of the cage that have been contaminated by the droppings of the sick bird, an infection can spread quickly through an aviary.

Line the Bottom of the Cage with Reinforced Sheet-Like Floor-Covering Material. A layer of uncoloured wrapping paper or, better still, slightly oiled non-woven tissue will keep the bottom of the cage clean. The absorbent tissue should be replaced every day. This procedure will keep the bird in good condition and produce the least amount of suspended dust particulates and bioaerosols in the indoor air. The dirt tray should also be removed and rinsed out. After this has been done, a new tissue can be replaced in the bottom of the cage. If this is done, food remnants and droppings will not accumulate in the cage. Grit or a cuttle bone can be hung in the cage so that the bird has easy access to calcium.

Isolate Sick Birds. Diseases quickly spread from one bird to another in cages or aviaries. Droppings and food remnants can accumulate to produce high concentrations of infectious matter. A sick bird must therefore be kept separately.

Keep the Breeding Cage Very Clean. Breeding cages should be disinfected before use to eliminate the bacteria, viruses and moulds that have accumulated in the cage. Failed breeding efforts can often be traced to the presence of lice and other parasites. During the breeding season, it is rarely if ever possible to clean the breeding cages. Never use loose sand in the breeding cages. The young birds become easily infected in the 1st week when they cannot fly and scratch over the bottom of the cage.

Daily Spraying Will Improve the Condition of the Bird's Plumage. Birds living indoors are clearly unable to bathe as they would in an aviary. Regular spraying should encourage them to preen normally, reducing the likelihood of feather plucking. There is nothing worse for the bird's plumage than lack of moisture. The relative humidity in tropical rain forests is between 60% and 70%, while it is between 30% and 40% in the home. Most parrots and budgerigars appreciate a light spray, however, although they may be nervous at first until they are used to

it. A clean plant sprayer with a fine nozzle which produces a mist of water droplets is ideal. It is best to spray the bird just before you clean out the cage, so that you can change the wet lining immediately afterwards. Before you begin, remove the food and water pots. Then, with the nozzle directed above the bird's head and the sprayer held at a suitable distance outside the cage, squeeze the handle. If the sprayer is used in this way, the bird will be moistened by a cloud of droplets falling from above rather than being struck directly by a jet of water. Although it may be startled at first, the bird should begin preening shortly afterwards. Spraying will help to improve the condition of the plumage and dampen down the feather dust.

Ventilate the Living Room Properly. Infectious bioaerosols can develop readily in a warm environment. No ventilation and a good warm hearth such as is customary in a cold winter are ideal circumstances for the spread of biological pollutants from the bird cages throughout the indoor air. To create optimum conditions for the birds, the food and water pots and dirt tray should be cleaned daily. The cage may be moved to another room or the kitchen, so that the living room can be aired out and vacuumed.

Do not Keep Birds in Bedrooms. In 24 h, we breathe between 10 000 and 15 000 l air. About 4000 l will be breathed in the bedroom. For health reasons, it is very important that the air here is as clean as possible. All children who keep caged pets in their bedroom run a severe risk of developing extrinsic atopic asthma.

Ventilate Exhibition Spaces and Pet Shops Properly. In 1987 an exhibition of birds in Zwijndrecht near Antwerp (DeSchrijver 1987) caused an epidemic of psittacosis infections in 8% of the visitors and 17% of the exhibitors. The exhibition space for 500 birds was too small, dusty and badly ventilated.

Glossary

allergen	Any antigen that causes allergy in a hypersensitive person. Pollens, fur, feathers, mould and dust may cause hay fever, and the fine dust particles produced by house and bird mites have been implicated in some forms of asthma.
alveolitis	Inflammation of the walls of the minute air sacs (alveoli) of the lung, the sites of gaseous exchange, is caused by inhaled inorganic dusts such as coal dust, silica and asbestos or by inhaled organic dusts from mouldy hay, straw, dovecotes or the cages of pet birds. Chronic alveolitis progresses slowly to the state of fibrosis, emphysema, and bronchiectasis.
antibody	A special kind of blood protein that is synthesized in lymphoid tissue in response to the presence of a particular antigen and circulates in the plasma to attack the antigen and render it harmless.
antigen	Any substance that the body regards as foreign or potentially dangerous and against which it produces an antibody.
aorta	The main artery of the body, from which all other arteries derive. It arises from the left ventricle.
aortic valve stenosis	Narrowing of the opening of the aortic valve due to fusion of the cusps that comprise the valve. It may result from previous rheumatic fever or infection of the lining of the heart. Aortic valve stenosis obstructs the flow of blood from the left ventricle to the aorta during systole and may be a cause of sudden death during exercise.
arbovirus	One of a group of RNA-containing viruses that are transmitted from animals to man by insects (i.e. arthropods — hence arthropod-borne viruses) and cause diseases resulting in encephalitis or serious fever.
artery	Blood vessel carrying blood away from the heart. All arteries except the pulmonary artery carry oxygenated blood.

bronchial tree — A branching system of tubes connecting the windpipe with the air sacs of the lung, including the bronchi and their subdivisions and the bronchioles.

bronchiectasis — Widening of the bronchi or their branches. It may result from infection or from obstruction. Pus may form in the widened bronchus so that the patient coughs up purulent sputum, which may contain blood.

bronchitis — Inflammation of the bronchi, characterized by coughing, the production of mucopurulent sputum, and narrowing of the bronchi due to spasmodic contractions. Acute bronchitis is caused by viruses or bacteria. Chronic bronchitis is not primarily an inflammatory condition, although it is frequently complicated by acute infections. The disease is particularly prevalent in Britain, Belgium, and the Netherlands in association with cigarette smoking, open air and indoor air pollution (atopens, microbes).

carcinogen — Any substance that, when exposed to living tissue, may cause the production of a cancer. Many chemicals known to produce cancer in laboratory animals have yet to be proved to do so in humans.

carcinoma — Any cancer that arises in epithelium, the tissue that lines the skin and internal organs of the body.

cardiomyopathy — Any chronic disease affecting the muscle of the heart. It can be caused by various conditions, including virus infections, alcoholism and vitamin B deficiency. The cause is often unknown. It results in enlargement of the heart.

case-control study — Comparison of one group of people who have a disease with another group free from that disease, in terms of variables in their backgrounds (e.g. bird keeping in those who have just had a nasal polyp surgically removed and in those who came to the hospital with a broken nose). In the more precise matched-pair study, every individual with the disease is paired with a control matched on the basis of (say) age, sex, or occupation in order to place greater emphasis on a factor in study.

chlamydia — A genus of minute virus-like microorganisms that cause disease in man and birds. Some chlamydia infections of birds can be transmitted to man (ornithosis, parrot disease).

clearance — Lung clearance is the rate at which inhaled gaseous and dust particles are removed from the bronchial tree to the throat.

cohort study — A systematic follow-up of a group of people for a defined period of time to observe their pattern of disease and/or cause of death. On the basis of factors prevailing at the outset of the study, two or more separate cohorts (bird keeping/ no bird keeping) may be identified and compared in relation to outcome.

colon carcinoma — Cancer of the colon, the main part of the large intestine. The colon has no digestive function but it absorbs large amounts of water and electrolytes from the undigested food passed on from the small intestine and resting in the colon. At intervals strong peristaltic movements move the dehydrated contents (faeces) towards the rectum.

colonization — Mass of microorganisms, usually bacteria, all of which are considered to have developed from a single parent cell.

congenital transposition of the great vessels — A congenital abnormality of the heart in which the aorta arises from the right ventricle and the lung artery from the left ventricle. Life is impossible unless there is an additional abnormality that permits the mixing of blood between the pulmonary and systemic (aortic) circulations. Few of those surgically untreated survive infancy.

conjunctivitis — Inflammation of the mucous membrane that covers the front of the eye and the inside of the eyelids (pink eye). Conjunctivitis is caused by infection (in which case it usually spreads rapidly to the other eye), allergy, or physical or chemical irritation.

demography — The study of the populations of the world, their racial make-up, birth rates, cases of a disease per 100 000, death rates, and other factors affecting the quality of life within them.

dissecting aortic aneurysm — Usually affects the first part of the aorta and results from a degenerative condition of its muscular coat. This weakness predisposes to a tear in the lining of the aorta, which allows blood to enter the wall and dissect the muscular coat.

ectoparasite — Parasite that lives on the outer surface of its host. Some ectoparasites, such as bed bugs, maintain only periodic contact with their hosts.

emphysema — The minute air sacs of the lungs are enlarged and damaged and as a result the surface area for the exchange of oxygen

	and carbon dioxide is reduced. Severe emphysema causes breathlessness which is made worse by infections. The patient may become dependent on oxygen.
encephalitis	Inflammation of the brain. It may be caused by a viral or bacterial infection.
endocarditis	Inflammation of the lining of the heart cavity and valves. It is most often due to rheumatic fever or results from bacterial infection. Permanent damage to the heart valves may result.
enteritis	Inflammation of the small intestine, usually causing diarrhoea.
eosinophilia	An increase in the number of eosinophils in the blood. Eosinophilia occurs in a variety of diseases, including allergies and parasitic infestations.
epidemiological study	The study of all forms of widespread disease that relates to infectious epidemics or to the environment and ways of life. It thus includes the study of the links between smoking and cancer, and diet and coronary disease, as well as infectious and allergic diseases transferred by pets to humans.
epithelium	The tissue that covers the external surface (skin) of the body and lines hollow structures (such as airways and intestines).
erysipeloid	An infection of the skin and underlying tissues, developing usually in people handling fish, poultry or meat. Infection enters through scratches or cuts on the hands, and is normally confined to a finger or hand, which becomes reddened.
erythematous plaques	Red and raised circular patches of the skin, resulting from local tissue damage, usually due to infection.
ethmoid sinus carcinoma	Cancer of the ethmoid sinuses, paranasal sinuses which open into the nasal cavity via the meatuses and consist of many spaces inside the ethmoid bone lined with mucous membrane.
Ewing's sarcoma	A highly malignant tumour of bone, occurring in children and young adults. It commonly arises in the limbs but may affect any bone.
fibrosarcoma	A malignant tumour of connective tissue. This type of tumour may affect any organ but is most common in the limbs,

	particularly the leg. Tumours arising in soft tissue have a considerably better prognosis than those arising in bone.
granuloma	A small nodular delimited aggregation, made up of small particles.
herpes	Inflammation of the skin caused by viruses and characterized by collection of small blisters.
herpes virus	One of a group of DNA-containing viruses causing latent infections in humans and animals. The herpes viruses are the causative agents of herpes and chickenpox. The group also includes the cytomegalovirus and Epstein-Barr virus.
histamine	Histamine is formed in the body by mast cells, found in nearly all tissues. It has pronounced pharmacological activity, causing dilatation of blood vessels (tissue damage, shock, migraine), acid production in the stomach (stress) and contraction of smooth muscle (for example in the lungs, asthma). It is an important local mediator of inflammations.
hyaline membrane disease	The condition of a newborn infant in which the lungs are imperfectly expanded. Otherwise known as respiratory distress syndrome, it is most common among premature infants in whom the surface tension of the air sac is still too high and surfactant is deficient.
hyperreactivity	Prone to respond strongly to the presence of a non-specific stimulus.
immune deficiency	Deficiency in the body's ability to resist infection. Immunity is afforded by the presence of circulating antibodies and white blood cells.
immunofluorescence	A technique for observing the amount and/or distribution of antibody or antigen in a tissue section. The antibodies are labelled with a fluorescent dye and applied to the tissue, which is observed through an ultraviolet microscope.
incidence rate	The number of new episodes of illness arising in 1000 individuals over an estimated period.
infertility	Inability in a woman to conceive or in a man to induce conception. Female infertility may be due to failure to ovulate or to disease of the inner mucous lining of the oviducts or the womb. Infections ascending the vagina may cause salpingitis, resulting in infertility. Male infertility may be due to spermatozoa in the ejaculate being defective either in motility or in numbers. The impotence occurs in

	these patients as a result of hormonal disturbances or of damage to the testicles following ascending or haematogenic infections.
intracellular	Situated inside a cell.
keratomalacia	A progressive disease of the eye due to vitamin A deficiency. The cornea softens and may become perforated. This condition is very serious and blindness is usually inevitable.
Koch's postulates	Koch described certain postulates which, he insisted, must be met before a causative relation could be accepted between a particular microorganism and the disease in question. First, the microorganism must be shown to be present in every case of the disease by isolation in pure culture. Second, it must not be found in cases of other diseases. Third, once isolated, the agent must be capable of reproducing the disease in experimental animals. Fourth, the agent must be recovered from the experimental disease produced.
lung cancer	Cancer arising in the mucous membrane of the air passages (bronchial cancer) or lung. It is a very common form of cancer, particularly in Belgium, the Netherlands and the United Kingdom. It is strongly associated with cigarette smoking and with exposure to air pollutants such as asbestos fibres or radon gas precipitated from fine rock dust particles which occur in the mines.
lung fibrosis	Thickening and scarring of the lining of the air sacs (alveoli) of the lungs, causing progressive breathlessness.
macrophage	A large scavenger cell present in the small tissue space between the alveoli and in these minute air sacs of the lung. They wander between cells and aggregate at focal sites of infection, where they remove bacteria or other foreign bodies from blood or tissues.
malignant	Describing a tumour that invades and destroys the tissue in which it originates and can spread to other sites in the body via the bloodstream and lymphatic system. If untreated such tumours cause death.
metaplasia	An abnormal change in the nature of a tissue. This may be an early sign of malignant change.
microbe/ microorganism	Any organism too small to be visible to the naked eye. Microorganisms include bacteria, some moulds, mycoplasmas, protozoa and viruses.
micrometre	One millionth of a metre. Symbol: μm.

mite	Microorganism belonging to a group that also includes the ticks. Most mites are small, averaging 1 mm or less in length. The house dust mites which cause allergic asthma are medically important. Birds have feather mites.
morbidity	The state of being diseased.
morbidity rate	The proportion of cases of a disease in a population usually expressed as the number per 100 000 at risk.
mortality	The proportion dying in a period, usually calculated as the number of registered deaths in a year, multiplied by 1000 and divided by the population at the middle of the year.
mucociliary system	Cilia and mucus production are particularly characteristic of the epithelium that lines the upper respiratory tract. A mucus layer and the beating of these cilia serve to remove particles of dust and other foreign material
mycoplasma	One of a group of minute non-motile microorganisms that lack a rigid wall and hence display a variety of forms. The *Mycoplasma pneumoniae* cause a pneumonia-like disease in humans.
nasopharynx	The part of the throat that lies above the soft palate.
neoplasm	Any benign (not cancerous) or malignant tumour.
oesophageal varices	Dilated veins in the gullet caused by obstruction of blood flow through the liver. Bleeding may occur.
ornithosis	An infectious disease of birds, due to a virus-like organism of the genus chlamydia. It can be transmitted to humans and causes symptoms resembling those of pneumonia.
oviducts	Either of a pair of tubes that conduct ova (egg cells) from the ovary to the womb.
pack-years	One pack of cigarettes per day for 1 year.
paroxysm	A sudden violent attack, for instance of coughing.
perianal	Beside the anus.
perinatal death	Infant death, in the period from about 3 months before to 1 month after the expected birth.
pneumonia	Inflammation of the lung caused by bacteria, in which the minute air sacs (alveoli) fill up with pus so that air is excluded and the lung becomes solid. The symptoms depend upon the amount of lung involved and the virulence of the bacteria.

polyp	A growth, usually benign, protruding from a mucous membrane. Polyps are commonly found in the nose and sinuses, giving rise to obstruction, chronic infection, and discharge. They are often present in patients with allergic rhinitis, in whom they may develop in response to long-term antigenic stimulation.
prevalence	Number of sick persons per 1000 individuals in a population at a particular time (point prevalence) or over a stated period (period prevalence).
pseudocyst	A fluid-filled space without a proper wall or lining, within an organ.
rectal carcinoma	Cancer of the rectum. The rectum is the terminal part of the large intestine, about 12 cm long, which runs from the sigmoid colon to the anal canal. Faeces are stored in the rectum before defecation.
rhinitis	Inflammation of the mucous membrane of the nose. It may be caused by a virus infection (acute rhinitis, common cold) or an allergic reaction (allergic rhinitis).
saprophyte	Any microorganism that lives and feeds on the dead and putrefying tissues or excreta of animals or plants.
sarcoma	Any cancer of connective tissue.
S.E.M./S.E.	(Standard error of a mean). The extent to which the means of several different samples would vary if they were taken repeatedly from the same population.
silicosis	A lung disease, produced by inhaling silica dust particles. It affects workers in mineral mining, stone-dressing, or sandblasting. Silica stimulates fibrosis of lung tissue which produces progressive breathlessness and considerably increased susceptibility to tuberculosis, but not to lung cancer.
spore	A small reproductive body produced by plants and microorganisms (e.g.*Chlamydia psittaci*). The spores of chlamydiae function as dormant stages of the life cycle, enabling the chlamydiae to survive adverse conditions.
sputum	Saliva mixed with mucus coughed up from the respiratory tract.
statistical significance	A difference between two groups is significant at the 5% level ($p < 0.05$) if the probability of that difference, or one more extreme than it, occurring by chance, is less than 5%.

subacute	Describing a disease that progresses more rapidly than a chronic condition but does not become acute.
subcutaneous tissue	Loose connective tissue, often fatty, situated under the dermis.
sulfa drug	Prevents the growth of bacteria.
T cell	Mediated cellular immunity, controls the defence of the lung tissue to intracellular infections. T helper cells kill infected cells with virus particles.
tick	Bloodsucking parasite belonging to the order of anthropods that also includes the mite.
tetracycline	Antibiotic.
toxoplasmosis	A disease of mammals and birds due to the protozoan *Toxoplasma gondii*, which is transmitted to humans via undercooked meat, contaminated soil or by direct contact. Generally symptoms are mild but severe infection of lymph nodes can occur.
trachea	The windpipe.
tumour pathology	The study of tumour processes with the aim of understanding and causes. This is achieved by observing samples of diseased tissue obtained from the living patient or at autopsy by the use of X-rays or biopsy. Lung tumours are divided into a number of types: epidermoid (having the appearance of the outer cornified layer of the skin), small cell, large cell or adenocarcinoma (showing a glandular growth pattern).
urticaria	An acute or chronic allergic reaction, known also as hives or nettle rash, in which red round weals develop on the skin, ranging in size from small spots to several inches across. These itch intensely and may last for hours or days. The cause is hyperreactivity to allergens, followed by histamine release.
vein	Blood vessels conveying blood towards the heart. All veins except the pulmonary vein carry deoxygenated blood from the tissues, via the capillaries, to the main vein ending in the right atrium of the heart.
xanthoma	A yellowish swelling in the skin resulting from deposits of fat. The presence of xanthomata is usually accompanied by a raised blood cholesterol level.

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