1. Is Sjögren’s syndrome contagious?
No.

2. Is Sjögren’s syndrome hereditary?
No, it is not hereditary. However, it does occur more commonly than normal in relatives of patients with Sjögren’s syndrome.

3. Do you get Sjögren’s syndrome through the wrong diet or lifestyle?
There is absolutely no evidence of this.

4. What is the life expectancy of a patient with Sjögren’s syndrome?
Life expectancy is virtually normal. Risks are only higher if a patient also has special complications such as specific rare lung disorders or non-Hodgkin lymphoma.

5. Can you ever completely get rid of Sjögren’s syndrome?
In principle no, but this does not mean that the symptoms will always remain the same. When treating Sjögren’s syndrome, we quite often see an improvement in the symptoms. Some patients have scarcely any symptoms after a time.

6. Is vaginal dryness also part of Sjögren’s syndrome and what can be done about it?
Yes, this is possible. Treatment is discussed in chapter 5.

7. Is it true that Sjögren’s syndrome can worsen or improve without there being any apparent reason?
Yes, Sjögren’s syndrome often takes an undulating course, with there being any clear cause for this.

8. Should a Sjögren’s patient get pregnant?
Yes, but ensure that you have sufficient water and eye-drops for the flight. The air in planes is very dry. Also take along (sugar-free) chewing gum, since this will help to combat ear problems (feeling of pressure, “muffled” hearing) due to a difference in air pressure in the aircraft and in your middle ear during take-off and landing. The Eustachian tube, which links the middle ear to the pharynx, only allows more air through when swallowing, yawning and chewing.

9. Should a Sjögren’s syndrome patient travel by plane?
Yes, but ensure that you have sufficient water and eye-drops for the flight. The air in planes is very dry. Also take along (sugar-free) chewing gum, since this will help to combat ear problems (feeling of pressure, “muffled” hearing) due to a difference in air pressure in the aircraft and in your middle ear during take-off and landing. The Eustachian tube, which links the middle ear to the pharynx, only allows more air through when swallowing, yawning and chewing.

10. How can you cope with the dreadful problem of fatigue?
Sometimes a cause for the fatigue can be found such as anaemia or an underactive thyroid gland. If known causes have been excluded, the only option is to “learn to live with it”. The best method is to spread activities throughout the day and the week and to avoid activities involving exertion that do not contribute to the quality of life. Be a bit egocentric where that’s concerned. See also chapters 5 and 6.

11. I went to a doctor who did a test to check the amount of tear fluid (Schirmer test). This was normal and the doctor said that this showed that I don’t have Sjögren’s syndrome. Is this correct?
No, approximately 20% of patients with Sjögren’s syndrome have a normal Schirmer test. The diagnosis of Sjögren’s syndrome is based on a combination of signs and symptoms and no single specific sign or symptom is essential for the diagnosis. See also chapter 4 on criteria for the diagnosis of Sjögren’s syndrome.

12. Is a lip biopsy essential for a diagnosis?
It depends. If there are both characteristic eye and mouth symptoms, the blood contains antibodies to SSA/Ro and/or SSB/La, the eye tests are abnormal and other causes of the signs and symptoms have been excluded, a definite diagnosis can be made without a lip biopsy. However, if there are no antibodies to SSA/Ro and/or to SSB/La, the lip biopsy is necessary to complete the diagnosis according to the American-European diagnostic criteria of 2002. The value of a lip biopsy is much less than thought previously as both the specificity and sensitivity are
too low. On the other hand, the (lip) biopsy may be the only way to exclude certain complications of Sjögren’s syndrome, e.g. a lymphoma. Furthermore, other diseases which affect the functioning of the salivary glands can sometimes be detected through a lip biopsy, e.g. sarcoidosis.

13. The eye specialist has done three tests: the Schirmer test, break-up time and the rose bengal staining test. Why are three tests necessary for the eyes and what do the results mean? The fact that three tests need to be done is that individually the tests say too little to be diagnostic. The three above-mentioned tests each measure something different. The tear film consists of three layers (see figure 20.1): a lipid layer, an aqueous layer and a mucous layer. The lipid layer is produced by the Meibomian glands in the eyelids. The aqueous layer is produced by the lacrimal glands and the mucous layer by the goblet cells in the conjunctiva. The break-up time (BUT) is reduced by an impaired lipid layer, the Schirmer test by an impaired aqueous layer while the Rose Bengal test is positive if the mucous layer is impaired. Blepharitis is the most likely cause of the eye symptoms if the BUT is diminished and the other tests are normal.

14. What is “sicca syndrome”? Sicca means dry. Sicca syndrome is used as a description for symptoms of eye irritation and dry mouth without it being possible to diagnose a disease. The name sicca syndrome suggests that the diagnosis is complete. It would be more accurate to refer to sicca symptoms or dryness symptoms without an objectifiable disease. The majority of patients with sicca symptoms in whom it was not possible to diagnose Sjögren’s syndrome, will not develop Sjögren’s syndrome in the future.

15. What is Mikulicz’s syndrome? In 1888, Dr Mikulicz reported a patient with bilateral, painless swelling of the lacrimal and salivary glands and diminished production of tears and saliva. This combination of abnormalities was subsequently called Mikulicz’s syndrome. Later, all kinds of diseases with swelling of the lacrimal and salivary glands were called by this name. Consequently, this name gradually became a repository for a variety of illnesses, including today’s Sjögren’s syndrome, certain forms of sarcoidosis, etc. This is precisely why the name is scarcely used anymore.

16. How long has Sjögren’s syndrome been in existence?
Probably as long as human beings have existed. Back in 1888, Mikulicz reported a man with dryness symptoms of the eyes and mouth and swelling of the lacrimal and salivary glands. Also in 1888, Hadden described a woman with dryness symptoms of the eyes, mouth and skin. He treated this woman successfully with pilocarpine (!). After this, a number of patients were described in medical journals whom we now can assume to have had Sjögren’s syndrome. But it was not until 1933 that Henrik Sjögren (figure 20.2), a Swedish ophthalmologist, described 19 patients with keratoconjunctivitis sicca (“dry eyes”), 13 of whom also had joint inflammation. From that time onwards, the name Sjögren’s syndrome was used, initially for the combination of keratoconjunctivitis sicca, dry mouth and (rheumatoid) arthritis. Later, the definition of Sjögren’s syndrome was changed into the combination of abnormalities of the lacrimal and salivary glands.

17. Is there any point in using pilocarpine if you have had Sjögren’s syndrome for 20 years? Can the salivary and lacrimal glands still be stimulated?
    Yes. The effect of pilocarpine is independent of the duration of the disease.

18. Can pilocarpine be used if you have both Sjögren’s syndrome and interstitial cystitis (bladder pain syndrome)?
    An undesirable effect of pilocarpine can be a need for more frequent urination due to contraction of the bladder muscles. So far, this does not appear to occur more frequently in patients with both Sjögren’s syndrome and interstitial cystitis than in other patients with Sjögren’s syndrome. At any event, it is no reason not to try it because if it should nonetheless lead to exacerbation of the bladder symptoms, you can always stop taking the pilocarpine.

19. Does pilocarpine have the same effect as saliva substitutes (sprays)? Is it advisable to change to pilocarpine? With whom should this be discussed?
    Pilocarpine stimulates the production of your own saliva, including the constituents it contains to protect against infection. Artificial saliva substitute is some times no longer necessary if pilocarpine has the desired effect, but there is no objection to using both. You can discuss this with your general practitioner and/or your specialist who is treating you for your Sjögren’s syndrome. Pilocarpine can also have a positive effect on the dryness of other mucous membranes, but is unfortunately not effective in all patients (see chapter 5).

20. Pilocarpine has only given me a moist nose. The dose was one capsule a day for three months. Is this correct?
    The dose was too low. The optimal starting dose is 5 mg four times a day. Depending on the effect and on any side effects, the dose can be gradually increased to a maximum of 10 mg four times a day or 5 mg eight times a day. As a general rule, the likelihood of both desirable effects and undesirable (but harmless) side effects increases as the dose is increased and reduces as the dose is reduced. In the United States it is claimed that the effect of pilocarpine is some times only felt after a few months of usage.

21. Can a general practitioner prescribe pilocarpine?
    Any medical doctor may prescribe pilocarpine. It may be worthwhile for the doctor to consult the pharmacist about this since some pharmacies refuse to supply pilocarpine in capsule form. The reason for this is that when capsules of 5 mg are made, one in a hundred capsules, for example, may contain 7 or 3 mg. From a medical point of view this is no problem, but the user needs to know this so as not to be surprised if one capsule has more or less (adverse) effects than another. The alternative is liquid form (less convenient) or the commercial preparation of pilocarpine (Salagen®). However, Salagen® is not reimbursed by health insurers in some countries. In addition to the advantage of accurate dosage, Salagen® also has a second advantage of being absorbed more slowly into the body than capsules. This consequently reduces the chance of sweating attacks occurring 30 minutes after taking the pilocarpine. Pilocarpine eyedrops should not be used for oral administration (“oral” = taking by mouth) because this is too inaccurate to be medically admissible.

22. Do you put on weight through taking pilocarpine?
    No, or at most only indirectly due to an increase in your sense of taste and consequently in your appetite.

23. Patients with Sjögren’s syndrome have a higher risk of developing non-Hodgkin lymphoma. When do you notice it, how can it be recognised, can it be caught in time, can it be detected at an early stage?
    The likelihood of a patient with Sjögren’s syndrome developing non-Hodgkin lymphoma (NHL) is 5-8%. The NHL usually is a so-called MALT (Mucosa Associated Lymphoid Tissue) lymphoma. Certain patients have a higher risk than others, for example if the salivary glands are continually enlarged and if the patient has
antibodies to SSA/Ro and/or SSB/La. Catching in time is not really the right expression because a lymphoma can only be diagnosed if it is already there. An alert doctor can at most diagnose it without needless delay. MALT lymphomas can, however, be successfully treated in virtually all patients. It is some times impossible to tell whether a tumour in a salivary gland or lymph node is malignant or not. Long-term use (5 or more years) of hydroxychloroquine (Plaquenil®) may possibly decrease the risk of MALT lymphomas. See also question 44.

24. Is it coincidence that several people in one family (aunt, niece) have Sjögren’s syndrome? No. Despite the fact that Sjögren’s syndrome is not hereditary, it is known that hereditary factors play a role in the likelihood of developing the disease. The chance of a second close relative of a Sjögren’s patient having the disease is approximately 12% (the normal chance for adults is about 0.4%).

25. If someone has dry eyes, dry mouth, dry tongue and osteoarthritis and the specialist says “it is not Sjögren’s”, what can it be? Osteoarthritis has no connection with Sjögren’s syndrome. Dryness can have many other causes such as diabetes, and underactive thyroid, high cholesterol and the use of certain drugs (see chapter 14). Whether the specialist is right or wrong depends on whether the correct tests have been carried out. Sometimes only a Schirmer test is carried out (measuring the amount of tear fluid with a filter paper) and if the result is normal the patient is told that he/she does not have Sjögren’s syndrome. This conclusion is not justified because the Schirmer test is normal in 20% of Sjögren’s patients.

26. Why is so little attention paid to acupuncture in Sjögren’s circles? I receive 5-6 acupuncture treatments once a year from a medical acupuncturist and this gives me sufficient tear fluid for a year. Acupuncture does not form part of “official” medicine, largely because no scientifically reliable study has been carried out into its possible effects. It should be remembered that acupuncture was the treatment used in China several thousand years ago. In today’s China, Sjögren’s patients are treated with the same drugs as in the western world, in addition to aditional Chinese methods of treatment.

27. Between what levels should the blood sedimentation rate of a Sjögren’s patient fluctuate? The erythrocyte sedimentation rate (ESR) depends on many factors, not only inflammation. Some Sjögren’s patients have a high concentration of IgG antibodies in their blood or anaemia, resulting in an increase in the ESR. In many Sjögren’s patients the ESR is either normal or only slightly increased (up to 40 mm for example). In the case of inflammation of the blood vessels (vasculitis), the ESR is often greatly increased, e.g. over 100 mm. The high ESR is in itself not dangerous, but is always caused by something. See also the chapter 15 on clinical investigations.

28. Is there a connection between Sjögren’s syndrome and thyroid disorders? Yes, according to the literature 15% of patients with Sjögren’s syndrome have or have had a thyroid disorder.

29. What causes gastrointestinal problems? Gastrointestinal problems can have many causes which may or may not be related to Sjögren’s syndrome. The clearest connection is with constipation, possibly because glands in the intestines produce less moisture, sometimes also due to the use of antiinflammatory drugs, the prostaglandin synthesis inhibitors (examples are aspirin, diclofenac, naproxen, ibuprofen, celecoxib, etoricoxib but not Plaquenil®). See also the chapter on gastrointestinal disorders.

30. I am a forty year old woman and have had frequent attacks of cystitis during the past year. Antibiotics don’t help. Cystitis is usually caused by bacteria from the intestines, for example Escherichia coli. If the cystitis occurs frequently and is not improved by antibiotics, when the next attack of cystitis occurs it should be ascertained whether the urine contains white and/or red blood cells (indicating inflammation) and whether the urine contains bacteria, preferably by a urine culture (indicating bacterial infection). If a person has symptoms of cystitis, but it is not caused by a bacterial infection, this may indicate interstitial cystitis-bladder pain syndrome (IC-BPS). This is probably an autoimmune disorder of the bladder (see the chapter on urogenital disorders).

31. Can Sjögren’s syndrome cause inflammation in the breasts? There is a form of inflammation in the breasts caused by lymphocytes, known as lymphocytic mastopathy. This closely resembles the abnormalities that occur in the large salivary glands in patients with Sjögren’s syndrome. However, lymphocytic mastopathy has
virtually only been described as a rare complication in people with longstanding insulin-dependent diabetes mellitus. It has also been described in the case of systemic lupus erythematosus and hypothyroidism (underactive thyroid gland). Very recently, a patient with Sjögren’s syndrome was reported with a non-Hodgkin lymphoma in the breast. Despite the fact that lymphocytic mastopathy has not been described so far in Sjögren’s patients, it may be assumed that this is likely. It can be difficult, moreover, to distinguish between lymphocytic mastopathy and lymphoma.

32. What is the difference between pilocarpine and pilocarpine hydrochloride?
The official name of pilocarpine is pilocarpine hydrochloride or pilocarpine HCl for short (see fig. 20.3). The abbreviation HCl is often omitted and there is no difference. A similar situation also applies to many other drugs. Examples are: bromhexine (hydrochloride) and hydroxychloroquine (sulfate).

33. What is CREST syndrome?
CREST is an abbreviation of the five most important features of this generalised autoimmune disease:
C - Calcinosis (local calcium deposits in the skin)
R - Raynaud phenomenon
E - Esophageal dysmotility: abnormal movements of the muscles in the esophagus (UK oesophagus)
S - Sclerodactyly (thickening of the fingers)
T - Teleangiectasia (small collections of dilated blood vessels in the skin)

Patients with CREST often have anticentromer antibodies in their blood. The name CREST is replaced now by the name limited systemic sclerosis.

34. What is scleroderma?
Scleroderma (systemic sclerosis) is a group of generalised autoimmune disease characterised by skin abnormalities (including an increase in connective tissue). The skin tightens and in some patients the lung and kidney functions are impaired. Almost all patients also have Raynaud phenomenon. There are different forms of scleroderma with a different prognosis. The most severe form is diffuse systemic sclerosis (“diffuse scleroderma”) involving the entire skin. This form is more often accompanied by lung and/or kidney disorders than the other forms.

In acroscleroderma, the skin lesions are limited to the
hands (and sometimes lower arms), feet (and sometimes lower legs) and nose. In morphea, the skin lesions are only found on certain areas of the trunk and/or limbs. The kidneys and lungs are not affected by this form of scleroderma. The skin lesions may also occur in linear bands and, due to the resemblance to a scar following a wound with a sharp instrument, this form is known as coup de sabre.

35. What is systemic lupus erythematosus?
Systemic lupus erythematosus (SLE) is a generalised autoimmune disease which more commonly occurs in women and non-white populations. The most common features are arthritis (joint inflammation), skin disorders (including a red butterfly rash on the face, see figure 20.5), sensitivity to sunlight, inflammation of the membranous sac around the heart (pericarditis) or of the pulmonary membrane (pleuritis), inflammation of the kidney (glomerulonephritis) and a low white blood cell count. The ANA (see chapter on clinical investigations) is positive and the anti-DNA in half the patients, particularly when the disease is active. The criteria for SLE are summarised in table 20.1. SLE can be diagnosed if four of the eleven items are present.

36. What is MCTD?
MCTD (Mixed Connective Tissue Disease) is a disease which forms a clinical overlap between systemic lupus erythematosus (SLE), myositis (inflammation of muscles) and systemic sclerosis (scleroderma). It is most likely a variant of SLE. On the basis of agreed criteria, in order to receive a diagnosis of MCTD a patient must have antibodies to RNP but not DNA.

### Table 20.1 Summary of the criteria for the diagnosis of systemic lupus erythematosus (American College of Rheumatology 1997)

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1.</td>
<td>malar rash</td>
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<tr>
<td>2.</td>
<td>discoid rash</td>
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<tr>
<td>3.</td>
<td>photosensitivity</td>
</tr>
<tr>
<td>4.</td>
<td>oral/nasopharyngeal ulcer</td>
</tr>
<tr>
<td>5.</td>
<td>arthritis</td>
</tr>
<tr>
<td>6.</td>
<td>pleuritis or pericarditis</td>
</tr>
<tr>
<td>7.</td>
<td>proteinuria &gt; 0.5 g/day</td>
</tr>
<tr>
<td>8.</td>
<td>neurologic/psychiatric disorder</td>
</tr>
<tr>
<td>9.</td>
<td>haematologic disorder</td>
</tr>
<tr>
<td>10.</td>
<td>anti-DNA, anti-Sm, or antiphospholipid antibodies</td>
</tr>
<tr>
<td>11.</td>
<td>antinuclear antibodies (ANA)⁴</td>
</tr>
</tbody>
</table>

37. What is sarcoidosis and is there a link with Sjögren’s syndrome?
Sarcoidosis or Besnier-Boeck disease is a disease which is sometimes difficult to distinguish from Sjögren’s syndrome. In 90% of the cases, sarcoidosis shows clear abnormalities on a lung x-ray. Figure 14.6 shows the most typical feature on a lung x-ray. Tissue examination often reveals granulomas accumulations of a specific type of cell, surrounded by lymphocytes (see figure 20.6 photo on the right). These abnormalities can also occur in lacrimal and salivary glands. In 10% of the patients, the lung x-ray shows no abnormalities. Sarcoidosis without lung abnormalities but with abnormalities in the lacrimal and salivary glands can be confused with Sjögren’s syndrome. However, a lip biopsy in a patient with sarcoidosis shows diffuse lymphocytic infiltration and often the above-mentioned granulomas. Blood tests can also support the possibility of sarcoidosis such as elevated lysozyme, angiotensin-converting enzyme
(ACE), calcium or vitamin D, which may occur in patients with sarcoidosis. Antibodies to SSA/Ro and SSB/La do not in principle occur with sarcoidosis (but do occur in 60-70% of the patients with Sjögren’s syndrome).

There have recently been a number of publications reporting patients with both sarcoidosis and Sjögren’s syndrome. Sarcoidosis occurs worldwide in an average of 1 per 5000 people, slightly more commonly in women than in men. The disease is more common in the negroid population and in Scandinavian countries (1:1600). 10-20% of known cases of sarcoidosis display no symptoms at all and the disease is only found by chance in a routine examination (e.g. a medical examination involving a lung x-ray). There must therefore be many people who “happen” to have both diseases. It is a simple matter to calculate that the chance of having both diseases in Scandinavian countries is 1:256.000 (Sjögren’s syndrome 1:160; sarcoidosis 1:1600; chance of both 1 per 160x1600).

38. Does Sjögren-Larsson syndrome have any connection with Sjögren’s syndrome?
No. Sjögren-Larsson syndrome (SLS) was first described in 1957 and consists of a combination of genetic ichthyosis (thickened fish-like skin), mental retardation and spastic paraplegia. SLS is an autosomal recessive genetic disease. Recessive means that the disease only occurs if two abnormal genes are present, one from each parent; autosomal means that the gene lies on one of the chromosomes 1-22, and not therefore on the 23rd gender-determining chromosome. The cause of the disease is a mutation (change) in the FALDH gene on chromosome 17 (FALDH is the abbreviation of Fatty Aldehyde DeHydrogenase), resulting in deficiency of the FALDH enzyme. Consequently metabolic products accumulate in the skin and nerve tissue.

39. Does Marinesco-Sjögren syndrome have any connection with Sjögren’s syndrome?
No. Marinesco-Sjögren syndrome is a rare autosomal recessive genetic disease (see answer to previous question) with cataracts, cerebellar ataxia (balance and coordination impairment due to an abnormality in the cerebellum), mental retardation, muscle weakness, short stature and hypogonadism (impaired function of the reproductive glands). It is unknown which gene is defective.

40. Does Gougerot-Sjögren’s syndrome have any connection with Sjögren’s syndrome?
Gougerot-Sjögren’s syndrome is the same as Sjögren’s syndrome. This version of the name is only used in French-speaking countries.

41. What is antiphospholipid syndrome?
Antiphospholipid syndrome (APS) is the combination of specific clinical features and laboratory diagnosis. The clinical features may be: thrombosis in veins or arteries or recurrent miscarriage. Many other features may be part of APS but are not included in the present diagnostic criteria such as low blood platelet count, livedo reticularis or aseptic necrosis of bone. The laboratory features are anti phospholipid antibodies (such as the lupus anticoagulant, anticardiolipin antibodies and antibodies to β₂-glycoprotein I). The physiological role of β₂-glycoprotein I is not known. Complexes of β₂-glycoprotein I and antibodies are not detected in the blood. The antiphospholipid antibodies interact with two β₂-glycoprotein I molecules. Via mechanisms that are not clarified to date, this binding leads to activation of endothelial cells and platelets and thrombosis (figure 20.7).

There are three forms of APS.

a. people who have APS without any other autoimmune disease have primary APS.

b. APS associated with a generalised autoimmune disease such as SLE, SCLE, MCTD, systemic sclerosis or Sjögren’s syndrome (so-called secondary APS).

c. there is also a form of APS associated with lupus-like syndrome.

Lupus-like syndrome is diagnosed if fewer than four items of the criteria for SLE are present (see table 20.1). By analogy with lupus-like syndrome, the term...
Sjögren-like syndrome could be introduced for people with 1-3 items of the criteria for Sjögren’s syndrome. It has been known for a long time that people with SLE sometimes have a positive syphilis reaction without having been in contact with the bacterium (Treponema pallidum) that causes syphilis. This is described as a false-positive syphilis reaction. It is now known that these false-positive reactions are caused by antiphospholipid antibodies.

42. I have the typical eye and mouth symptoms for Sjögren’s syndrome and the Schirmer test is very low. However, the lip biopsy was normal. Is this possible and have I got Sjögren’s syndrome or haven’t I? A lip biopsy can be normal in Sjögren’s syndrome, see also chapter 4 on diagnosis. Whether or not a diagnosis of Sjögren’s syndrome can be made in this situation depends on other information (e.g. other abnormal findings, exclusion of other diseases which could cause the same symptoms and signs, etc). Occasionally the lip biopsy has not been correctly performed. It sometimes proved to have little or no salivary gland tissue and is therefore impossible to assess. Recent research has also shown that smoking can cause a lip biopsy to be negative.

43. I have Sjögren’s syndrome and now BOOP has also been diagnosed. What is this and what connection does it have with Sjögren’s syndrome? Bronchiolitis Obliterans Organizing Pneumonia (BOOP) is called organizing pneumonia (OP) today. OP is a lung disease in which granulation tissue (scar tissue) causes narrowing or closure of the small branches of the respiratory tract (bronchioles). This lung abnormality has various causes, e.g. infections (adenovirus, cytomegalovirus, influenza, Legionella pneumophila), drugs (gold preparations, methotrexate, sulfasalazine), autoimmune diseases, transplantation and radiation.

If there is no association with another disease, the term cryptogenic organizing pneumonia or idiopathic OP is used. The course of the disease can vary per person. If the lung abnormalities increase, the patient is normally treated with prednisolone. In three-quarters of the patients the OP will then completely disappear, but 5% of patients die from the disease. Patients with the idiopathic form often recover following treatment with the antibiotic erythromycin. In the literature, 5-10 patients have been described with Sjögren’s syndrome and OP. The relationship is uncertain and probably indirect. See also the chapter on pulmonary disorders.

44. Patients with Sjögren’s syndrome have a higher risk than normal of getting a lymphoma. What are lymphomas? Lymphomas are malignant growths mainly consisting of lymphocytes, specific white blood cells (see chapter 15). There are two main categories: Hodgkin lymphoma and non-Hodgkin lymphomas. It is only non-Hodgkin lymphomas (NHL) which occur more frequently than normal in Sjögren’s syndrome. A NHL occurs if lymphocytes (B-lymphocytes, T-lymphocytes or NK cells) undergo a change from normal cells to malignant cells which are capable of uncontrolled growth and spreading. The malignant cells divide so as to form identical copies (clones). Most (85%) of NHL come from B-lymphocytes at some stage of their development. Lymphomas can occur anywhere in lymphatic tissue, such as lymph nodes, in intestines and in central nervous system. Symptoms depend on where they occur. In a lymph node this is swelling of the node. In addition, there may be other general symptoms such as fever, fatigue, night sweats, weight loss or itchy skin.

The diagnosis is based on examination of tissue, often a biopsy. Imaging is used to determine the location and spread. There are almost 40 different types of NHL. 13 of these types represent 90% of cases in the western world. With regard to the spreading of NHL, the following four stages are differentiated:

- stage I: disease in only one lymph node
- stage II: disease in a number of lymph nodes on one side of the diaphragm
- stage III: disease in lymph nodes above and below the diaphragm
- stage IV: the disease is also found outside the lymph nodes

Treatment depends on the type of NHL, the size and spread of the tumour and can vary from watch and wait with close monitoring, radiation therapy, chemotherapy, immunotherapy to stem cell transplantation. Patients with Sjögren’s syndrome have a 44x increased risk compared to other people of developing NHL. The percentage of Sjögren’s patients who develop NHL is 5-8%. NHL associated with Sjögren’s syndrome are usually MALT lymphomas. MALT is an abbreviation of Mucosa-Associated Lymphoid Tissue. These lymphomas are slow growing B-cell lymphomas. In around half the cases the lymphomas occur in the salivary glands. After treatment, the prognosis for MALT lymphomas is generally speaking much better than for other types of lymphoma.
45. There are many types of artificial tears available. What is the difference between the different brands? Which are the best and how often should you use them?

Artificial tears are watery solutions to which an ingredient is added to give them greater viscosity (stickiness) so that they will adhere better to the eye. The differences between the different products lie between the added ingredients and the addition of preservatives. This latter aspect is important if a specific preservative cannot be tolerated. Eye gels have a higher viscosity than artificial tears. Artificial tear inserts dissolve slowly and consequently are effective for a long time. Table 20.2 gives an overview of a number of types of artificial tears and eye gels. In addition, there are eye drops which contain medication such as an anti-inflammatory or anti-allergy agent, etc. These should only be used if there is a special reason.

The choice between the different drops, gels and inserts can only be made by the user, in other words a question of trying them out. Generally speaking, the worse the eye disorder, the more watery the artificial tears need to be. An insert can only be used if there is sufficient tear fluid during the day to dissolve it. If this is the case, 1 insert per day is often sufficient.

46. Since Sjögren’s syndrome is an inflammatory condition, why can it not be treated with penicillin or something similar?

Inflammation is the body’s response to tissue damage. Tissue damage can have different causes, such as mechanical (e.g. a cut), heat (burn), cold (frostbite), radiation or infection. Infection is the spreading and

Table 20.2 Composition of a number of types of “artificial tears”

<table>
<thead>
<tr>
<th>main ingredient</th>
<th>preservative</th>
<th>(brand)name</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbomer</td>
<td>thiomersal</td>
<td>Dry Eye® eye gel</td>
</tr>
<tr>
<td></td>
<td>thiomersal</td>
<td>Thilo Tears® eye gel</td>
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<tr>
<td></td>
<td>cetrimide</td>
<td>Vidisic® eye gel</td>
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<td>dextran 70/hypromellose</td>
<td>polyquaternium-I</td>
<td>Duratears® eye drops</td>
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<td>hyprolose</td>
<td>none</td>
<td>Lacrisert®</td>
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<td>benzalkoniumchloride</td>
<td>hypromellose eye drops</td>
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<td>Hypromellose Monofree</td>
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<td>hyaluronan (“hyaluronic acid”)</td>
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<td>thiomersal</td>
<td>methylcellulose eye drops</td>
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<tr>
<td>polyvidon</td>
<td>none</td>
<td>Duratears Free®</td>
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<tr>
<td></td>
<td>benzalkoniumchloride</td>
<td>Oculotect® eye drops</td>
</tr>
<tr>
<td></td>
<td>none</td>
<td>Oculotect Unidose® eye drops</td>
</tr>
<tr>
<td></td>
<td>benzalkoniumchloride</td>
<td>Protagens Mono 2%®</td>
</tr>
<tr>
<td></td>
<td>cetrimide</td>
<td>Protagens® eye drops</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vidisic PVP Ophthiole® eye drops</td>
</tr>
<tr>
<td>polyvidon/polyvinylalcohol</td>
<td>chlorbutanol</td>
<td>Tears Plus® eye drops</td>
</tr>
<tr>
<td></td>
<td>none</td>
<td>Tears Plus Unit Dose® eye drops</td>
</tr>
</tbody>
</table>

Some artificial tears are available preservative-free in special bottles (Comod system). Once the bottle has been opened, the artificial tears will keep for 3 months.
multiplying of a micro-organism (e.g. bacterium, virus or fungus) in living tissue. If this causes disease, it is called an infectious disease. Treatment with penicillin or some other antibiotic has no point unless the inflammation is caused by a bacterial infection.

47. Can Sjögren’s syndrome cause stones in the salivary glands?  
There is no evidence that Sjögren’s syndrome is more likely to lead to stones in the salivary glands than normal.

48. Do patients with Sjögren’s syndrome have more likelihood of developing a tumour in the salivary glands?  
Tumour means nothing more than swelling and a swelling can be benign or malignant. As is well known, some Sjögren’s patients have unilateral or bilateral swelling of the salivary glands. In this sense, they have tumours in the salivary glands more frequently than normal. But this question is probably referring to malignant tumours such as cancer or malignant lymphomas. The only malignant disorders of the salivary glands in Sjögren’s syndrome that occur more commonly than normal are non-Hodgkin lymphomas (see also answer to question 44).

49. What is the difference between thirst and a dry mouth?  
Thirst is a sensation which is normally felt if the body dehydrates. Thirst ensures that we drink. Once the body has received sufficient liquid, the thirst sensation subsides again.  
A dry mouth is caused by dryness of the surface of the mucous membranes in the mouth. Drinking helps as long as the liquid is present on the mucous membranes, a clear difference from thirst. If you have a dry mouth, you usually need to drink when eating dry food. There are different causes of thirst (see table 20.3).

50. Can a patient with Sjögren’s syndrome have dental implants?  
Yes, Sjögren’s patients do not differ from other people in this respect. This is important because the likelihood of dental problems is much higher than normal in patients with Sjögren’s syndrome. It is only if the patient is using drugs which greatly suppress the immune system that there are likely to be more problems with attachment of the implant to the bone. Implants need to be looked after and this is especially the case in people with insufficient or abnormal saliva. The question as to whether implants will be the solution for an individual person can only be answered by the dentist treating that person.

51. Is it true that the amount of saliva you produce decreases as you grow older?  
Yes and no. It is true that older people on average produce less saliva than younger people. However, this has nothing to do with age but is simply caused by the fact that elderly people are more likely to have illnesses or use medication which causes less saliva to be produced.

52. What is the difference between Raynaud phenomenon and Raynaud disease?  
A number of diseases and situations are known in which Raynaud phenomenon can occur. These may be autoimmune diseases (e.g. systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, Sjögren’s syndrome), diseases leading to narrowing of the arteries, pulmonary hypertension (high blood pressure in the pulmonary arteries), neurologic disorders (e.g. disorders of intervertebral discs, tumours of the spinal cord, carpal tunnel syndrome), blood diseases which make the blood more viscous, damage due to repetitive movement (e.g. frequent

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### Table 20.3 A number of causes of thirst

- physical exertion
- dehydration (diarrhoea, vomiting, heat, infection, diuretics)
- hormone disorders (e.g. overactive thyroid)
- diabetes mellitus
- diabetes insipidus (see box below)
- antihistamines, alcohol, caffeine, marihuana
- high sodium level in the body
- brain damage
- psychogenic

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**Diabetes insipidus**

Diabetes insipidus is a disease in which the pituitary gland produces too little ADH (antidiuretic hormone). This may have a variety of causes and some forms are considered to be an autoimmune disease. The result is that the kidney cannot concentrate the urine, resulting in voiding of a great deal of dilute urine and extreme thirst.
use of heavy drilling machine, playing the piano) and use of certain drugs (e.g. ergotamines and beta-blockers).

If Raynaud phenomenon occurs without one of these known situations or diseases being present, the condition is called primary Raynaud phenomenon or Raynaud’s disease. On the basis of this classification, over half the people with Raynaud phenomenon have Raynaud disease.

53. Is it helpful to keep to a special diet for Sjögren’s syndrome?

No. The same applies to Sjögren’s patients as to everyone: eat healthy food with sufficient variation and fresh products. Many patients realise themselves that they can better avoid highly spiced or acid food because this can cause mouth complaints. Since quite a number of patients suffer from constipation, high-fibre food is important, but that also really applies to everyone.

54. Can I improve my resistance through diet, food supplements or extra vitamins?

Not really. Resistance mainly concerns the ability to avoid getting ill when infected by viruses or bacteria. So you can have resistance to virus A or bacterium B. The term resistance refers to the combination of all ways in which we prevent or fight infectious diseases. If you eat a healthy diet, there is usually no point in taking extra vitamins. There are a number of exceptions to this rule. In the Netherlands, people with a dark skin often produce insufficient vitamin D because Dutch sunlight is too weak for them. Extra vitamin D may be necessary for them. Many people with white skins have been found to have a vitamin D deficiency as well. Always discuss vitamin D treatment with your doctor.

55. May I take pilocarpine by putting a few drops from a bottle of pilocarpine eye drops in a glass of water?

No, absolutely not. The quantity of pilocarpine that you would swallow in this way is insufficiently accurate and can lead to severe overdosing. Eye drops with pilocarpine are used to treat certain forms of glaucoma (increased eye pressure) and are not suitable for the treatment of eye complaints in Sjögren’s syndrome.

Permissible forms of taking pilocarpine for Sjögren’s syndrome are:

- oral mixture prepared by the pharmacy: accurate, but inconvenient
- capsules prepared by the pharmacy: moderately accurate, but convenient
- commercial tablets (Salagen®): accurate, convenient, not reimbursed by health insurers in some countries

56. I have osteoarthritis. Should I now take calcium tablets?

There is no point in taking calcium tablets for osteoarthritis unless you have osteoporosis and/or obtain too little calcium from your diet. There is a misunderstanding behind this question concerning the terms osteoarthritis (wear and tear of joints) and osteoporosis (loss of mineral density of bone tissue). Osteoarthritis is a chronic condition characterised by the softening and breakdown of cartilage in the joints. This leads to a reaction by the underlying bone, causing the growth of new cartilage and bone. Over a period of time osteoarthritis gradually increases, causing pain and limited motility of the joints. Osteoarthritis is the most common joint condition with the likelihood of developing it increasing with age: in 1% of the population under the age of 30 years to more than half the population over the age of 50 years. There are different types of osteoarthritis and specific risk factors.

Obese people are more likely to get osteoarthritis and less likely to get osteoporosis. Damage to joints also gives a higher risk of osteoarthritis. Long-term repetitive stress to certain joints in certain professions also increases the risk of osteoarthritis in these joints. There is no known treatment which slows down the progression of osteoarthritis. Treatment therefore consists simply of alleviating the symptoms (physiotherapy, painkillers) and if necessary dealing with known risk factors (e.g. obesity).

Osteoporosis is characterised by low bone mineral density and an increased risk of bone fractures. There are also specific risk factors for osteoporosis, such as being Caucasian, a history of osteoporosis in close blood relatives, smoking, excessive alcohol consumption, vitamin D deficiency, low dietary calcium intake, slight body build, too little exercise, early menopause, low testosterone level, use of corticosteroids (e.g. prednisolone) and diseases such as rheumatoid arthritis, an overactive thyroid (hyper thyroidism) and anorexia. Treatment generally consists of correcting all risk factors where possible and use of drugs which combat bone loss.

57. One of my pupils is larger than the other and does not respond to light. Has this anything to do with Sjögren’s syndrome?

You probably have an Adie pupil. This is a harmless