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What's new in insurance medicine?



Obstructive sleep apnoea syndrome

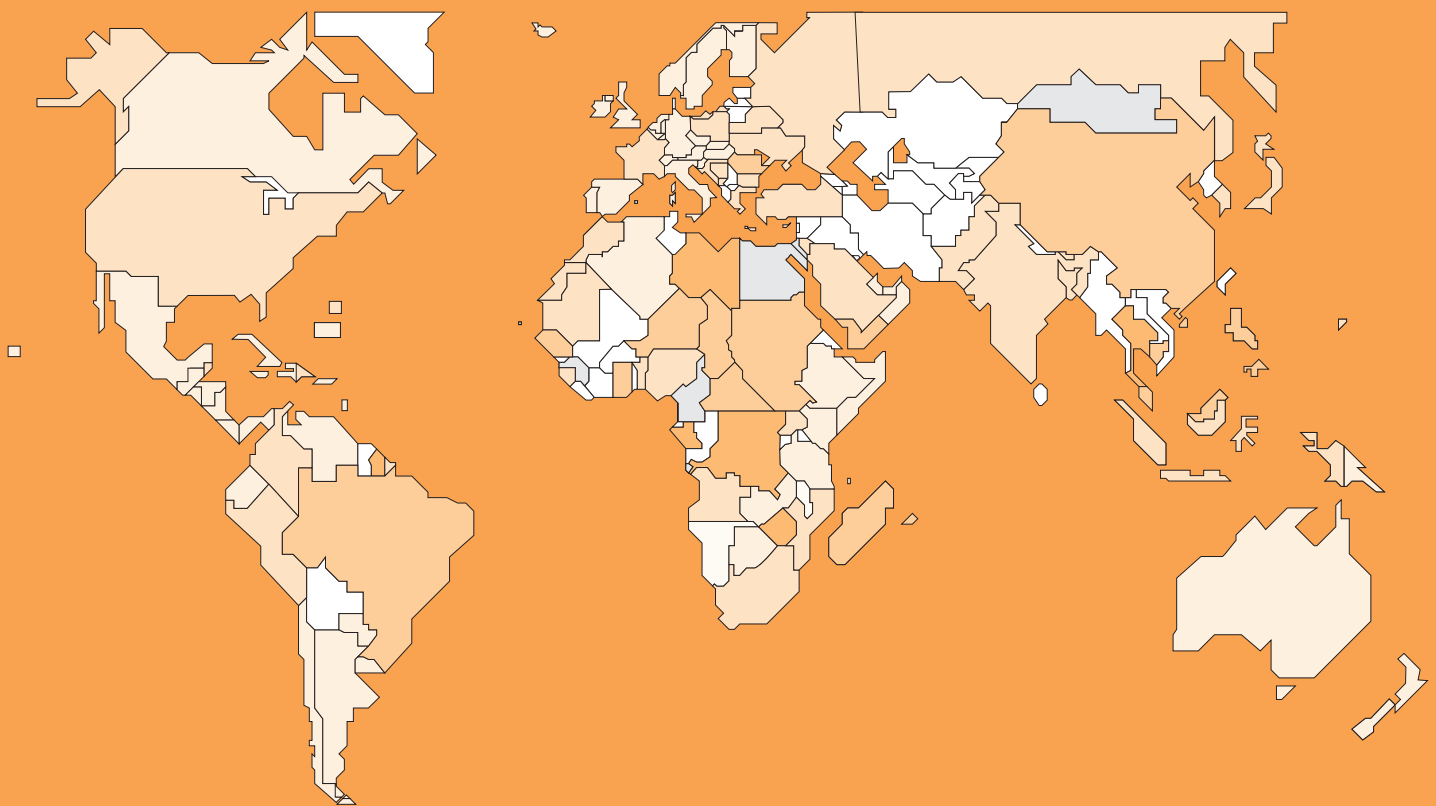


Electron beam tomography



Automatic external defibrillation





- No data
- < 1
- 1-2.49
- 2.5-4.99
- 5-10
- > 10

Global prevalence of hepatitis C
Based on published data, update 1999
Source: WHO (figures given in % of the population)

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Chronic hepatitis C – Medical aspects for insurance

Chronic **HEPATITIS C** is a viral infection of epidemic proportions. First discovered in 1989, the **HEPATITIS C VIRUS (HCV)** belongs to the family Flaviviridae. Hepatitis C viruses can be divided into six different **GENOTYPES** and further differentiated into a number of recognized genetic subtypes. These show geographical variations in prevalence, specific routes of transmission and particular requirements for treatment. As more than one infection with different subtypes is possible, a previous infection does not give any protection against a new infection. The incubation period is

up to 180 days. Damage to liver cells is caused by specialized cells of the body's own immune system and not by the virus itself.

Immunological processes associated with HCV infection can also involve other organs, e.g. the kidneys (glomerulonephritis) or the joints (arthritis). The development of a vaccine to protect against HCV infection is not to be expected in the near future.

EPIDEMIOLOGY OF HEPATITIS C

Worldwide, about 170 million people (approx. 3% of the world's population) are infected. The highest prevalence is seen in African countries, the eastern Mediterranean and the west Pacific region.

In Europe and North America, hepatitis C causes

- 70% of all chronic viral hepatitis;
- 40% of all cirrhosis of the liver;
- 60% of all primary hepatocellular carcinomas (HCC);

in addition

- an estimated 8,000–10,000 deaths per year in the USA;
- costs of more than US\$ 600m for HCV-related liver disease in the USA.

TRANSMISSION

Today, the only route known for certain is the parenteral transmission of HCV by the entry of blood from an infected person into the circulation or tissues of the recipient.

At the time of diagnosis, the origin of the infection can no longer be ascertained in the majority of people infected with HCV.

Using very sensitive laboratory procedures, it is possible to detect HCV in other body fluids such as saliva, sweat, tears, breast milk and seminal fluid. On the basis of previous investigations, however, it has to be assumed that the transmission of HCV via body fluids other than blood is not very likely and cannot be responsible for the high number of sporadic HCV infections (with no recognizable source of infection).

Nor can the question of sexual transmission be answered with any degree of certainty. In large study populations, transmission rates in the order of 1–3% have been reported.

The average vertical transmission rate of HCV from mother to child during pregnancy is approximately 6%.

TREATMENT OF CHRONIC HEPATITIS C

Great advances in the treatment of chronic hepatitis C have been made in recent years. Even five years ago, a prolonged reduction of HCV below the detection limit could be achieved in less than 16% of patients, while today this is the case for more than 50% of patients, thanks to combination therapy with **PEG-INTERFERON** and **RIBAVIRIN** (two effective antiviral drugs). Typical long-term sequelae of chronic hepatitis C, **CIRRHOSIS OF THE LIVER** and **HEPATOCELLULAR CARCINOMA**, can probably be prevented in this way.

The primary aim of therapy is the elimination of HCV from the serum within six months of starting treatment. Viral genetic material, **HCV RNA**, is measured in the blood by **POLYMERASE CHAIN REACTION (PCR)**, a highly sensitive method of determination for viruses. Prospective studies show that in 95% of patients successfully treated with PEG-interferon and Ribavirin, HCV RNA cannot be demonstrated with PCR even years after the end of therapy.

WHEN IS TREATMENT GIVEN?

- Raised transaminases
- Demonstration of HCV RNA in serum
- Histologically confirmed chronic hepatitis

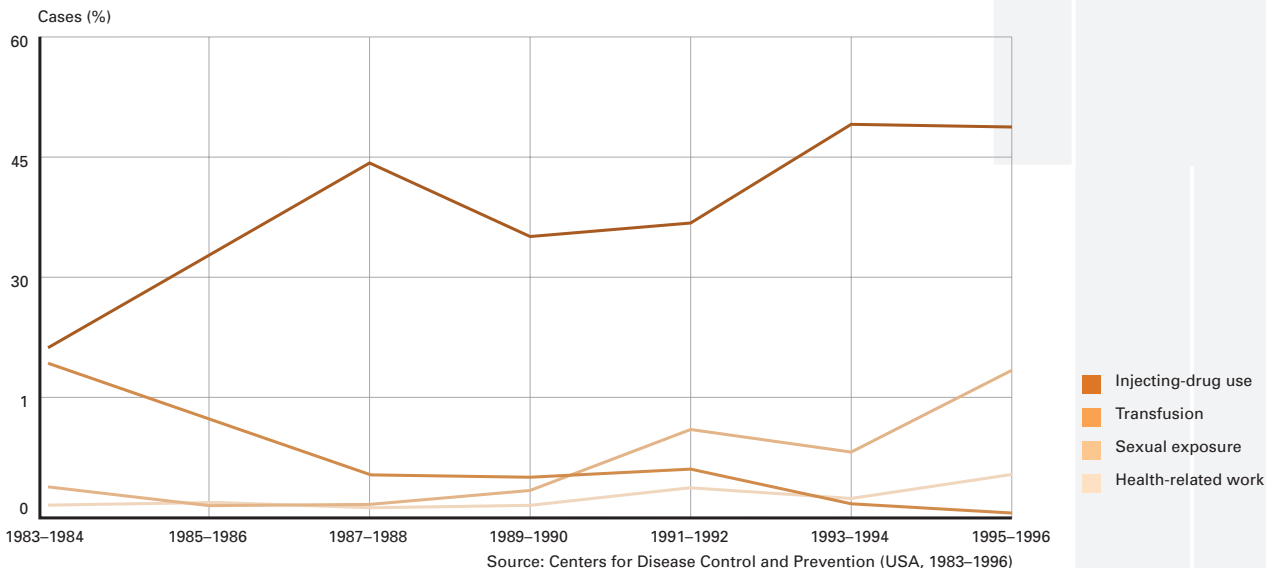
POSITIVE PREDICTORS FOR TREATMENT SUCCESS WITH COMBINATION THERAPY

- HCV genotypes 2 and 3
- Low viral load at the start of treatment
- Age < 40 years
- Female
- Still no serious damage to the liver (as shown by liver biopsy)

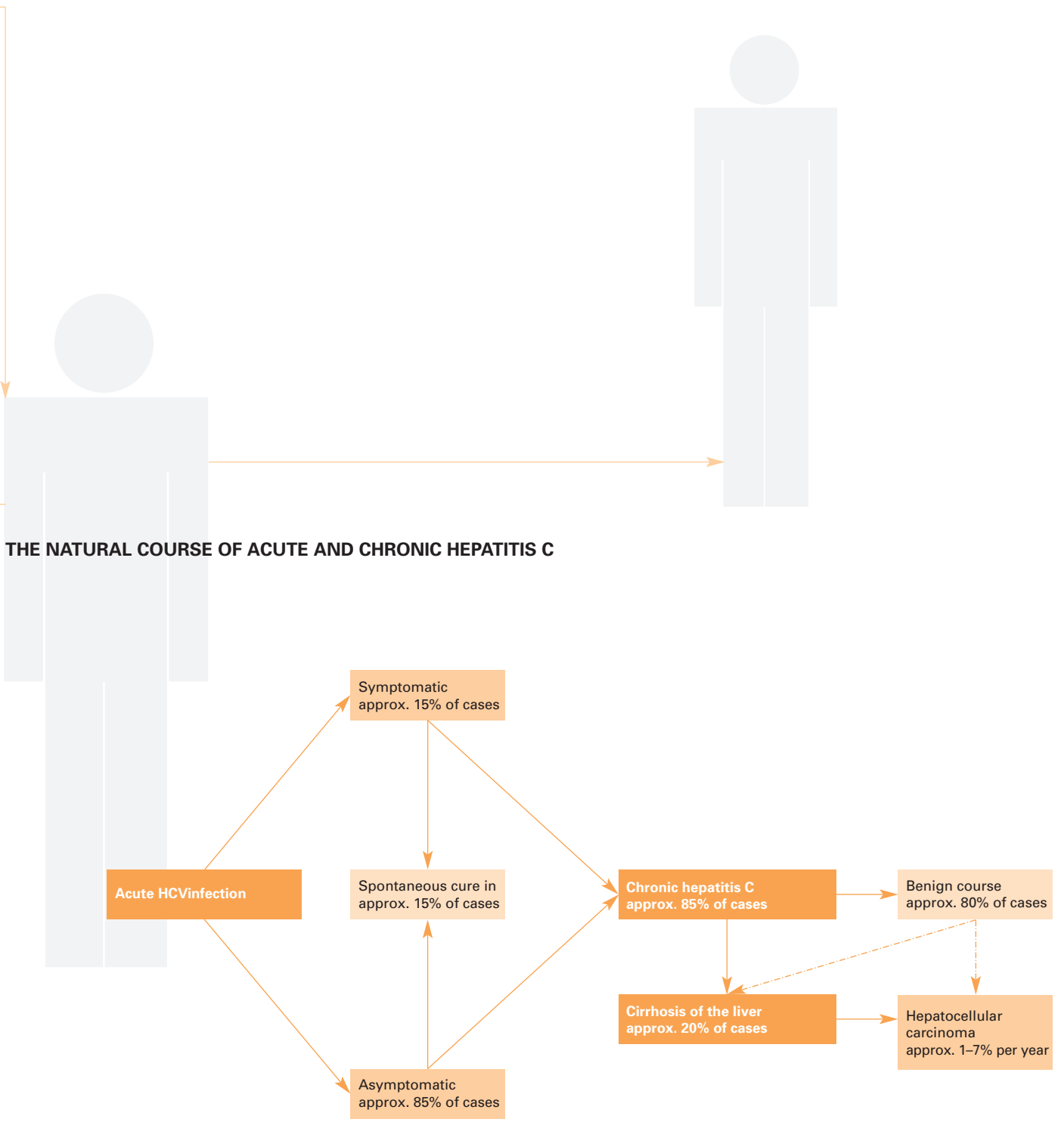
WHEN IS TREATMENT SUCCESSFUL?

- Transaminases return to normal
- HCV RNA no longer demonstrated with PCR within a maximum of six months after the start of treatment
- Improvement in the histology of the liver (regression of fibrosis and inflammatory changes)

THE MOST IMPORTANT ROUTES OF HCV TRANSMISSION



THE NATURAL COURSE OF ACUTE AND CHRONIC HEPATITIS C



“According to information from the WHO, approximately 170 million people – i.e. 3% of the world’s population – are infected with hepatitis C virus and thus have the potential risk of suffering from cirrhosis of the liver and/or hepatocellular carcinoma.”

Important aspects for the risk assessment of chronic hepatitis C

START OF THE INFECTION: Frequently not known, as the acute infection is asymptomatic in some 85% of those affected. Only 15% have symptoms of jaundice, tiredness, upper abdominal pain, etc. Retrospective elucidation of the time of infection is sometimes possible through taking a careful history and asking about blood transfusions in the past or intravenous drug misuse. If the levels of liver enzymes are raised without any symptoms, chronic viral hepatitis must always be considered in the differential diagnosis.

COURSE OF THE DISEASE: Approx. 85% of HCV infections run a chronic course. Chronic hepatitis C first becomes symptomatic 10–20 years after the infection. It may appear sooner if there are other hepatotoxic factors, e.g. alcohol consumption. Hepatic cirrhosis and hepatocellular carcinoma may develop as a result.

PROGNOSIS: Depends on the extent of the liver damage at the time of diagnosis, the disease activity, the viral load and the genotype, as well as cofactors causing liver damage. If HCV RNA is no longer detected after combination therapy with PEG-interferon and Ribavirin (standard therapy), the transaminases and liver function tests are normal, and the histology of the liver rules out any serious hepatic damage, the prognosis is probably very good. Liver damage which has been induced by chronic hepatitis C may partially regress on treatment.

HCV ANTIBODIES (ANTI-HCV): Proteins, known as immunoglobulins, produced by specialized immune cells and targeted against HCV can be determined in the blood. They provide evidence of an infection but no conclusions can be drawn as to the activity of the disease. However, about 80% of anti-HCV positive patients are also HCV RNA positive. Findings of positive anti-HCV must be checked by a confirmatory test, since false positive results have been reported. Anti-HCV tests first become positive 1–5 months after the onset of the illness (**diagnostic window**) and are therefore not suitable for excluding an acute infection. The infection can only be diagnosed by the determination of virus-specific HCV RNA in the blood. As a rule, the antibodies can still be found in the blood even after the disease has been cured.

HCV RNA: Genetic material of HCV, the earliest measurable marker of infection with HCV. It provides evidence of infection, shows that the affected person is infectious, and persists when the infection follows a chronic course. Quantitative determinations of HCV RNA indicate the viral load and are important for the assessment of therapeutic success. The **viral load** is the quantity of virus or HCV genetic material that is present in the blood. It is reported in terms of virus equivalent or as the number of (virus) copies per millilitre of blood. The viral load may lie anywhere be-

tween “not detected” and a values of hundreds of million copies per millilitre.

TRANSAMINASES (GOT, GPT, GAMMA-GT): **Liver enzymes** which act as biocatalysts to accelerate and maintain metabolic processes in the liver. If there is cell damage, they enter the bloodstream and the raised levels measured provide valuable information about the nature and extent of liver disease. Gamma-GT is the most sensitive parameter of damage to hepatic cells and the biliary system. Normal liver enzymes do not rule out chronic hepatitis C but, as a rule, the disease follows a more gradual course in patients with chronic hepatitis C and normal liver enzymes.

ALPHA-FETOPROTEIN (AFP): Tumour marker (protein that is produced with the development and growth of cancer). A large increase in AFP suggests cancer of the liver (hepatocellular carcinoma) but may also be seen with other types of cancer or an acute or chronic hepatitis. Conversely, a normal AFP does not exclude hepatocellular carcinoma.

LIVER FUNCTION TESTS: Albumin, bilirubin, cholinesterase, coagulation tests (INR/PTT). These results provide information about the metabolism and synthesis taking place in the liver and may detect a weakness of liver function, e.g. due to hepatic cirrhosis as a result of chronic hepatitis C.

LIVER BIOPSY: Taking a tissue sample from the liver with a special biopsy needle inserted through the abdominal wall under ultrasound guidance. Biopsies serve to diagnose and monitor the progress of various liver diseases. Histological examination of the tissue under the microscope gives the most accurate picture of the extent of liver damage.

SONOGRAPHY (ULTRASOUND SCANNING): Procedure that gives an image of the different regions of the body by means of ultrasound waves. The size and consistency of the liver (e.g. presence of tumour, fatty changes, cirrhosis, etc.) can be seen. The sensitivity and specificity of this method depend greatly on the skill of the examiner.

PEG-INTERFERON: Interferons are proteins that, in addition to their anti-viral effects, have inhibitory effects on cell growth, as well as immunomodulating and anti-tumour properties. Pegylated interferons (PEG-interferons) are representatives of a new generation of interferons with a particularly prolonged duration of action. Treatment of chronic HCV infections using a combination of PEG-interferon with ribavirin causes a lasting reduction of the virus to concentrations below the detection limit in up to 60% of patients. Even in those patients infected with genotype 1 (70% of infections) who do not respond so well to treatment, this figure is still 50%. Whether this is equivalent to a cure is still the subject of scientific investigation.

Risk assessment

NEGATIVE HCV-RNA (after therapy)

- Negative HCV RNA at least one year after stopping PEG-interferon/Ribavirin therapy (for life insurance); if the application is made less than one year after completion of treatment, tariffs as for HCV RNA positive or postpone. Application during therapy: postpone at least until end of treatment
- Transaminases, liver function parameters (cholinesterase, albumin, PTT), AFP in normal range
- Normal liver histology (there must be current histology findings from at least one biopsy, otherwise tariff as HCV RNA positive)

Life insurance	50
Disability insurance	Postpone two years after end of treatment, then refer to Munich Re
Health insurance	Acceptance with medium to high supplement possible in individual cases

POSITIVE HCV RNA (after or without therapy)

- Transaminases, liver function parameters, AFP in normal range

Life insurance	150
Disability insurance	In gen., decl.
Health insurance	Decl.

- Transaminases raised
- Liver function parameters and AFP in normal range

Life insurance	Weighting depends on the level of transaminases
Disability insurance	In gen., decl.
Health insurance	Decl.

GGT normal x	GPT normal x				
	1.1–1.5x	1.6–2.0x	2.1–2.5x	2.6–3.0x	> 3.1x
1.1–1.5x	150	175	200	225	Postp./decl.
1.6–2.0x	150	175	200	225	Postp./decl.
2.1–2.5x	175	200	225	250	Postp./decl.
2.6–3.0x	200	225	250	300	Postp./decl.
> 3.1x	Postp./decl.	Postp./decl.	Postp./decl.	Postp./decl.	Postp./decl.

Postp. = postpone decl. = decline



Only those who sleep well have a good day! – Obstructive sleep apnoea syndrome

Sleep overcame the lorry driver in broad daylight while he was reversing. The rude awakening came a few seconds later, when he found himself in the excavation pit into which he had driven his six-ton vehicle. This example illustrates a condition which many of those affected are not even aware of: **OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS)**.

This term is taken to mean frequent cessations of airflow, lasting more than ten seconds, during sleep, almost always accompanied by heavy snoring, and which lead to a reduction of the oxygen levels in the blood.

Obstructive sleep apnoea syndrome is caused by a narrowing of the upper airway due to floppiness of the pharyngeal musculature. This floppiness is due to loss of muscle tone (relaxation) during sleep. The result is “collapse” with narrowing (obstruction) of the upper airway. Complete collapse results in apnoea and partial collapse in hypopnoea. If the collapse is only slight, vibrations of the airway mucosa and muscles occur, giving rise to the typical sounds of snoring.

The cessation of airflow triggers **AROUSALS** (sudden awakenings) which interrupt sleep, causing it to lose its regenerative function. The consequences are daytime sleepiness, reduced performance and an increase in cardiovascular and peripheral vascular diseases. At least 2% of the female and 4% of the male population aged between 30 and 60 years suffer from OSAS, often associated with a metabolic syndrome.

DIAGNOSTICS

In a **SLEEP LABORATORY**, simple snoring can be differentiated from sleep apnoea by carrying out an overnight **POLYSOMNOGRAM**. This is a diagnostic procedure to measure more than twenty body functions during sleep, such as brain and muscle activity, eye movements, breathing through the nose and mouth, snoring, heart rate and oxygen levels in the blood. One important parameter is the **APNOEA HYPOPNOEA INDEX (AHI)**, i.e. the sum of all cessations in breathing (apnoea) and reductions in breathing (hypopnoea) of at least 10 seconds duration, per hour of night-time sleep.

PROGNOSIS

AHI < 20/h – slightly raised mortality of those affected in comparison with the general population
AHI > 20/h – markedly raised mortality of those affected in comparison with the general population, especially if associated with a metabolic syndrome

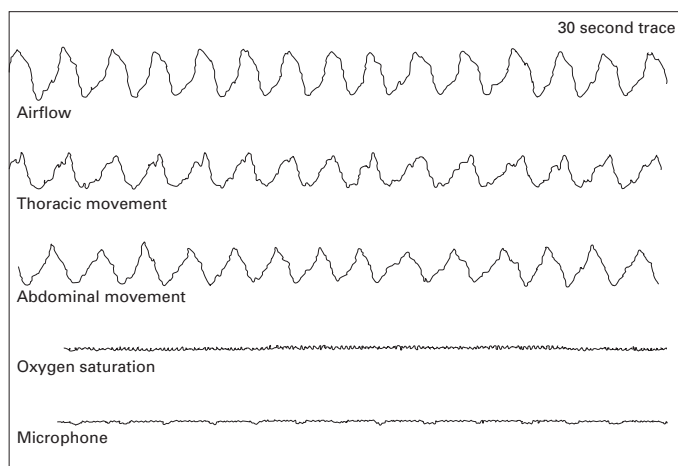
THERAPY FOR OBSTRUCTIVE SLEEP APNOEA SYNDROME

- Change in lifestyle (weight reduction, reduction of nicotine, alcohol, sedative consumption)
- **N-CPAP** (nasal continuous positive airway pressure)
- Maxillary surgery (long-term success clearly worse than n-CPAP)

Obstructive sleep apnoea syndrome: Risk assessment

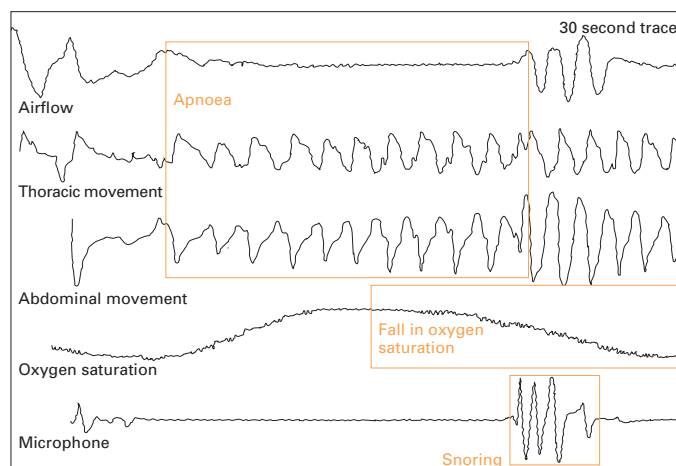
		Life	Disability	Accident	Health
Without CPAP or operation	AHI > 20				
	< 45 years	200	In gen., decl.	In gen., decl.	In gen., decl.
	> 45 years	100	In gen., decl.	In gen., decl.	In gen., decl.
	AHI < 20				
< 45 years	100	RMO	x2	In gen., decl.	
> 45 years	50	RMO	x2	In gen., decl.	
Successful CPAP or operation	< 45 years	100	RMO	x2	In gen., decl.
	> 45 years	50	RMO	x2	In gen., decl.

decl. = decline RMO = Refer to medical officer



Extract from a polysomnogram

Normal sleep



OSAS

NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (N-CPAP)

N-CPAP appliances create a positive pressure in the upper airways by means of a blower, with the airflow directed into the patient's airway through a tube and a nasal mask. The positive pressure causes a pneumatic bracing of the muscles in the pharyngeal wall which prevents the collapse of the upper airway. As a rule, side effects such as dryness of the mucosa and irritation of the skin under the nasal mask can easily be overcome with the appropriate medication.

The success of operative or apparatusive treatment should be checked by polysomnography within three months. Further follow-up examinations should be carried out at least once a year (recommendation of the German Association of Pneumology). The increased mortality due to obstructive sleep apnoea syndrome can be significantly reduced with continuous positive pressure ventilation.

ORGAN TRANSPLANTATION AND INSURABILITY – An example from practice

Female applicant born in 1964

Risk life insurance, duration of policy 23 years, sum insured €194,290

MEDICAL HISTORY

- No significant medical history prior to 1995
- Orthotopic **LIVER TRANSPLANTATION** on 31.3.1995 for fulminating hepatic failure of unclear origin
- Re-transplantation on 3.4.1995 because of thrombosis of the hepatic artery (main artery of the liver) of the first donor organ
- 5.1995 to 6.1995 cytomegalovirus infection and mild rejection of the transplanted liver
- Partial resection of the small intestine because of bowel obstruction due to adhesions 5.2000 und 1.2001
- Recurrent respiratory tract infections
- Birth of two healthy sons (2.1997 and 12.2000)
- Immunosuppression with cyclosporin, azathioprine and prednisolone
- Very good compliance (follows all directions)

FINDINGS

- Laboratory tests: normal liver function parameters, creatinine, blood glucose, blood picture. Hepatitis serology negative
- Hospital report (course of hospital admissions clearly documented)
- Normal ECG, lung function and chest X-ray. Blood pressure 120/75 mm Hg

LIVER TRANSPLANTATION

Because of the increasing imbalance between organ supply and demand, various methods have been developed to increase the supply of organs. These include split liver transplantation (division of the liver into two complete transplantable grafts) and live donor liver transplantation. The lack of organs means that up to 20% of patients on the waiting list die before they can receive a transplant. Success of transplantation depends mainly on suppressing the rejection reaction with immunosuppressant drugs which have to be taken for the rest of the patient's life.

In general, the safety profile of **IMMUNOSUPPRESSANTS** includes side effects of an increased risk of infection, increased rate of malignant tumours (ten-year risk following liver transplantation: 7–8%) bone marrow depression, hypertension, diabetes mellitus, renal failure, neurological disturbances and osteoporosis. Pregnancy after liver transplantation is possible but with a calculated risk, and is unusual evidence of a return to a higher quality and perspective of life.

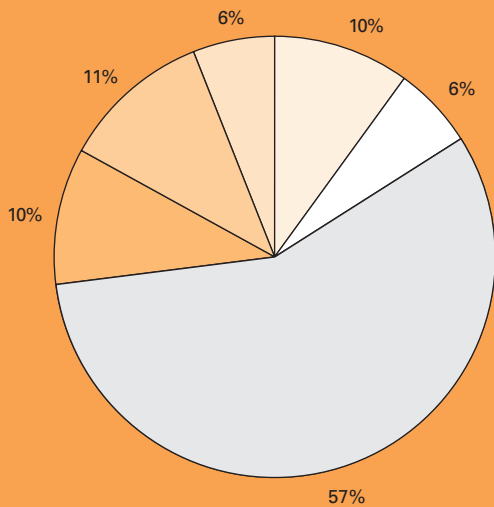


Risk assessment: Liver transplantation

- Wait at least three years after transplantation
- No serious rejection reactions in the past
- Age of the recipient (problematic with < 2 years and > 60 years) and nature of the liver disease for which the transplantation was required
- No severe systemic disease (arteriosclerosis, diabetes mellitus, etc.)
- Current laboratory status (liver enzymes, hepatitis serology, creatinine, blood picture)
- Information on current immunosuppressant therapy

Life insurance	15‰*
Disability insurance	Decl.
Health insurance	Decl.

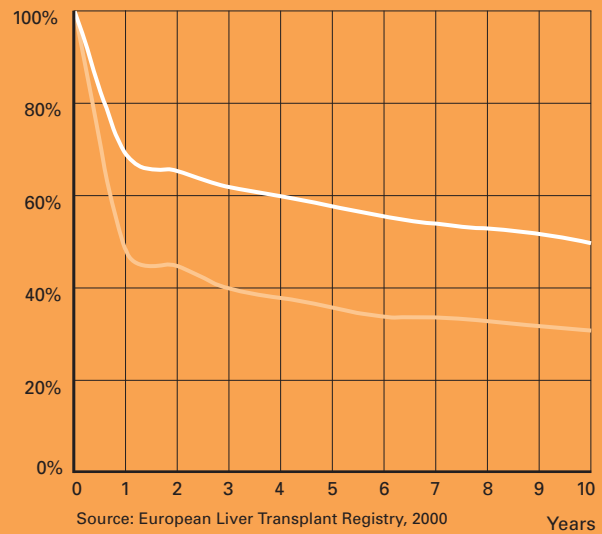
*For the entire duration of the policy: (maximum 15 years)



Source: European Liver Transplant Registry, 2000

Indications for liver transplantation in Europe

- Cirrhosis 57%
- Malignancies 10%
- Cholestasis 11%
- Metabolic diseases 6%
- Acute liver failure 10%
- Other 6%



Source: European Liver Transplant Registry, 2000

Survival rate of patients following liver transplantation in Europe

- 1968-1987
- from 1988

DIAGNOSTICS

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Prostate-specific antigen – Value for risk assessment

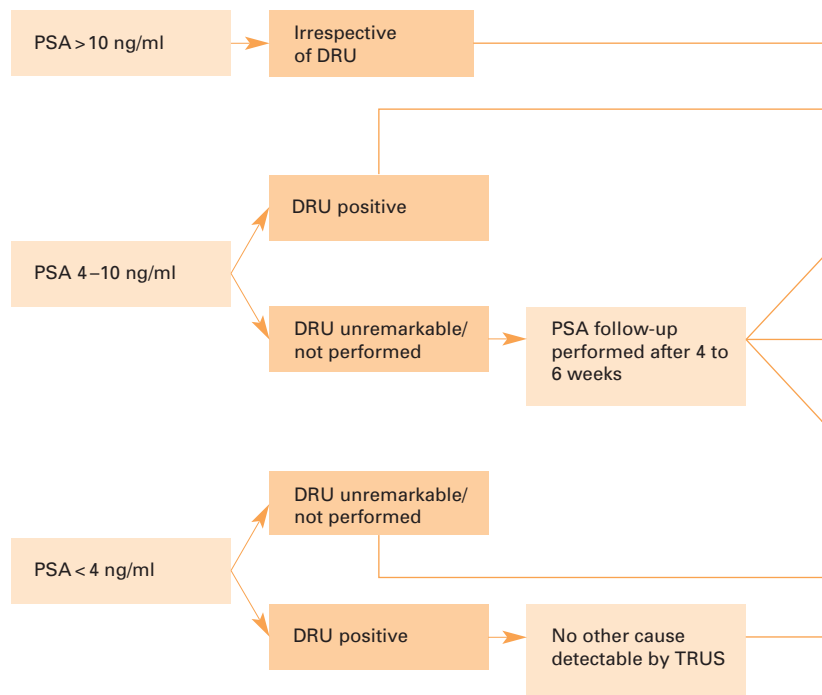
PROSTATE-SPECIFIC ANTIGEN (PSA) is a protein formed by the cells of the prostate. It is present in prostatic secretion and serves to liquefy the ejaculate. It also passes into the blood in small amounts, where it can be detected by a laboratory test. A small proportion of the PSA exists in the blood in free form, but the greater part is bound to proteins. The assay usually comprises total PSA only. There is some scientific evidence to suggest that the distinction between benign and malignant prostatic diseases can be improved by measuring free and bound PSA separately and comparing these results with one another. The probability of malignant prostatic disease is stated to be lower if the free PSA fraction makes up more than 15% of the total PSA, but higher if this proportion is lower than 15%.

ELEVATED PSA LEVELS ARE FOUND

- in **PROSTATIC CARCINOMA**,
- in benign enlargement of the prostate and prostatic inflammation,
- after vigorous exertion.

METHODS FOR THE DETECTION OF PROSTATIC CARCINOMA

- Digital rectal examination (DRU)
- PSA value
- Transrectal ultrasound (TRUS)
- Prostatic biopsy and histological examination



PSA – PROS AND CONS

- Malignant disease (cancer of the prostate) is found in roughly one-third of men with raised values, the probability being the greater the higher the PSA concentration is above normal.
- Combination with DRU improves the early recognition rate by about three times.
- Cancers can be more frequently detected at an early stage when they can be successfully treated.
- There is some danger of over-diagnosis, which will expose the patient to physical and mental stresses, because the provisional diagnosis of prostatic carcinoma made on the basis of raised PSA levels alone remains unconfirmed in two-third of cases.
- Thirty per cent of prostatic cancers remain undiscovered because the test is still insufficiently sensitive.

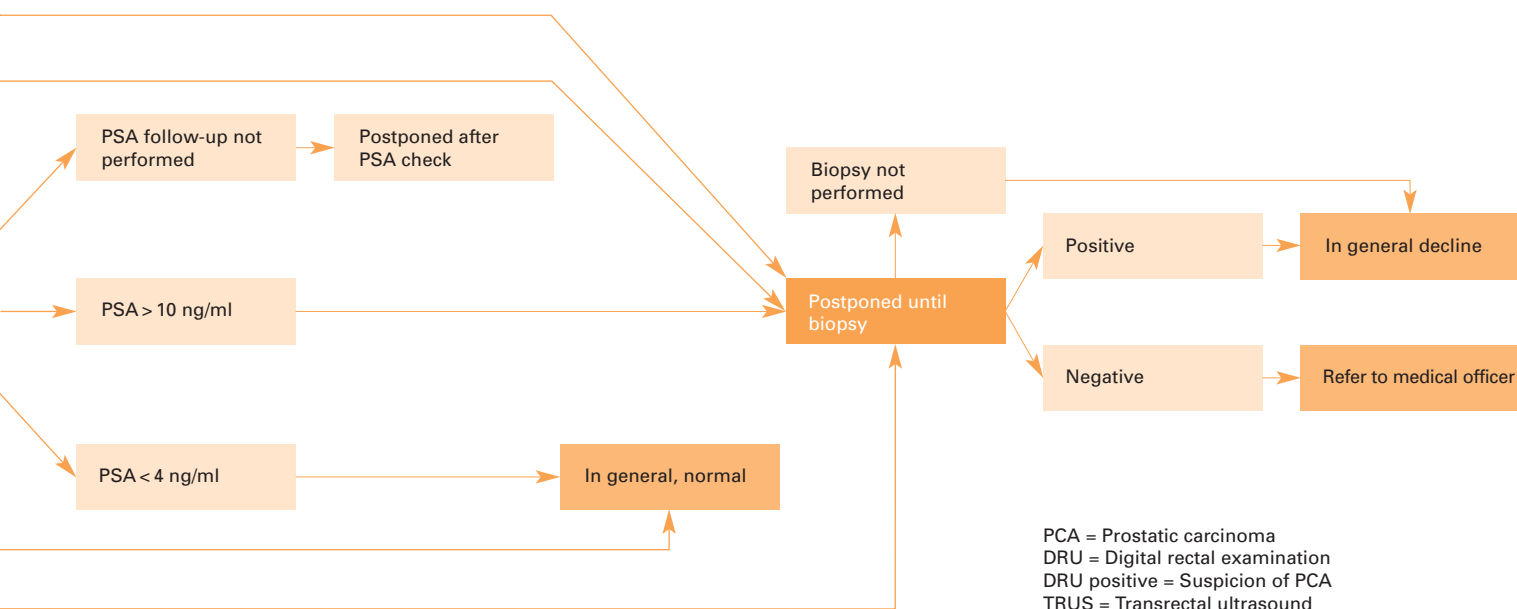
- Some patients whose cancer might otherwise have remained unrecognized for the rest of their lives are at risk of over-treatment because it would not cause any seriously troublesome symptoms.
- Because prostatic carcinoma usually progresses fairly slowly, the commonly older patients will die in many cases from some other disease.

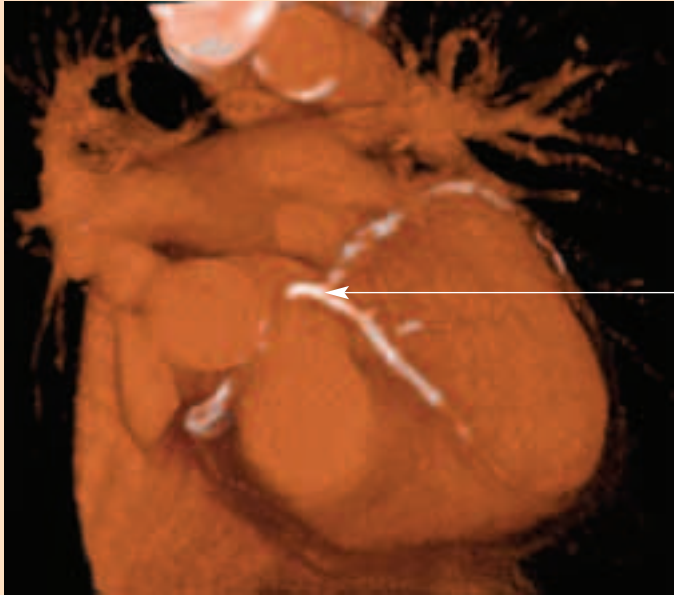
VALUE OF THE PSA FOR THE FOLLOW-UP OF PROSTATIC CARCINOMA

- Detectable PSA readings, of whatever level, after radical removal of the prostate are nearly always early signs of recurrence or progression of the cancer.

Patient group	Predictive value in %
DRU positive	21-51
PSA <= 4 ng/ml	26.1
4.1-9.9 ng/ml	31.5
> 10 ng/ml	52.9
DRU positive and PSA 4.1-9.9 ng/ml	40.8
DRU positive and PSA > 10 ng/ml	69.1

Positive predictive value PSA and/or DRU for prostatic carcinoma





Coronary calcification

3-D image of the heart using the ultra-fast spiral-CT scanning equipment

Electron beam tomography: A future screening tool for coronary heart disease?

Up to 50% of all myocardial infarcts involve patients who have had no symptoms beforehand and who are unaware that they have coronary heart disease. In such cases timely therapeutic intervention might improve the prognosis even in asymptomatic patients. In “at-risk patients”, when the doctor is disinclined to recommend cardiac catheterisation, a **CORONARY CALCIFICATION CHECK** is now increasingly often performed. Coronary calcification is an important component of coronary atherosclerosis. Exact measurements are now feasible by **ELECTRON BEAM TOMOGRAPHY (EBT)** and new multi-detector spiral-CT equipment. The examination takes only 35 seconds, during which the patient has to hold his or her breath. During this time the computer tomograph scans the heart in cuts of only a few millimetres. These serial cuts are then assembled to give detailed three-dimensional pictures of the heart and coronary vessels. Whereas the gain in prognostic confidence provided by this examination is still disputed, it is already being promoted by its most zealous proponents as the screening tool of the future and has even been recommended for risk assessment for life insurance. What view can be taken of this “cardiac diagnosis without catheterization”?

The American Heart Association (AHA) has now published a consensus document giving a detailed appraisal of the method. According to this document, coronary calcification determination in asymptomatic persons does not provide a better estimate of the probability of coronary heart disease than that given by a risk model based on the usual factors – blood pressure, cholesterol, smoking, blood sugar and age. The examination can at best provide evidence that a patient who has previously appeared to be at moderate risk must in fact be assessed as being at serious risk. Conversely, a low “calcium burden” in a patient with a high CHD risk profile might indicate that the patient in fact has a lower risk of developing CHD. The AHA does not recommend wide adoption of the method. Even for risk assessment, the value of coronary calcification measurements remains very low, in view of the well-established methods of risk appraisal by the risk factors listed above.

Up to 50% of all myocardial infarcts involve patients who have had no symptoms beforehand and who are unaware of their coronary heart disease.

Therapy

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Selective COX-2 inhibitors – Current state of knowledge

Selective **COX-2 INHIBITORS** (e.g. Celecoxib and Rofecoxib) represent a new generation of painkillers which are included in the pharmaceutical class of **NSAIDs***. Through selective inhibition of cyclooxygenase 2, a naturally occurring enzyme, they act against pain, inflammation and fever.

COX-2 inhibitors have similar efficacy to the classic analgesics but, because of their selective actions, have a lower rate of adverse effects on the gastrointestinal tract. These undesirable effects include ulceration of the stomach and duodenum, which can lead to serious complications and have a high risk of death.

Large-scale surveys in the USA give estimates of about 107,000 cases requiring hospital treatment and some 16,500 deaths each year as a result of these side effects. This number of deaths is in the same order of magnitude as the annual deaths from road traffic accidents in the USA.

Even though significantly fewer gastrointestinal ulcers occur with COX-2 inhibitors, the CLASS and VIGOR studies have shown that these dangerous adverse reactions cannot be completely eliminated.

Both the new COX-2 inhibitors and the classic NSAIDs give rise to increased fluid retention in the body tissues, which means that their use can be problematic in patients with cardiac and renal diseases, or high blood pressure.

A potentially increased risk of myocardial infarction and cerebrovascular accident with COX-2 inhibitors (in contrast to classic NSAIDs) has not yet been completely ruled out.

A definitive assessment of long-term risks is difficult, as the physiological function of cyclo-oxygenase 2 in humans has not yet been fully elucidated.

In comparison with classic NSAIDs, COX-2 inhibitors have additional therapeutic potential and may be used in the future to treat Alzheimer's disease or as co-therapy for various types of cancer. Even if it is possible, this vision of the future can only be realized if COX-2 inhibitors prove their efficacy in humans for the current permitted indications and no undesirable adverse or life-threatening drug reactions with long-term use are observed. The introduction of Celecoxib on the market in 1999 was one of the most successful drug launches in the whole of pharmaceutical history. Sales of Celecoxib are estimated to be in the region of US\$ 3bn per year, which makes Celecoxib one of the most successful drugs in the world.

In particular with novel drugs, harmful effects may arise that can be attributed to development errors and that could not be determined in this form at the time of the original marketing authorization. This should be borne in mind when considering the question of **DRUG LIABILITY**. A case of drug liability arises if a defective drug causes the death or not inconsiderable damage to the health of a person when it is has been used correctly.

*NSAID = non-steroidal anti-inflammatory drug; cortisone-free anti-inflammatory analgesic (popular examples: aspirin, diclofenac, ibuprofen).

Gastric banding – Surgical therapy for extreme obesity

The World Health Organisation (WHO) has designated obesity as the greatest of all chronic health problems. Data from the CDC (Centers for Disease Control) show that in 1999 61% of all US citizens (20–74 years) were overweight, 27% of this group having a **BODY MASS INDEX (BMI)** of 30 kg/m² or more.

Especially problematic are extremely obese patients with a BMI > 40 kg/m², for whom the success rate of long-term conservative therapy (diet, behavioural therapy, drugs) is only 3–10%. The hazards of obesity and its status as a disease are clearly defined in the Guidelines of the German Obesity Society, the World Health Organisation and the National Institute of Health. According to these guidelines, obesity is not only a disease leading on to the metabolic syndrome, to coronary heart disease, arteriosclerosis and cancers (Framingham study, Nurses’ Health Study), but is in itself associated with increased risks.

experimental procedure, but a scientifically evaluated mode of treatment, provided it is carried out by competent surgeons and physicians with interdisciplinary experience in this field.

In gastric banding a silicone band is introduced under laparoscopic vision and is placed round the stomach like a belt. The stomach is thereby narrowed like a sandglass with a small upper pouch and a passage into the remainder of the stomach below. The diameter of the passage or portal has to be adjusted every month for the first six months. It is regulated by a balloon incorporated into the band, this balloon being connected to a reservoir implanted under the skin (port), so that it can be filled or emptied by a needle inserted through the skin. Stretch stimuli from the newly created pouch ensure rapid adjustment of the feeling of satiation.

The gastric band can theoretically be left in the body for the patient’s lifetime, but in roughly one quarter of the patients it has to be removed because of side effects or insufficient weight loss. The band can be removed laparoscopically with little difficulty. Complications (displacement of the band or leakage, expansion of the pouch, infections, etc.) are infrequent. Within four years after a successful operation, 80% of the patients will achieve a reduction in BMI to below 30 kg/m², with 60% of all patients retaining the reduction beyond this four-year period. Since 1993 a gastric band has been inserted in over 60,000 patients worldwide. The surgical costs amount to about €4,000 per patient.

The adoption of minimally invasive surgical techniques opens new therapeutic approaches with low risks of side effects for this seriously at-risk group of patients with extreme obesity. Given systematic risk-benefit appraisal, integration of the patients into an interdisciplinary care system, and operations which are performed in accordance with the rules of good surgery, these modern techniques may well claim to be the treatment of choice for extreme obesity which has not responded to conservative measures.

WHO classification	
	BMI (kg/m ²)
Normal weight	18.5–24.9
Pre-obesity	25–29.9
Obesity Grade I	30–34.9
Obesity Grade II	35–39.9
Obesity Grade III	40 or more

SURGERY FOR OBESITY

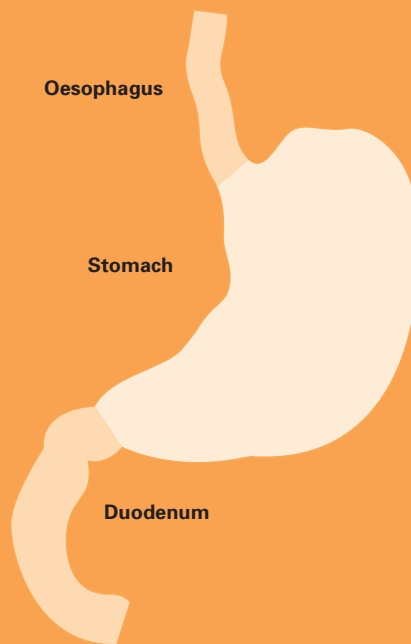
Surgical measures may be considered for selected patients with a BMI > 40 kg/m², and for those having particularly serious associated diseases from a BMI of 35 kg/m² upwards, for whom conservative measures have been tried and failed. At the beginning of the nineties, Kuzmak’s technique of laparoscopic **GASTRIC BANDING** was introduced as a minimally invasive surgical procedure, and is now accepted as the best operative method. It is in no sense an

The World Health Organisation (WHO) has designated obesity as the greatest of all chronic health problems.

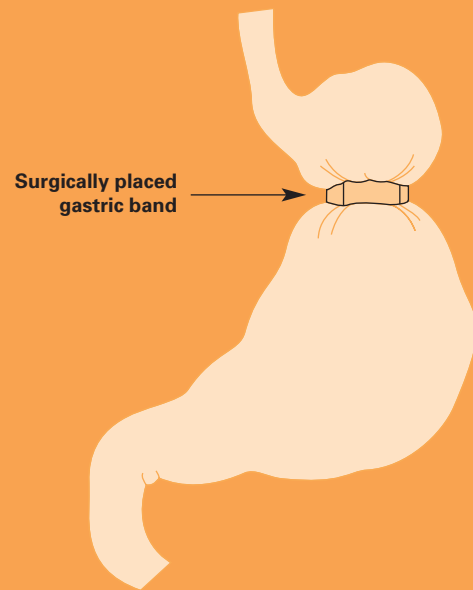
Gastric banding: Risk assessment

Time since surgery	Life	Disability	Health
Single surgery			
< 6 months	Postpone	Postpone	In general, decline
6 months to 3 years	50*	Postpone	In general, decline
> 3 years	In general 0*	In general 0* + exclusion clause: gastric banding	In general, decline
Repeated surgery	Refer to medical officer	Decline	Decline

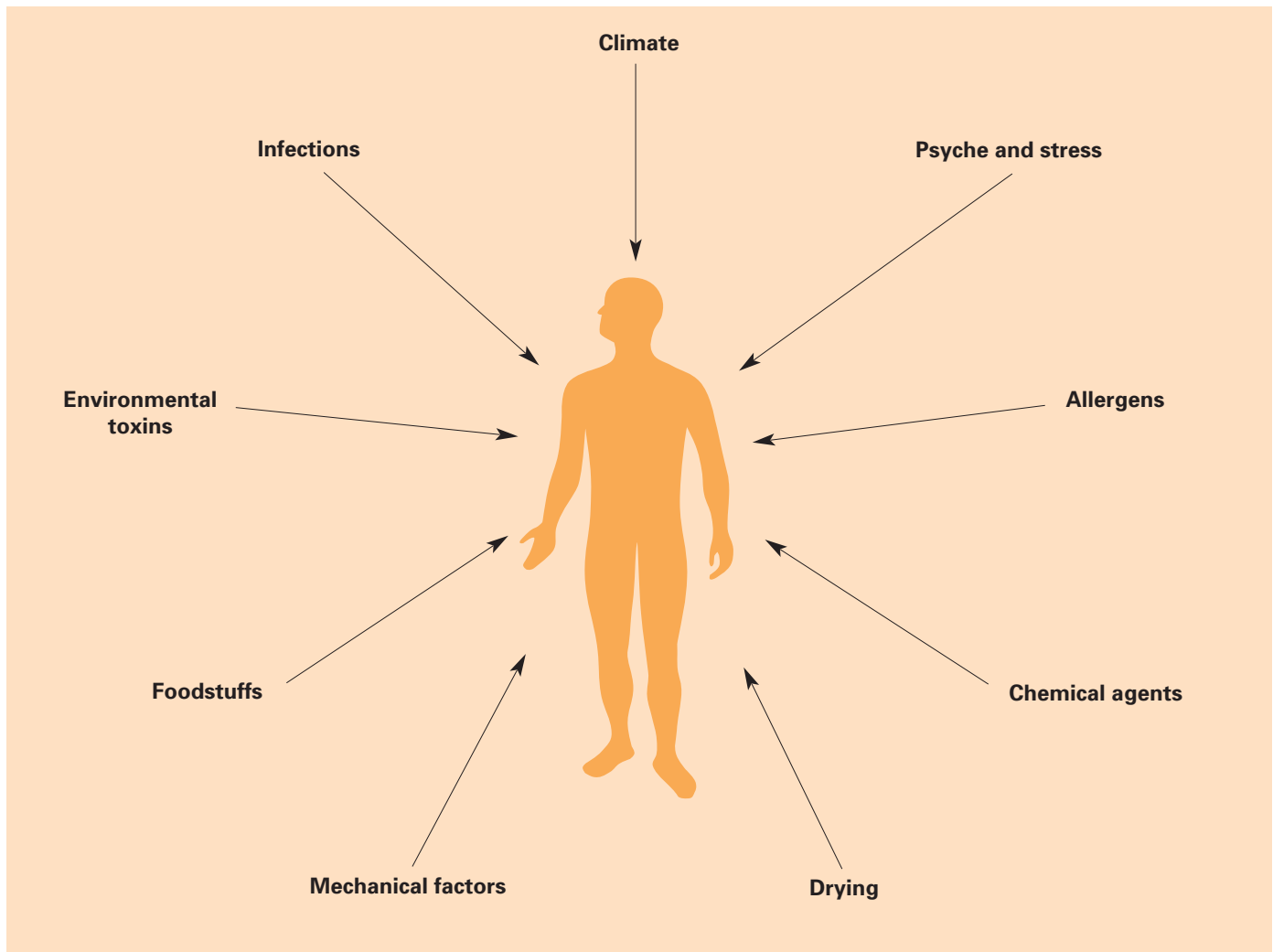
*Plus loading for current BMI



Before gastric banding



After gastric banding



Triggers of neurodermatitis

The worldwide prevalence of neurodermatitis in industrial countries is around 10% and is tending to rise.

Tacrolimus ointment – New hope for the treatment of a common disease, neurodermatitis

The worldwide prevalence of **NEURODERMATITIS** in industrial countries is around 10% and is tending to rise. This condition is therefore one of the most frequent of all chronic skin diseases. In Germany alone it affects almost four million people, in particular infants and pre-school children.

The disease frequently clears up of its own accord during childhood, but in occasional cases it constitutes a lifelong burden. Even in adult life, the disease can break out for the first time.

Although cortisone is highly effective in the treatment of neurodermatitis, it does have a number of possible side effects such as thinning of the skin. Long-term use or application to certain parts of the body is therefore inadvisable. An agent of comparable efficacy but with lower risks of side effects has therefore been the objective of many years' research. This goal now seems to have been achieved. A new ointment containing the active agent **TACROLIMUS** (Protopic TM) shows highly promising results for the treatment of neurodermatitis.

NEW THERAPEUTIC OPTIONS

Tacrolimus belongs to the group of immunosuppressants and has so far been employed in transplantation medicine. Applied locally, it penetrates the skin arriving in the cells of

the immune system, where it acts by several mechanisms to suppress the immunological over-reaction associated with neurodermatitis and has beneficial effects on both the allergic and the inflammatory reaction.

In international clinical studies comprising more than 10,000 participants worldwide, tacrolimus has been documented as showing good efficacy without systemic or serious local side effects. Unlike cortisone, tacrolimus is therefore suitable for the long-term treatment of neurodermatitis.

Tacrolimus ointment has now been licensed in Japan, the USA and Switzerland for the treatment of atopic dermatitis in children and adults; a licence for Germany is expected by the end of 2002.

The price is roughly €220 for 60 g ointment (0.1%), approximately ten times higher than for corticosteroid ointments. Should tacrolimus ultimately prove to be the product of choice for neurodermatitis, this will entail daily costs of €20 to €30 (depending on the severity and extent of the disease) and will impose a heavy financial burden on health insurers.

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A life-saving shock – Automatic external defibrillation

In Germany, **SUDDEN CARDIAC DEATH** is the number 1 cause of death outside hospitals. Every year about 100,000 people die of sudden cardiac arrest in Germany. This mode of death exceeds traffic deaths by a factor of twelve. In more than three-quarters of cases, sudden heart death is preceded by ventricular fibrillation. The chances of prevention are limited by the fact that there are no previous warning signals in roughly half the cases.

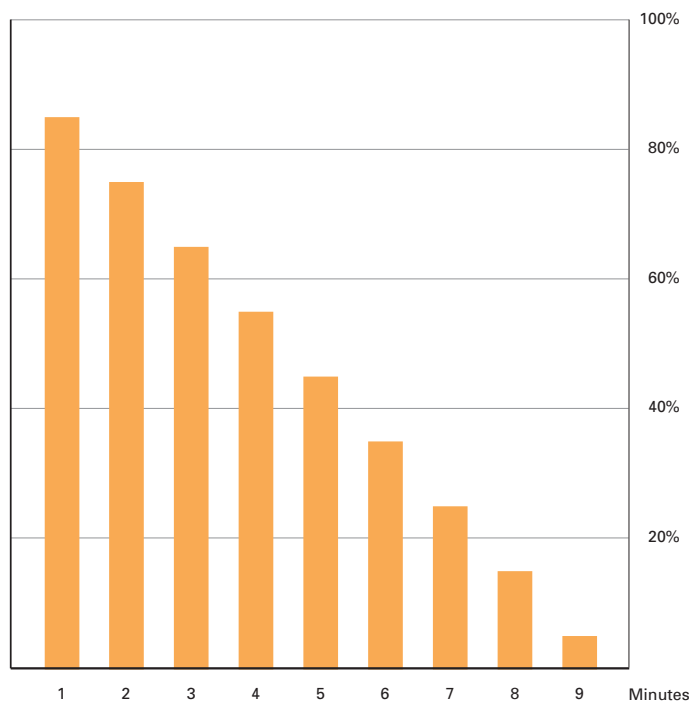
In **VENTRICULAR FIBRILLATION** the heart muscle operates in such an uncoordinated fashion as to be equivalent to cardiac arrest. The resulting lack of oxygen will very quickly lead to irreversible brain damage.

The only effective treatment for ventricular fibrillation is immediate electrical **DEFIBRILLATION**, backed up by the basic measures of resuscitation (artificial ventilation, cardiac massage). Electrical defibrillation is performed by applying large electrodes and delivering an electrical impulse to the patient's chest. This is intended to interrupt the uncoordinated fibrillation of the heart muscle fibres, and convert it into a coordinated action. However, the probability of successful defibrillation is seriously limited by the time factor (see illustration).

Industry has developed modern **AUTOMATIC EXTERNAL DEFIBRILLATORS (AEDs)**, which record the patient's ECG via electrodes, evaluate it and, if ventricular fibrillation is present, recommend defibrillation. In many countries, defibrillation by trained lay people is already accepted as part of basic resuscitation, and is gaining acceptance in Germany as well. Studies in the USA and Europe have demonstrated the effectiveness of early defibrillation.

Automatic defibrillators can be installed in many places such as industrial plants, sports facilities, banks, insurance companies and subway stations. The cost of a defibrillator is €2,000–4,000. Given wide coverage and training of the population, the numbers of deaths from sudden ventricular fibrillation can be significantly reduced.

Chances of surviving ventricular fibrillation in % depending on time. Already after five minutes there will be irreversible brain damage.



Automatic external defibrillation (AED)

Coated stents – Of great promise for preventing coronary restenosis?

BALLOON DILATATION of coronary stenoses (angioplasty/PTCA) has revolutionized the management of coronary stenoses. Yet even these techniques have their limitations: in some 40% of patients the symptoms reappear within the first six months. Many patients will ultimately have to undergo a bypass operation if a further attempt at balloon dilatation has not brought lasting success. Genuine improvement in the prognosis was achieved only by the introduction of **STENTS** at the beginning of the 1990s.

These small metal mesh tubes are inserted into the coronary vessel and then expanded. Although the restenosis rate – renewed narrowing of the arteries that have been treated – is lower, it still remains the chief problem. The essential cause of restenosis is the proliferation of arterial wall cells. At a time in which stents are being employed with increasing frequency, the so-called in-stent restenosis has now become the problem child of invasive cardiology. It was therefore obviously necessary to find ways of inhibiting this lethal cell proliferation.

Irradiation has long been used to arrest the growth of tumours. Excessive scar formation after operations can also be treated by irradiation in very low doses. Various methods are now being tested to bring radioactive radiation to bear on the arterial wall.

In intracoronary **BRACHYTHERAPY** the affected segments of vessel are irradiated so as to stop unwanted cell proliferation. An alternative procedure makes use of stents which themselves emit radiation. Initial clinical studies have given highly encouraging acute results and follow-up figures. However, the manufacture of these radioactive stents re-

quires elaborate equipment and they need special facilities for storage and handling. **DRUG-ELUTING STENTS** are therefore likely to be adopted more rapidly. By coating the stent with a cytostatic drug, cell proliferation can be blocked in a controlled way and without systemic side effects. The handling of the stent is uncomplicated and, in contrast to brachytherapy, no elaborate safety precautions are necessary.

PTCA IN FIGURES

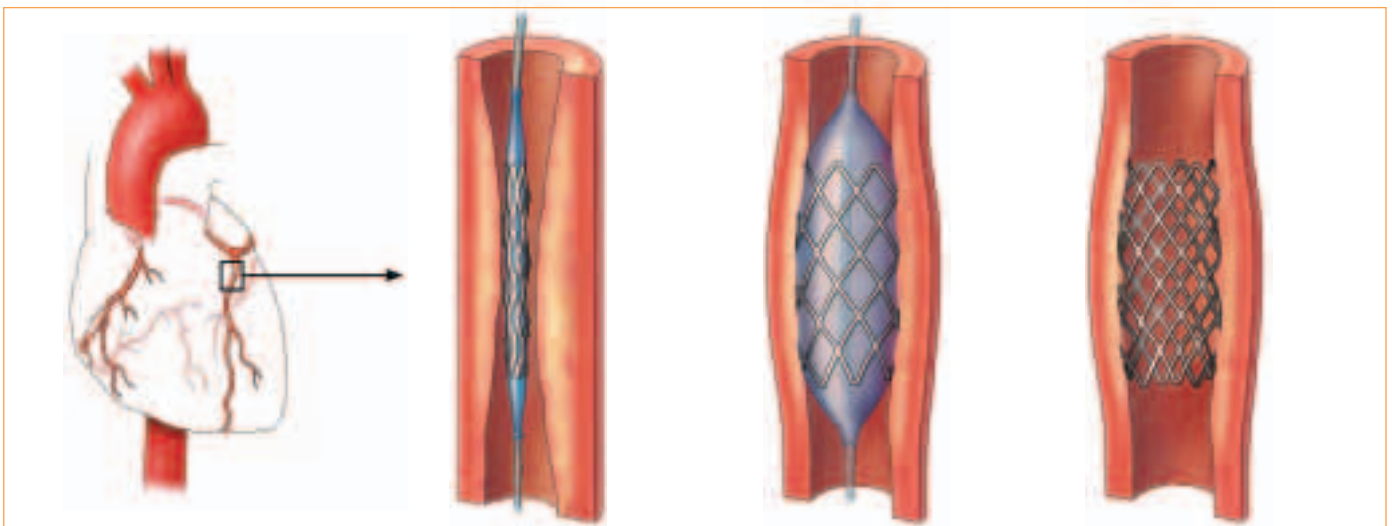
In Europe more than 400,000 patients undergo examination "therapeutic cardiac catheterization" every year.

In the USA in 1999 stents were implanted in an average of 80% of angioplasty cases; in France in the year 2000 the figure was as high as 94%.

One out of five of these patients will require further treatment for in-stent restenosis within a few months.

AND THE COSTS?

In-stent restenosis nowadays presents a significant clinical and economic problem. In Germany alone, the insurance funds pay out more than €0.5 bn for coronary angioplasties. Further reduction in the numbers of second and third operations on diseased coronary arteries would therefore be welcome not only to patients, but also to the health insurance companies.



Insertion of an intracoronary stent into a coronary artery

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