International Journal of Technology Assessment in Health Care, 15:4 (1999), 767–778.

TECHNOLOGY ASSESSMENT REPORTS

REPORT FROM THE CATALAN AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT (CAHTA)

Review of the Scientific Evidence of the Clinical and Economic Implications of Resistance of Enterococcus to Vancomycin

Recently, the advent and extension of vancomycin-resistant enterococci (VRE) has raised the awareness of the professional community, given that this antimicrobial is used as first-choice therapy for multiresistant gram-positive bacteria. The objectives are:

1. To know the prevalence of VRE;
2. To identify the risk factors of the appearance of VRE; and
3. To study, by means of a review of economic studies, the economic impact implied by the appearance of resistance to the antibiotic at hospital, health care, or society level.

METHODS

Data Sources

Bibliographic search in databases: MEDLINE (1989–97), Current Contents (1996–97), HealthSTAR (1992–97), and the Cochrane Library (2nd edition, 1997). Additionally, articles from bibliographic references, gray literature, and personal communications were included.

A systematic review of the scientific evidence was conducted.

RESULTS

Vancomycin-resistant enterococci are present in third-level hospitals, especially in intensive medicine units, and at least two strains have been detected in the community.

The risk factors identified in the acquisition of VRE are the administration of vancomycin and cephalosporins, the long-term therapy with vancomycin, hemodialysis, stay in intensive care units, and long-term stay in hospitals and/or intensive care units.

Other risk factors have been described but have only been assessed in a single study of those identified in this paper. These factors are: use of multiple antibiotic therapy, administration of aminoglycosides or macrolides, invasive abdominal processes, duration of therapy with cephalosporins, prior nosocomial infection, use of a central venous catheter, use of Foley probes, wound infections, renal failure,

https://doi.org/10.1017/S0266462399234162 Published online by Cambridge University Press

proximity of another patient with VRE, exposure to nursing staff caring for a VRE patient, gastrointestinal colonization with VRE, stay in more than one ward, vascular disorders as concomitant disease, administration of metronidazole, and patient age.

Ten economic assessment studies have been found related to the use of vancomycin and the appearance of resistances. None of the studies included comparative analysis of the costs and consequences of two or more alternatives against the appearance of bacterial resistances to antibiotics. The studies identified performed a cost analysis in some partial aspect related to resistances: a) administration costs of antibiotics, including the acquisition, preparation, and dosing of antibiotics; b) the cost incurred by the appearance of resistances (direct, indirect, and externalities costs); and c) the economic consequences of the antibiotic prescription therapies. None of the identified studies was made in the context of our health care.

CONCLUSIONS AND RECOMMENDATIONS

Catalonia is one of the areas where VRE strains have been found. Due to the worldwide extension of the problem of bacterial resistances and the potential of transmission to meticilin-resistant *Staphylococcus aureus*, a multiresistant organism that poses a difficult therapeutical challenge (actually, low-sensitivity strains have been found in Japan and the United States), it is necessary to control both multiresistant organisms and to prevent the appearance of new resistant strains. The task of making the professional community aware of the crisis implied by the bacterial resistance should not be ended. Continued training may play a very important role in it.

In order to control nosocomial infections of resistant organisms, certain isolation measures should be diffused and fulfilled. As regards the prevention of the appearance of new resistant strains, professionals should develop clinical practice guidelines based on the available evidence, mainly at hospital level but also in primary care.

It would be convenient to promote research in the field of bacterial resistances (both at the molecular level and regarding the favorable risk factors) and in research and development, addressed to the synthesis and production of new antimicrobials. The discovery of the mechanism of resistance should help fight those organisms presenting this characteristic, and it also means an important step for the research of new drugs against them.

Economic studies focused on our context should be carried out, mainly concerning the resistance to vancomycin and about antibiotics in general, with measurement of the economic impact of nosocomial infections and the strategies for its prevention and control. A social or health care system perspective should be included in the studies, in order to account not only for the costs that may be implied by the appearance and treatment of resistances in the hospitals, but also for the negative externalities placed upon other centers and the rest of society.

Studies should be carried out on the cost and health care implications generated by resistant organisms. Thus, the first approach is to carry out effectiveness, safety, and utilization studies; economic analysis studies comparing the cost and the results of different prevention strategies for the transmission of the existing resistances should also be undertaken.

Copies of this report are available in Catalan, and abstracts are available in Catalan, English, and Spanish from Area de Comunicacio, Documentacio i Gestio Operativa, Agencia d'Avaluacio de Tecnologia Medica, Travessera de les Corts,

131-159, Pavello Ave Maria, 08028 Barcelona, Spain; Tel: 34-3-227-2900; Fax: 34-3-227-2998; Email: agranado@dsss.scs.es or tparada@dsss.scs.es; Website: http://www.aatm.es.

REPORT FROM THE DANISH MEDICAL RESEARCH COUNCIL AND DANISH INSTITUTE FOR HEALTH SERVICES RESEARCH AND DEVELOPMENT

Consensus Statement on Depression: A Common Illness to be Treated?

A medical consensus conference on depression was held in Copenhagen, Denmark, on March 1–3, 1999. The consensus panel addressed the following questions: a) When does dejection constitute depression? b) What do we know about the causes of depression? c) How frequent is depression among different sections of the population? d) Which forms of treatment are available? e) Can several forms of treatment be combined with advantageous results? f) What happens if treatment is not received? g) Should the present organization of efforts be changed? h) What are the costs of depression and treatment of depression? i) Are there areas of research that should be enhanced?

The panel notes that depression is a common illness, as every year it affects more than 200,000 in a Danish population of 5.1 million inhabitants. As a medical diagnosis, depression denotes a prolonged state of dejection, emotional emptiness, self-recrimination, lack of energy, apathy, anxiety, sleep disorders, and lack of appetite. Emotional life contains a series of phenomena such as mood (with a duration of weeks or months), emotions (brief signals as outbursts of anger or joy), passions (often lasting for years), and finally pure feelings (e.g., it hurts if you hit yourself). Depression differs from emotion and passion in that it is a prolonged emotional state that progresses until settling into an immobile, long-term state of dejection. However, diagnosing a patient as depressed requires that the condition can be distinguished from normal emotional fluctuations and other resembling mental disorders. States that wrongly may be taken for depression include grief, adaptation reactions, dysthymia, anxiety, alcohol abuse, dementia, and seasonal affective disorder.

The panel notes that there is no clear borderline between normal psychological reactions, including grief, and an actual depression, just as it is not possible to define clear and unambiguous distinctions between mild/moderate and moderate/severe depression.

At present, the diagnosis "depression" is made in accordance with the World Health Organization (WHO) ICD-10 classification, 1992 edition, which classifies mental and behavioral deviations without a description of the trigger of the depression. The degree of depression severity is determined by means of the Hamilton Scale. Despite all diagnostic efforts, it is difficult to determine whether individual cases are cases of dejection or mild depression, as the ICD-10 classification only registers similarities and is incapable of determining decisive differences. Detecting depression in children and young people constitutes a special problem, because the diagnostic classification has been developed primarily for adults.

The panel notes that the cause of depression is not known. This fact makes it appropriate to consider depression as a multifaceted illness, where biological as

well as psychosocial conditions are of significance. Studies show that the risk of becoming afflicted by depression is at least doubled if close relatives suffer from depression. The risk of an identical twin developing a depression if the other twin has had one is approximately 60%, whereas the risk among fraternal twins corresponds to that of siblings, 10–15%.

In a biochemical perspective, communication between nerve cells in the brain is the basis for brain functions (activity of thought, emotions, mental well-being, etc.). Each nerve cell is in contact with other nerve cells by means of threadlike extensions, and communication takes place by means of neurotransmitters. This system is complex, as there are various types of transmitters and receptors. Moreover, the same transmitter may have activating as well as repressive functions. Drugs that reduce the amount of transmitters (such as serotonin and noradrenaline), thus reducing the amount available for binding to receptors, can trigger a depression, whereas drugs that increase transmitter concentrations — tricyclic antidepressants, SSRI, and others — can be used for treating depression. The first depression episode occurs more frequently in people who find themselves in psychosocially stressful situations, whereas subsequent episodes often occur without any known external cause. Depression occurs more frequently among people from lower social groups, divorcees, widows, widowers, and people who have had a stressful childhood, but the cause for this is not known.

In a psychosocial perspective the three lines of explanation are enhanced. According to Freud's theory, loss of and separation from significant persons during childhood can cause depression, but the viability of the theory is not supported in the literature.

According to the cognitive theory, depression is a result of negative thought patterns and not in itself the result of the individual's present external circumstances. Cognitive therapy focuses on detecting and correcting inappropriate thought patterns, and is often combined with behavioral exercises with a view to teaching the individual to control situations that would previously lead to negative, self-destructive thinking.

According to the vulnerability–stress model, it is assumed that depression is caused by an interplay between biological disruptions that may be hereditary and external causes in the form of psychosocial stress, particularly loss and/or rejection, or severe physical illness. In biologically predisposed individuals, external conditions may lead to a shifting of the mental balance, causing that person to develop depression.

The panel notes that depression is a widespread illness, and that 3% of the Danish population suffers from depression at any given time. The risk of suffering from depression at some point during a life span is 15–20%, even higher if there is a family history of predisposition to depression. Seventy percent of all patients with depression have more than one period of illness, and approximately 10% of all patients develop chronic depression.

Depression seems capable of starting in childhood, and 0.5% of all children between the ages of 2–6 show symptoms of depression, making it reasonable to assume that an actual illness is at work. The frequency of depression increases with age and is as great in puberty as among adults. Before puberty, depression occurs among girls and boys with equal frequency, whereas in puberty depression occurs twice as frequently among girls as among boys.

Depression among the elderly increases with age and often has serious consequences. Approximately 5% of all individuals over the age of 65 are estimated to

suffer from depression, but incidences are far more frequent among elderly people in institutions.

When the panel evaluated the effectiveness of treatment, it considered a number of acute effects, measured as the ability to reduce/eliminate the number and/or severity of the symptoms of depression.

In cases of mild depression, use of antidepressants does not have a proven effect greater than placebos, while psychotherapy has. There is some evidence that supportive conversations and patient instruction (psycho-education) are a relevant option with first-time episodes of mild depression. Medical treatment using tricyclic antidepressants (TCA) is seldom used for mild depression, and electroconvulsive treatment (ECT) is never used.

In cases of moderate and severe depression, the use of antidepressants (TCA and SSRI) has a proven effect greater than placebos. According to Danish studies, the effect of treatment with TCA is greater than the effect of treatment with SSRI for patients with severe depression. Studies show that approximately 60% of all patients experience an effect from antidepressants. Some studies indicate that psychotherapy could have an effect in cases of moderate depression, whereas other studies indicate that this is not feasible. There is a consensus that psychotherapy on its own would not be an effective method of treatment of severe depression, but it can supplement the otherwise relevant medical treatment. ECT treatment has a proven effect for approximately 80% of patients with very severe depression where medical treatment has not proven effective.

Long-term effects are measured as the ability to keep the patient free from symptoms or to prevent new depression over a longer period of time. The panel notes that there is no reliable knowledge available on long-term relapse frequency, but the following examples outline the trend. Drug treatment has a greater long-term effect than placebos, and the risk of a relapse is more than 10 times greater for patients with severe depression who cease drug treatment than for patients in continuous medical treatment. Cognitive therapy (accompanied by medical treatment) leads to fewer relapses than medical treatment of limited duration.

The panel finds that certain states of depression will profit from both medical treatment and psychotherapy. If emphasis is placed on medical treatment, it is recommended that such treatment is accompanied by a supportive conversation with the patient and with his or her closest relatives. In cases of moderate to severe depression, medical treatment should be supplemented by patient instruction, and in some cases by actual psychotherapy.

If left untreated, the depression period of individual patients will usually last 3–12 months, but longer periods can occur. Antidepressive treatment can shorten a period of depression, thus easing what is often a painful and socially disabling state for patients with depression. Patients with insufficiently treated severe depression have a risk of committing suicide 10–35 times greater than that of the rest of the population. The risk of a patient having one or more subsequent episodes of depression is approximately 70%. No conclusive evidence exists that treatment of individual episodes lowers the risk of subsequent depression episodes, but unverified observations seem to suggest this. On the other hand, maintenance treatment with antidepressants, which may be viable for patients with frequent episodes of depression, significantly reduces the number of subsequent depression episodes. The risks of not identifying and treating depression must be considered in light of the fact that only 50% of all patients with depression consult their doctor. Besides pharmacological maintenance treatment, it seems that cognitive psychotherapy, when maintained during nondepressive periods, can reduce the risk of new depression episodes.

Approximately 10% of patients with depression develop chronic depression. It is important to treat patients with a depression episode with a sufficient dosage and for a sufficiently long period of time. If treatment is discontinued too soon, the patient risks a rapid relapse of the depression, with all the appertaining consequences. For this reason, treatment of depression should be extended to cover at least 6–12 months, a fact that may be difficult to understand for some patients, who feel entirely recovered after a few weeks of treatment and who may experience side effects from the medicine.

Today, all patients in Denmark with a health problem of any description, including mental problems, can consult their general practitioner for an assessment of their problem. It is possible to have an appointment with the doctor quickly, at the latest 5 days after calling to make the appointment, and the doctor's clinic is only a short distance away. Moreover, doctor and patient are often previously acquainted, a fact that increases the opportunities for recognizing even small changes in the patient's mood.

When encountering a patient with potential depression, on the basis of the first consultation the doctor may arrive at a reliable diagnosis and initiate relevant treatment, he may suspect depression, he may assume that the patient suffers from another somatic or mental disorder, or he may assume that the patient suffers from an existential problem.

On suspicion of depression, the general practitioner can ascertain the diagnosis in subsequent consultations or refer the patient to:

- A private psychiatrist. This often involves great distances and long waiting time (up to 12 months is not unusual). There are only approximately 110 private psychiatrists in Denmark (population 5 million). The number of consultations per patient per year is limited.
- A private psychologist. Here, the patients have to pay the full fee for consultations themselves. Most general practitioners have no special knowledge of the professional qualifications of individual psychologists and do not know beforehand the type of psychotherapy their patients will receive, and consequently cannot offer their patients guidance.
- A psychiatric hospital with a view to hospitalization, outpatient treatment, treatment at a day care ward, or further treatment in the Danish district psychiatry scheme. Hospitalization is only a real option for severely depressed and highly suicidal patients. Experience shows that the interdisciplinary efforts offered by teams in district psychiatry are best suited for chronic and psychotic patients and less suitable for patients with depression.

The panel recommends that the general practitioners retain their position as gatekeepers and stay in charge of the distribution of patients to primary and secondary health care facilities. They should, however, be given better opportunities for receiving assistance in situations where they feel uncertain. In future, opportunities should be opened for referring patients to limited types of therapy with a private psychologist without patients having to pay for it themselves.

Within the hospital system, patients with depression should be physically segregated from psychotic patients and addicts. Establishment of depression clinics/departments (as provided in the County of Funen), with a maximum limit on the length of time a patient has to wait for an initial assessment with a view to diagnosis and treatment, is recommended.

The panel finds it positive that there are strong patient organizations that can assist in outlining the scope of the problem, thus strengthening the basis for allocating funds for treatment and research.

No Danish empirical materials/studies with information on the direct and indirect costs of depression are available. If the results of foreign studies are used as the basis for an estimate of Danish costs, the figures arrived at vary from approximately DKK 5.5 billion to approximately DKK 9.5 billion per year. Direct costs alone vary from almost DKK 700 million to just above DKK 2.7 billion (all amounts in 1997 prices). These figures demonstrate that depression constitutes a significant economic problem.

Within psychiatric epidemiology, psycho-pharmacological research, and genetic research, Denmark has research groups of global reputation. The Danish research community is characterized by having relatively small research groups that have difficulties in attracting talented scientists, and by having difficulties competing with large foreign research communities.

The panel has identified a series of specific topics for research as potential areas for concentrated effort: neuro-research and psychosocial research with a view to outlining the causes of depression, assessments of the effect of psychological and pharmacological treatment on mild depression, optimization, and assessment of long-term treatment, research on the incidence, diagnosis, and treatment of depression in children and the elderly, and health economic research with a view to mapping the costs of depression to assess the cost-effectiveness of new and usually expensive forms of treatment.

The full text of the consensus statement, in English or Danish, is available from Bent Danneskiold-Samsøe, M.Sc., Senior Research Associate, DSI Danish Institute for Health Services Research and Development, Dampfaergevej 22, P.O. Box 2595, DK-2100 Copenhagen, Denmark; Tel: +45 35 29 84 58; Fax: +45 35 29 84 99; Email: bd@dsi.dk.

REPORTS FROM THE SPANISH AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT (AETS)

Ultrasonography in Primary Health Care

Purpose of assessment: To assess the usefulness and convenience of including ultrasonography as a diagnostic tool in primary health care services provided by the Spanish National Institute of Health.

Clinical review: structured overview.

Data sources: MEDLINE database (1974–97), the Cochrane Library, reports from agencies for health technology assessment included in INAHTA, and external expert comments.

Review process: internal expert review.

Content of report/main findings: From 30 to 70% of sonograms requested by general practitioners showed pathologic findings. No studies were found that rigorously assess either the benefits that can be rendered by sonography when performed by general practitioners or the effectiveness of using specific forms requesting sonographs performed by radiologists. The only economic evaluation found (a direct cost estimation) had methodological flaws that make it impossible to draw any conclusion on the alleged cost reduction of sonography when performed by general practitioners. The high variability of the estimates, the number of participants, and the serious methodological flaws of the evaluations do not allow for

conclusions on the effectiveness of training general practitioners in performing ultrasounds. No model for training general practitioners in sonography had been adopted by health authorities in any country. However, no binding character recommendations exist.

Recommendations: The medical literature on this subject is scanty, most studies included in this review provide poor evidence, and flaws in their design and methodology preclude drawing conclusions on the performance of ultrasound by general practitioners. The only studies available refer to obstetric ultrasound, which in the Spanish primary health care system is usually carried out by gynecologists. Pilot studies should be carried out to further explore these issues.

Surgery for Epilepsy

Purpose of assessment: To review the current indications, outcomes and use of epilepsy surgery in Spain. To assess present and future needs for presurgical evaluation and surgical treatment for medically refractory epilepsy. To describe diagnostic and treatment procedures and requirements for service provision.

METHODS

A search of scientific literature in the MEDLINE database (1995–97) has been carried out, using the MeSH keywords epilepsy/diagnosis, temporary lobe/surgery, cerebral cortex/surgery, psychosurgery; studies on presurgical evaluation, diagnostic tests, and effectiveness of the different surgical procedures have been retrieved; reports and documents related with surgery for epilepsy have been consulted in the database of INAHTA and the Cochrane Library. Information related to the frequency and type of surgical treatment for epilepsy in Spain has been obtained from a specific hospital survey.

RESULTS

The protocol of patients' selection for the surgical indication should maximize the results with the minimum risk for patients. An established consensus does not exist on the protocols of patients' selection for presurgical evaluation, on the best diagnostic strategy, or the most appropriate surgical procedure for each indication.

The scientific evidence of the surgery for epilepsy effectiveness comes mainly from studies describing series of cases. The comparison of results among the studies carried out in different countries outlines substantial difficulties, due to the great heterogeneity of the indication, time of pursuit, surgical procedure used, the criteria adopted to select patients, changes of procedures over time, and selected outcomes.

At the present time, good results are achieved with several techniques in selected patients, and these results are now obtained with safer procedures in the presurgical evaluation and smaller risk of neuroligic sequels and adverse effects. In the short term the surgery for epilepsy reduces the frequency of the seizures, although in a variable way according to clinical situation and intervention type. The results attained in patients with epilepsy of the temporary lobe and with located lesions are very good (temporary lobectomy and lesionectomy) (67–69% free of seizures), with follow-up of 1 to 2 years. The results are worse in patients with extratemporal epilepsy (45% free of seizures).

The available long-term data suggest that the results of the surgery in patients with mesial temporal sclerosis, in spite of their short-term effectiveness, worsen

with time (50–68% without crisis). High relapse percentages are observed at 1 year of follow-up (14%). Most of the recurrent seizures after surgery are similar to the presurgical seizures; the probability that they will continue is 80%, and the probability that they end up being drug-resistant is 85% when recurrent seizures happen during the first year and 50% when they happen later.

The measures of results have been based fundamentally on the decrease of the frequency of the seizures after the intervention. There is little evidence of the long-term effects of the surgery (complications, morbidity, and mortality) as well as the global impact of the intervention in patients' quality of life and social integration. It has been estimated that 5–15% of the patients need another surgery. In 37–63% of the patients the new operation is able to control the seizures, depending on the type of surgical procedure and the affected lobe.

Assuming the values of incidence and prevalence obtained in developed countries as well as the percentages of drug-resistant candidates for surgical intervention, it is estimated that in Spain 75 to 300 new cases a year would benefit from surgery. Furthermore, it would be necessary to add to these incidence cases the accumulated prevalent cases (1,000 at 5,000) that could benefit from the surgery. Some estimates indicate that at the present time about 1,500 epileptic patients in Spain could benefit from the surgery. As a whole, the number of medically refractory epilepsy patients receiving intervention in Spain is no more than 100–150 patients a year, although many of them would not be classified as patients with essential or primary epilepsy. Most of the surgeries are performed in Madrid and Barcelona, where the majority of patients are referred. There is a deficit of resources dedicated to surgical treatment for epilepsy and limited use of this therapeutic option.

RECOMMENDATIONS

Resources should be allocated to presurgical evaluation research and protocols for the patients' selection, to advance knowledge of the clinical utility of complex, invasive, and expensive diagnostic procedures and more efficient diagnostic strategies. In the same way, research protocols of surgery outcomes should be established according to medium- and long-term outcomes, complications, and adverse effects of the different intervention alternatives.

The achievement and maintenance of excellence in surgery for epilepsy demands a low activity volume. This implies the need to concentrate current demand with a few surgical units in order to achieve the optimal number of operations and the maximum level of quality of the procedures. Probably no more than four to five highly specialized epilepsy surgery units (providing invasive diagnostic procedures) could provide treatment of high quality and cover the Spanish population's needs. Additionally, other centers could carry out a high volume of interventions that demand less complex diagnostic and therapeutic procedures (secondary epilepsy, temporal lobe).

One unit of surgery for epilepsy endowed with the necessary resources could obtain a high activity level, handling 50 to 100 patients a year. Currently, this intervention volume is far below the activity levels of most of the centers of the world. In fact, the demand for treatment, although it is growing, would not reach that activity volume. However, as we have estimated (75–300 new cases added annually to the prevalent cases), the potential demand for treatment could create a substantial increase in activity in the near future.

Some of the existing units, with the necessary support, could offer surgical treatment to 30 patients a year. The units that have accumulated a high level of experience should consolidate and continue concentrating most of the support and surgical activity. In turn, these units must become reference centers, facilitating research activities for effective and efficient procedures and training.

It would be convenient to establish standard requirements for epilepsy surgery units to guarantee adequacy of resources and high-quality procedures.

Effectiveness and Safety of Penile Prosthesis

Purpose of assessment: To assess the effectiveness and safety of penile prosthesis in the treatment of impotence for public consideration.

Clinical review: Structured overview.

Data sources: MEDLINE database (1983–97); reports from AHCPR: "Diagnosis and Treatment of Impotence" and NIH: "Consensus Development Conference Statement." A survey was conducted in five hospitals in Madrid (Spain).

Review process: External expert comments.

Content of report/main findings: Mechanical malfunction ranged from 3 to 33% (best outcomes were reported with malleable, modern inflatable devices like Mentor Alpha I, AMS 700CX, AMS 700CXM, and AMS700 Ultrex Plus). Worst outcomes were with old devices, the one-component inflatable device, and the modern three-component AMS Ultrex. Surgical complications ranged from 4 to 20% (best outcomes were with malleable and modern three-component inflatable devices; worst with old inflatable devices, AMS 600, previous Peyronie disease, reimplantation, and AMS Ultrex because of S-shaped penis deformity). Infection rates ranged from 2 to 5% (worst outcomes were those on corticosteroid therapy and those with diabetes).

Effectiveness has been assessed considering two outcomes: second-year survival rate of first prosthesis and sexual satisfaction. Survival ranged from 29 to 100%. Most of the studies use inflatable devices with three components. With these devices the survival ranged from 45 to 100% and had sexual satisfaction rates from 72 to 96%. The best outcomes with all three components were reported with Mentor Alpha I, AMS 700 CX or CXM, and AMS Ultrex Plus. These outcomes are poorer than those achieved with the old three-component inflatable devices and with the modern three-component AMS Ultrex and AMS 700.

Few studies of two-component inflatable devices were found. The survival rate for these devices ranged from 29 to 100%, with a sexual satisfaction rate of 59 to 65%. The data for one-component devices show a 2-year survival rate of 64 to 90%, and with malleable devices from 82 to 96%.

A survey conducted in five hospitals in Madrid reported a high variability in the number of procedures: penile prostheses were implanted in 1 to 10% of the cases of impotence attended, and a high variability between but not within hospitals in the kind of prosthesis implanted (in some hospitals only malleable devices and in others only three-component inflatable devices).

Recommendations: Since this procedure is a surgical technology, with a high degree of irreversibility in case of failure, the penile prosthesis should be considered as the last therapeutic option. The public health care coverage of the impotence disorder must be better defined. The penile prosthesis implantation should not be considered as common practice in the Spanish health care system. Its use should

be controlled and considered as a technology to be assessed with the appropriate methodology and performed in hospitals with research capabilities.

Copies of these reports are available in Spanish and abstracts are available in Spanish and English from the Agencia of Evaluación de Tecnologías Sanitarias (AETS), Instituto de Salud Carlos III, Ministerio de Sanidad y Consumo, c/Sinesio Delgado, 6 - Pabellón 3, 28029 Madrid, Spain; Tel: 91-387-7840 or 91-387-7800; Fax: 91-387-7841; Email: hertoran@iscii.es; Website: http://www.isciii.es/aets.

REPORT FROM THE SWISS SCIENCE COUNCIL PROGRAMME ON TECHNOLOGY ASSESSMENT

Technology Assessment of Xenotransplantation

Xenotransplantation research, as a part of biomedical research, investigates the question of whether it is possible to take living organs, tissues, or cells from animals and transplant them into humans. It is hoped that the xenotransplantation of organs will close the widening gap between the growing demand for organs and the limited supply of donor organs; cellular xenotransplantation aims at providing first or improved therapies for a variety of diseases.

In this report the present state of the art in the xenotransplantation of animal organs, tissues, and cells into humans and its possible future development are reviewed. Moreover, medical–scientific, economic, ethical, social, legal, and safety issues related to xenotransplantation are analyzed with special emphasis on the situation in Switzerland. The report is intended to provide an objective and comprehensive information bases and to contribute to forming an informed opinion about xenotransplantation, to assessing xenotransplantation in a differentiated way, and to decide on its future development.

Xenotransplantation of organs, if feasible at all, will not be a routine clinical procedure before 15 to 20 years' time because medical–scientific questions must be resolved that may turn out to be much more complex than anticipated. During this period of approximately two decades, xenotransplantation will have only minor effects on the improved supply of organs but will make organ allocation, which is problematic already, even more difficult during this period. Moreover, xenotransplantation in principle harbors the risk that new infective agents might be transferred from animal to man. Present knowledge is not sufficient to assess this risk. It is an issue of the current scientific and political debate to develop and implement appropriate safety measures and precautions in order to minimize the risk of infection for the patient and the general population. There is a call for action in Switzerland.

With respect to its economic, legal, ethical, and social aspects, xenotransplantation is a very controversial issue. Inherent to xenotransplantation are controversial questions such as, for example, how to balance interests of individuals against social interests, under which conditions and for which purposes animals may be exploited by man, whether potential health and economic benefits are allocated to individuals while risks have to be taken by society, to which extent social and administrative decision-making processes are influenced by lobby groups, etc.

Against this background is the question of how important xenotransplantation is considered in Switzerland when compared with possible alternatives, and under

which conditions and prerequisites this option is to be pursued further and eventually used in clinical practice.

It is recommended that this question be discussed in Switzerland in a broadly based, deliberately initiated social discourse on xenotransplantation. This discourse should fulfill the criteria transparency of the discussion and decision-making processes, communication ability of the participants, openness with respect to the result of the process, real possibilities to influence the process, and confidence in this form of opinion-forming and decision-making. Possible measures comprise more detailed and complementary technology assessment studies on cellular xenotransplantation and on transplantation medicine, different forms of information and discussion, and the instrument of a consensus conference. The results should be adequately considered in the political decision-making process.

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