



Background information on Preconception Care and Screening

This document gives a brief overview of Preconception Care and Screening (PCCS). It focuses mainly on information and activities that are relevant to reducing the burden of congenital disorders.

What is Preconception Care?

Preconception care is the entire range of measures that can be adopted before conception to promote the health of the expectant mother and her child.

Preconception care is a key opportunity for preventing congenital disorders. Most women do not know they are pregnant in the early weeks and so they and the fetus may be exposed unknowingly to harm during the most sensitive period of fetal development. Therefore measures to encourage a healthy lifestyle and minimise harmful exposures need to be initiated before conception and continue for at least the first few weeks of the pregnancy. Prevention of some recessive genetic congenital disorders may also be possible through preconception carrier screening programmes.

Preconception care involves risk assessment, health promotion, health education and intervention. It requires involvement not only of health care providers involved in reproductive, prenatal and postnatal care, but also of employers, legislators and those responsible for the control of environmental health hazards and infectious diseases.

Types of programmes of Preconception Care

Programmes can be targeted at:

- The **entire community**, regardless of intention to conceive - for example programmes of rubella vaccination or folic acid fortification. This approach has

the advantage of reaching couples who have an unplanned pregnancy. Globally it is estimated that approximately 41% of pregnancies are unplanned¹.

- **All individuals in a particular population** – for example a programme of preconception care delivered by primary health care professionals to all couples who want to have children
- **High risk individuals** – those who want to conceive a child and have known risk factors, for example couples with a genetic condition through the paternal or maternal line, or women who have diabetes, drink heavily or smoke.

A combination of these approaches is likely to be most effective.

Preconception care to reduce congenital disorders can be divided into prevention of conditions with non-genetic causes (for example, conditions caused by alcohol consumption, iodine deficiency, rubella or syphilis infection) and for conditions with genetic or partly genetic causes (for example, congenital cardiac abnormalities, neural tube defects, haemoglobin disorders, Down's syndrome and glucose-6-phosphate dehydrogenase deficiency).

Preconception care can take the form of an integrated programme covering the full range of relevant conditions. An integrated programme of preconception care could consider the following:

- Family planning
- Folic acid supplementation and fortification
- Iodine and iron deficiency management
- Minimisation of exposure to teratogens including alcohol, drugs, tobacco and illegal drugs
- Minimisation of exposure to workplace/environmental teratogens including pesticides and herbicides
- Minimisation of infectious disease exposure, including syphilis, rubella, and cytomegalovirus (CMV)
- Chronic disease control, particularly diabetes, epilepsy and obesity
- Review of medication, both prescribed and over the counter, and advice to avoid non-essential medications
- Review of obstetric and gynaecological history
- Genetic disease management, particularly haemoglobin disorders, cystic fibrosis and other recessive single gene disorders.

Additional information in relation to specific conditions is available in other Toolkit documents such as those on neural tube defects (which examines folic acid fortification and supplementation), congenital hypothyroidism and iodine deficiency, teratogens, fetal alcohol spectrum disorder, congenital rubella and congenital syphilis and on sickle cell disease and thalassaemia.

In most countries delivery of preconception care is at best fragmented. A notable exception is Hungary, where preconception screening is integrated into a complete

¹ Singh S, Sedgh G and Hussain R Unintended Pregnancy: Worldwide Levels, Trends, and Outcomes. *Studies in Family Planning* 2010, 41,4,241-250

programme of preconception care. Examples of preconception care programmes are described in Appendix 1.

More commonly, preconception care addresses a particular condition in the preconception period, for example folic acid fortification to prevent neural tube defects, or carrier screening for haemoglobin disorders. Advice may be offered to women at high risk, such as those with complications in previous pregnancies, or with chronic diseases that pose risks to the fetus.

The success of preconception care programmes in high and lower income countries may be directly related to the availability and accessibility of health care for women. WHO identifies reproductive health care as being an essential element of the continuum of maternal and child health care and calls for a reformulation of programmes from the vertical (condition based) to those offering a wide range of services. In many low and middle income countries (LMIC), primary and community health care providers fulfil roles that are taken on by more highly-trained and specialist personnel in higher income countries. Enabling these providers to assume more responsibility for the care and prevention of congenital disorders requires education, training, and the strengthening of the human and technical infrastructure within which they work.

Family planning programmes as part of Preconception Care

A family planning approach to preconception care enables a woman and her partner to prepare for pregnancy and provide the best environment possible for a healthy pregnancy and birth of a healthy child. Parents can be informed of the essential micro and macro nutrients and the importance of avoiding specific exposures such as to alcohol, drugs, certain medications and other teratogens. Chronic conditions such as diabetes and epilepsy can be controlled. Infections such as syphilis can be screened for and treated and rubella vaccination administered. Family planning can directly reduce the number of children being born with congenital disorders.

For example by reducing the number of births to women of advanced maternal age there is a reduced risk of having a child with Down's syndrome and other chromosomal abnormalities. Couples with a child with a single-gene disorder or those in consanguineous partnerships (where there is a genetic disorder) may decide to reduce their family size if aware of the increased risk of bearing a child with a congenital disorder.

Preconception Care to minimise environmental causes of congenital disorders

Diet

Folic acid supplementation and fortification to prevent neural tube defects and other malformations

Periconception folic acid supplementation has been shown to be very effective in reducing the incidence of neural tube defects. Supplementation should begin at least 4 weeks before planned conception and continue for 8 weeks after conception. Food fortification can provide much of the folic acid necessary for women who wish to

become pregnant but depends on the level of folate fortification in each country, the foods fortified and variations in consumption of fortified foods with the result that women may be advised to take supplements as well.

Iodine

Iodine deficiency is the main cause of preventable brain damage in childhood. It occurs primarily in areas where there are low iodine levels in the soil, mainly in LMIC. Iodisation of salt has been chosen by the WHO as the best strategy to prevent iodine deficiency as salt is consumed universally and at a stable rate throughout the year. The addition of 20-40 parts per million of iodine to salt, based on the assumption of an average salt consumption of 10g/day, is recommended².

Iron and other micronutrients

Iron deficiency is the most common cause of anaemia in women and children. In young children iron deficiency anaemia delays psychomotor development and impairs cognitive performance. Other micronutrients such as vitamin A and vitamin D should also be considered. However, excessive vitamin A levels are teratogenic. Women of child bearing age should consume no more than 3,000 µg of vitamin A a day and those who are pregnant should avoid over consumption of products containing high concentrations of vitamin A, such as liver products or crustaceans³.

Exposure to teratogens

Alcohol

Alcohol consumption increases the risk of spontaneous abortion and fetal death and can cause a range of conditions which persist throughout the child's life. These include fetal alcohol syndrome, which involves characteristic cranial/facial abnormalities, prenatal and postnatal growth deficiency and central nervous system dysfunction, and fetal alcohol spectrum disorder (FASD). FASD describes the spectrum of physical, mental, behavioural and learning disabilities that can result from prenatal exposure to alcohol.

There is a dose related relationship between congenital abnormalities and alcohol consumption but to eliminate these risks, alcohol should be avoided completely both in the periconception period and during pregnancy.⁴ Evidence suggests that binge drinking is more harmful to the fetus than the regular drinking of smaller quantities of alcohol. Binge drinking is also a risk factor for unplanned pregnancies.

Family planning and reproductive health services should ensure that women who may be planning a pregnancy are aware of the harmful effects of alcohol on fetal development and direct women to appropriate support to reduce their alcohol consumption before pregnancy. For moderate drinkers, brief educational intervention programmes have been successful in reducing alcohol intake overall as well as the

² De Benoist B. *Iodine status worldwide: WHO global database on iodine deficiency*. Geneva: Dept. of Nutrition for Health and Development, World Health Organization; 2004.

³ European Food Safety Authority. Scientific Committee on Food. Scientific panel on dietetic products, nutrition and allergies. *Tolerable upper intake levels for vitamins and minerals*. 2006.

⁴ Sokol RJ, Delaney-Black V and Nordstrom B. *Fetal Alcohol Spectrum Disorder*. JAMA 2003;290(22):2996-2999.

number of binge drinking episodes. Alcohol consumption among heavy drinkers is generally only reduced through intensive educational programmes and supervision⁵.

Smoking and other recreational drugs

Smoking increases the risk of congenital disorders such as limb deficiencies⁶, orofacial clefts⁷ and gastroschisis⁸.

It is estimated that a third of the world's population aged 15 years or older smoke, including 12% of women. The proportion of women who smoke in high income countries is estimated to be 24% compared to 7% in LMIC, but smoking by women is increasing in LMIC by about 3.4% per year. Globally each year approximately 12 million women smoke during pregnancy.

Advice and support on smoking cessation should be given to women and their partners before pregnancy. Nicotine replacement therapy such as nicotine patches or chewing gum can be helpful before conception but their effects on the unborn child have not been studied sufficiently to recommend their use immediately before or during pregnancy.

Other recreational drug use such as cannabis, cocaine, opiates and amphetamines have adverse effects including increased risk of fetal death, low birthweight, post natal withdrawal symptoms and subsequent developmental and concentration disturbances. These drugs should be avoided immediately prior to and during pregnancy.

Environmental teratogens

Congenital disorders may be caused by exposure to harmful environmental factors through mutagenic action before pregnancy or teratogenic effects after conception. The mutagenic action may occur in the mother or father. After conception the highest risk of harm from teratogens is usually in the first trimester, when most organ development is taking place.

Environmental teratogens include exposure to radiation, mercury, lead and other heavy metals, pesticides, herbicides and organic solvents. Congenital abnormalities linked to exposure to environmental teratogens include limb reduction defects, neural tube defects, neurological damage and orofacial clefts. In some cases, an increased risk of congenital abnormalities has been linked to both maternal and paternal exposure, suggesting that damage has occurred before conception. Thus it is important to control exposures to environmental mutagens and teratogens before pregnancy.

⁵ Floyd RL, Weber MK, Denny C, O'Connor MJ. *Prevention of fetal alcohol spectrum disorders*. Dev Disabil Res Rev 2009; 15(3):193-199.

⁶ Czeizel AE, Kodaj I, Lenz W. *Smoking during pregnancy and congenital limb deficiency*. BMJ 1994; 308(6942):1473-1476.

⁷ Little J, Cardy A, Munger RG. *Tobacco smoking and oral clefts: a meta-analysis*. Bull World Health Organ 2004; 82(3):213-218.

⁸ Boer K, Steegers-Theunissen RPM, Steegers EAP. *Pre-conception care*. In: Macklon N, Greer I E, Steegers E, editors. Textbook of Periconceptional Medicine. London: Informa Health Care; 2009.

Infectious diseases

Infectious diseases that can be transmitted via foods (for example salmonella, campylobacter, and listeria) and parasites that can be transmitted from animals (*echinococcus multicularias* and *toxoplasma gondii*) can cause serious illness and premature birth. Steps to reduce risk include ensuring that eggs and meat are cooked thoroughly, and hygienic practice during preparation, cooking and serving of food. Farm/animal waste should be avoided; if this is impossible and the practice of hand hygiene, is important after contact.

Sexually transmitted diseases (STDs)

The point of transmission of infectious diseases to a child during pregnancy can vary, HIV, syphilis and hepatitis B can be transmitted during pregnancy or labour if the mother is infected. Chlamydia, gonorrhoea, herpes genitalis can be transmitted during labour.

More newborn infants are affected by congenital syphilis than by any other neonatal infection⁹. Syphilis is endemic in parts of Africa, Asia and Latin America. Every year, between half a million and 1.5 million infants are born with congenital syphilis, which is estimated to be responsible for 1.3% of deaths among children under 5. A single dose of penicillin to the mother early in pregnancy prevents infection in the fetus. However, recognition of the disease during the later stages of the pregnancy, or provision of inadequate prenatal care, may prevent timely diagnosis and treatment. Where screening as part of prenatal care is judged not to be reaching the target population, reproductive and family planning services would be an appropriate setting for screening and treatment of STDs. If these infections are identified in good time they can be prevented from infecting the child.

Rubella

Rubella can cause serious congenital disorders if the mother contracts the virus in the first 16 weeks of pregnancy. Symptoms of congenital rubella syndrome (CRS) include congenital cataracts, hearing impairment, patent ductus arteriosus, hepatosplenomegaly, thrombocytopenia, and mental retardation. Worldwide it is estimated that over 100,000 infants are born with congenital rubella syndrome each year in non-pandemic years; yet it may be that, due to under-reporting, the true incidence could be more than double this estimate¹⁰.

Prevention through vaccination in childhood or before conception is very effective. Vaccination during pregnancy is not recommended. In 2008 rubella vaccination was being given as part of EPI (Expanded Programme on Immunisation) in 127 countries – 40% of the global birth cohort. However, there is a marked gradient of vaccine use between the highest and lowest income countries, with many of the lowest income countries not including rubella in their vaccination programmes.

WHO recommends that rubella vaccination of children should only be implemented if uptake rates of 80% or greater can be maintained on a long term basis. Otherwise

⁹ *The global elimination of congenital syphilis: rationale and strategy for action*. Geneva, World Health Organization;2007.

¹⁰ Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS. *Rubella and congenital rubella syndrome: global update*. Rev Panam Salud Publica 2003; 14(5):306-315.

low childhood vaccination rates can lead to an increase in rubella infection among susceptible women of child bearing age. To address this problem, if rubella immunisation of children is put into place, rubella vaccination of women should be introduced at the same time or earlier. Where measles eradication programmes are already in place, a rubella component should be added through the use of the MMR vaccine.

Increasing use of MMR vaccines by private health care providers in countries where there is no national programme of vaccination is a concern in that it may increase the number of children born with CRS. Such countries may need to consider introducing national rubella vaccination programmes for women of child bearing age.

CMV (Congenital Cytomegalovirus) infection

Approximately 40,000 babies infected with CMV are born in the US each year (about 1 in 150 live births). Of these approximately 400 die and 8,000 have permanent CMV related disabilities including hearing loss, visual impairment and intellectual disability¹¹. Following infection, the virus is found in urine, saliva, tears, semen and cervical secretions and can persist for months or years. Direct contact with these secretions appears to be necessary for transmission. As with other herpes viruses, persons with CMV develop life long latency after primary infection.

Both primary infection and reactivation are asymptomatic in most children and adults but transmission from mother to fetus occurs commonly and can result in significant illness. The highest risk of transmission is from women who contract their primary infection during pregnancy, with transmission to approximately a third of fetuses.

There is no effective vaccine for CMV and knowledge about the infection is poor, both in the general public and among health professionals. Prevention should focus on raising awareness, particularly in women of child-bearing age, and on reducing the risk of infection by promoting hygienic practices such as thorough hand washing after exposure to body fluids, and avoiding the sharing of utensils.

Control of chronic diseases

Chronic diseases can complicate a pregnancy and result in poor health outcomes for the newborn, so the management of the condition both before and during pregnancy needs to be considered. Most research has focused on diabetes and epilepsy. Diabetes in particular is a major concern as rates are increasing rapidly in many countries.

Diabetes

The incidence of gestational diabetes mellitus (GDM) is between 1-5%. Between 0.2-0.3% of pregnancies occur in women with pre-gestational diabetes. Up to 25% of infants of diabetic mothers have neonatal complications and there is also an increased risk the child will develop diabetes. Major congenital abnormalities are approximately 3-5 times higher in infants of diabetic mothers and are the most

¹¹ Rasmussen SA, Erickson JD, Reef SE, Ross DS. *Teratology: from science to birth defects prevention*. Birth Defects Res A Clin Mol Teratol 2009; 85(1):82-92.

common form of perinatal death among these infants¹². Congenital disorders associated with maternal diabetes include cardiovascular, central nervous system (CNS) and musculoskeletal abnormalities. Since most pregnancies are not recognized clinically until two or more weeks after conception, strict glycaemic control is often started after the critical period of embryogenesis has begun and may be inadequate to prevent adverse pregnancy outcomes. Therefore it is important to ensure that women who have diabetes or who have experienced gestational diabetes in a previous pregnancy achieve good control of blood glucose before conception as well as throughout pregnancy.

A meta-analysis of studies on preconception care in diabetic women relating to studies published between 1970 and 2000 showed that the pooled prevalence of serious congenital abnormalities in children of women who have received preconception care was significantly lower than when no preconception care was received (2.1% versus 6.5%)¹³.

Epilepsy

Epilepsy has a prevalence of 5.25 per 1,000. A third of people with epilepsy are women of reproductive age. In pregnant women with epilepsy the incidence of births with congenital disorders has been reported to be 7.1%, compared to 2.3% for women without epilepsy. The most common malformation in children born to women with epilepsy is cardiovascular defects (in particular ventricular septal defects, 1.8%). There are also significantly higher rates of hernia, ear/neck/face malformations, cleft lip and spina bifida¹⁴. Antiepileptic drugs are frequently teratogenic and are associated with adverse pregnancy outcomes. However, risks associated with seizures in pregnancy are generally greater than risks associated with anti-epileptic drugs, so it is important to establish good clinical management of epilepsy before and during pregnancy.

Medication

It is important that women who are intending to conceive are made aware of the potentially harmful impact of medications on early fetal development. All medications being used in the period prior to the pregnancy and during pregnancy and breastfeeding should be reviewed by a doctor or pharmacist. In general a woman should take as little medication as possible during pregnancy, including traditional herbal remedies, homeopathic medicines and over the counter drugs.

Other factors influencing pregnancy outcomes

Other adverse effects on pregnancy outcomes are obesity, anorexia, high paternal or maternal age and a history of repeated spontaneous abortions and stillbirths. Obesity is associated with gestational diabetes and hypertension in the mother and congenital abnormalities in the child. For example, neural tube defects are 1.5-3.0

¹² Eriksson U J. *Congenital anomalies in diabetic pregnancy*. Seminars in Fetal & Neonatal Medicine 2009; 14(85):93.

¹³ Ray JG, O'Brien TE, Chan WS. *Preconception care and the risk of congenital anomalies in the offspring of women with diabetes mellitus: a meta-analysis*. QJM 2001; 94(8):435-444.

¹⁴ Meador K, Reynolds MW, Crean S, Fahrbach K, Probst C. *Pregnancy outcomes in women with epilepsy: A systematic review and meta-analysis of published pregnancy registries and cohorts*. Epilepsy Research 2008; 81(1):1-13.

times more common in children of obese women¹⁵. Anorexia also increases risk of spontaneous abortion and cardiovascular disease in mothers and increases the risk of diabetes in the child at a later age.

Preconception Screening

Screening for the risk of congenital disorders can take place in the preconception, prenatal and postnatal periods. Preconception screening has the advantage of identifying at risk individuals at a point in time when they have the widest range of personal and reproductive choices. However, preconception screening can be difficult to deliver if preconception health care programmes are not in place or if only limited groups of prospective parents have the opportunity to access the healthcare. For non-genetic disorders, preconception screening involves an assessment of exposure to known environmental risk factor(s), for example through a screening questionnaire or specific tests where possible. There are few examples of systematic programmes of this type, but such screening may be beneficial for increased risk population subgroups, for example agricultural workers and for women likely to experience closely spaced pregnancies as in this latter case, nutritional and vitamin supplements, most notably folate could be provided.

Preconception carrier screening for genetic conditions

Preconception genetic screening aims to detect carriers of recessive genetic conditions, who have a one in four chance of having a child affected by the condition but are themselves asymptomatic and therefore usually unaware of their risk. A carrier may manage their risk by choosing not to marry another carrier, by electing not to have children if their partner is a carrier, or by undergoing prenatal diagnosis to determine if the fetus is affected.

Some recessive genetic conditions are more frequent among specific ethnic groups or occur more commonly in a particular location, due to founder effects. For example cystic fibrosis (CF) is more common among people from Western Europe, the Mediterranean region and the Middle East. Sickle cell disease is more common among people of African origin, and thalassaemia among people of Mediterranean origin, the Middle East and South Asian origin.

Single gene disorders are more common in LMIC for two main reasons. Firstly, some disorders such as the haemoglobin disorders confer protection against malaria and so have selective advantage in populations where malaria is endemic; secondly higher rates of consanguineous marriage in some LMIC increase the rates of these disorders (increased chance that both parents carry the same recessive mutation).

Carrier screening for haemoglobin disorders

The haemoglobin disorders (thalassaemias and sickle cell disease) are particularly amenable to preconception screening as they are familial and are caused by a limited number of mutations. The majority of people with haemoglobin disorders are born in lower income countries, where lack of access to safe blood transfusions and

¹⁵ Galtier-Dereure F, Boegner C, Bringer J. *Obesity and pregnancy: complications and cost.* Am J Clin Nutr 2000; 71(5 Suppl):1242S-1248S.

expensive iron chelation therapy lead to the death of many patients with thalassaemia in childhood or adolescence.

Population-wide preconception carrier screening programmes for thalassaemia are in place in several countries including Iran, Sardinia, Cyprus, Saudi Arabia and Bahrain (see Appendix 3). In some countries carrier screening is a stand-alone programme, while in others it is integrated within wider reproductive health services. Carrier screening programmes have proved highly successful, reducing the birth rate for thalassaemia by 70-90%. Key features of these programmes include:

- Extensive educational campaigns to raise awareness of the condition and how it can be prevented. Target groups include healthcare workers, secondary school students and couples intending to marry
- Carrier testing may be carried out during adolescence but most programmes test couples intending to marry. One member of the couple is tested first, and only if he/she tests positive is the other member tested
- Carrier testing is accompanied by genetic counselling about reproductive risk. Carrier couples are free to marry if they wish to do so
- Successful programmes are characterised by effective organisation (often with centralised laboratory facilities serving regional/outreach clinics), agreed protocols and guidelines for all aspects of the programme; and procedures for laboratory accreditation, quality control, staff training, audit and evaluation.

Some other countries, for example Pakistan and India, target preconception screening at couples or communities where a family history of the condition and/or high levels of consanguinity suggest increased risk.

Carrier screening for G6PD deficiency

Preconception screening for glucose-6-phosphate dehydrogenase deficiency (G6PD) can in theory be undertaken through screening a couple for carrier status. However, there are difficulties in this approach due to the number of different alleles for the condition, lowering the sensitivity of the screening test. Bahrain is one of the few countries where screening for G6PD deficiency is currently incorporated within a screening programme for haemoglobin disorders.

Carrier screening for cystic fibrosis (CF)

Cystic fibrosis is an autosomal recessive condition caused by mutations in the gene that regulates CFTR – the cystic fibrosis transmembrane conductance regulator. The main feature of the disease is chronic pulmonary disorders, resulting in frequent lung infections, commonly starting in the first months of life. The pancreas may also be involved. The condition is only treatable to a limited extent and even with good medical care, average life expectancy is only 35 years. Prevalence varies in different ethnic groups, with 1 in 30 Caucasians, 1 in 60 Africans and 1 in 90 Asians being mutation carriers.

Preconception carrier screening for CF is available in some countries, either as a private or state-funded service, but it is rarely organised as a systematic programme. More often, carrier testing is targeted at couples who have a family history of the condition or where one member of the couple is known to be a carrier.

Carrier screening for Tay Sachs disease

Tay Sachs disease is an autosomal recessive condition that has a higher prevalence among the Jewish population of Ashkenazi origin (largely Eastern European origin). Tay Sachs disease is fatal in early childhood and there is currently no effective treatment or cure. Preconception carrier screening and prenatal screening programmes have been set up in Israel, parts of the USA, Australia, Canada and the UK. The Tay Sachs screening programmes have been very successful at decreasing the number of infants born with the disease.

Cost-effectiveness of interventions

An integrated preconception care programme developed in Hungary (see Appendix 1) resulted in reduced prevalence of congenital disorders and was inexpensive (US\$150 for a couple not needing referral to secondary services), though formal cost-effectiveness data are not available.

Preconception care that reduces the prevalence of particular congenital disorders has also been shown to be cost-effective, although many of the studies have been undertaken in high income settings and so may not be directly transferable to a low income setting. For example, in the United States, the cost of fortifying food with folic acid to help prevent neural tube defects is about US\$10 million, compared to an estimated cost of US\$400 million (including US\$158 million in direct medical expenditure) for treating the 500-550 cases prevented. In a review of cost-effectiveness studies for rubella vaccination in high income countries, all studies found that the intervention was cost-effective.

Also in the US, preconception care of women with diabetes was calculated to save US\$34,000 (1992 US\$) per care recipient as a result of fewer complications in pregnancy and childbirth, and lower incidence of congenital disorders.

What are the main ethical, legal and social issues to consider?

Autonomy and informed consent

Preconception care and screening are ideally carried out on a voluntary basis and with informed consent – in certain countries this is not the case.

In most Western countries, women or couples who are at high risk of having children affected by congenital abnormalities are nevertheless free to marry and to have children, as the value of individual autonomous choice is considered paramount. This may mean that they have greater choice in selecting a partner. However, in other countries and among some cultural groups, there may be a high value placed on obligations to family and society which may limit marital choice.

In high income countries there is often resistance to the genetic testing of children and adolescents on the basis that their future decision-making may be compromised by providing genetic testing before they are able to make a decision for themselves. However in countries where teenage pregnancy is common or where arranged

marriages are made based on the choice of couples made in childhood, it may be appropriate to undertake genetic testing earlier.

Attitudes to termination of pregnancy

Preconception care and screening may be particularly important in countries where abortion is illegal or unacceptable for religious reasons. In several countries, however, the availability of preconception services that enable couples to know their risk of having an affected child has led to pressure for laws to be changed so that abortion is allowed in cases of severe fetal abnormality.

Access to services

Efforts should be made to achieve equity of access to preconception care and screening. In some cases, specific targeting of services at disadvantaged groups may be justified if these groups are more likely to be exposed to environmental or behavioural risk factors. If women or couples with lower socioeconomic status do not know about services, or cannot afford or access them, their families may disproportionately bear the burden of preventable congenital abnormalities, further widening social inequalities.

Although programmes of preconception screening, particularly for genetic conditions, aim to reduce the birth prevalence of these conditions, it is important that high-quality services remain available and accessible for affected children.

Anxiety caused by screening

As parents become more informed, this may result in increased anxiety about a future pregnancy, especially where prospective parents were not formerly aware of potential risks. It is important to make the distinction between controllable and non-controllable risks.

Stigma and discrimination

Women (or men) who are identified by preconception care and screening programmes as carriers of recessive genetic conditions may encounter stigma and discrimination, or even become unmarriageable. For this reason the preferred option may be to test couples after marriage.

KEY REFERENCES

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RELATED TOPICS

Prenatal screening
Newborn screening
Congenital heart disease
Fetal alcohol spectrum disorder
G6PD deficiency
Haemoglobin disorders
Congenital hypothyroidism
Neural tube disorders
Teratogens
Consanguinity

APPENDIX 1 EXAMPLES OF PRECONCEPTION CARE INITIATIVES

Preconception care in Hungary

Hungary's Optimal Family Planning Service is a national service providing free peri-conception care delivered by specially trained nurses. The service is incorporated within primary care. The programme is a 3 stage process, with 4 visits.

- First stage: explanation of preconception care, consent for participation in the programme and check up examination. Couples or individuals at specific risk due to genetic disease risk or as a result of maternal disease referred to appropriate secondary care services
- Second stage: advice on optimum nutrition and physical exercise; on avoiding alcohol, smoking and unnecessary drugs; and on identifying and avoiding workplace hazards. Further medical examination and/or treatment undertaken if indicated by the initial check-up examination. Contraception discontinued. Menstrual history and measurement of basal body temperature used to detect hormonal dysfunction and to determine ovulation day
- Third stage: immediately after first missed menstrual period. Confirmation of pregnancy, and early pregnancy care (e.g. ultrasound scan, referral to prenatal services). Farewell visit at 10-12th week of gestation with discharge summary of peri-conception care. Pregnant women asked to send the last page of their completed health certificate at the end of the pregnancy which includes details of the pregnancy outcome.

Amongst those who had received the programme, there was a significant reduction in congenital abnormalities (20.6/1,000 newborns compared to 35/1,000) as well as other benefits such as early identification of fertility problems, reduction in the numbers of ectopic pregnancies and higher birth weights. Importantly, the majority of couples are positive about participation in the programme and efforts to involve male partners in preparation for conception help in developing attitudes of responsible fatherhood.

The Netherlands

In the Netherlands there have been a number of preconception care initiatives. For example, an outpatient preconception care clinic at the University Medical Center of Nijmegen evaluates potential pregnancy risk and preconception interventions for women referred by health professionals because of complicated obstetric history, a chronic illness or congenital abnormality in a previous child. A study in Nijmegen from 1996-2000 showed that preconception care in secondary health care helped to minimise risk factors such women.

Hong Kong and China

The 'pre-pregnancy preparation service' established and partly subsidised by the Family Planning Association of Hong Kong is a private scheme which includes medical testing, health assessments, counselling and information for couples planning a family. Couples are charged about US\$75 for a consultation and blood

test for HIV and other diseases. Every year 4-5,000 people use the service. In China before 2003 couples were required to undergo a medical examination before they were allowed to marry which included health education and mandatory HIV testing. This requirement was discontinued in 2003, resulting in a drastic reduction in the number of couples using this service.

The Philippines

In the Philippines, a multi-disciplinary team of doctors and nurse midwives travels to specified areas for 1-3 days per month and offers a service of screening pregnant women for a number of risk factors and non-pregnant women of reproductive age for chronic medical conditions. Family planning services are also provided.

Russia

The Russian Association of Gynaecologists and Obstetricians, in response to an alert that the state of maternal and child health was one of crisis proportion, have developed and implemented the People's Health Movement with the aim of promoting health throughout the stages of a woman's reproductive life. Preconception services inclusive of family planning have been developed.

Belgium

The Office de la Naissance et de l'Enfance has established a national preconception care campaign to educate all women of reproductive age and all health professionals involved in the care of women and children of the importance of preconception health care.

United States

CDC recommendations on preconception care

In the US the CDC along with 35 organisations that make up the Select Panel on Preconception care issued following recommendations for preconception care.

- **Recommendation 1.** Individual Responsibility Across the Lifespan. Each woman, man, and couple should be encouraged to have a reproductive life plan. The target population for preconception health promotion is women, from menarche to menopause, who are capable of having children, even if they do not intend to conceive.
- **Recommendation 2.** Consumer Awareness. Increase public awareness of the importance of preconception health behaviors and preconception care services by using information and tools appropriate across various ages; literacy, including health literacy; and cultural/linguistic contexts.
- **Recommendation 3.** Preventive Visits. As a part of primary care visits, provide risk assessment and educational and health promotion counseling to all women of childbearing age to reduce reproductive risks and improve pregnancy outcomes.
- **Recommendation 4.** Interventions for Identified Risks. Increase the proportion of women who receive interventions as follow-up to preconception risk screening, focusing on high priority interventions (i.e., those with evidence of effectiveness and greatest potential impact).
- **Recommendation 5.** Interconception Care. Use the interconception period to provide additional intensive interventions to women who have had a previous

pregnancy that ended in an adverse outcome (i.e., infant death, fetal loss, congenital disorders, low birthweight, or preterm birth).

- **Recommendation 6.** Pre-pregnancy Checkup. Offer, as a component of maternity care, one pre-pregnancy visit for couples and persons planning pregnancy. SPPC encourages the use of a broad definition of maternity care that includes the addition of a pre-pregnancy visit and the recommended prenatal and postpartum visits. The addition of this pre-pregnancy visit is an essential step toward improving pregnancy outcomes, particularly for those planning pregnancy.
- **Recommendation 7.** Health Insurance Coverage for Women with Low Incomes. Increase public and private health insurance coverage for women with low incomes to improve access to preventive women's health and preconception and interconception care.
- **Recommendation 8.** Public Health Programs and Strategies. Integrate components of preconception health into existing local public health and related programs, including emphasis on interconception interventions for women with previous adverse outcomes.
- **Recommendation 9.** Research. Increase the evidence base and promote the use of the evidence to improve preconception health.
- **Recommendation 10.** Monitoring Improvements. Maximize public health surveillance and related research mechanisms to monitor preconception health.

APPENDIX 2

AN EXAMPLE OF A PRECONCEPTION GENETIC SCREENING PROGRAMME

As in the case of integrated preconception care programmes, there are very few examples of integrated preconception genetic screening programmes encompassing a range of genetic disorders. An integrated programme exists in Bahrain.

Bahrain

Bahrain has high rates of haemoglobin disorders, G6PD deficiency, other autosomal recessive conditions and severe metabolic disorders. Low rates of unplanned pregnancy and pregnancy outside of marriage make preconception care easier to target in such societies.

In 2004 a law was issued mandating premarital screening and counselling for hereditary, sexually transmitted and other common diseases. There is a separate risk assessment for men and women who are asked about consanguinity, medical and surgical history, infection history including STDs, family genetic history, smoking, alcohol and drugs use, pregnancy readiness and past obstetric and contraception history if relevant. A physical examination is undertaken and a blood test taken which includes testing for haemoglobin disorders, G6PD deficiency, rubella antibodies and syphilis. Some individuals are also screened for HIV and hepatitis B. On a second visit the results are discussed and counselling and management is provided, including immunisation against rubella. An information booklet is given out which covers a broad range of topics relating to preconception care. At risk couples are then referred on to the genetic clinic. Although attendance is compulsory there is no compulsion to take the advice. In 2009 a review of those attending a premarital genetic clinic found that of 1,566 clients answering a questionnaire, 70% reported that the services were excellent.

APPENDIX 3

EXAMPLES OF HAEMOGLOBINOPATHY SCREENING PROGRAMMES

Thalassaemia screening in Iran

The cost of treating 15,000 patients for thalassaemia in Iran in 2000 was estimated by the WHO as being US \$200 million. Premarital carrier screening for thalassaemia is mandatory. Governmental and private laboratories are members of an accredited national professional laboratory network for thalassaemia screening, follow national screening protocols based on international guidelines, participate in quality control and attend regular educational courses.

Prospective couples are referred by marriage registrars (many of whom are clergy) to a designated local laboratory for premarital screening. The man's thalassaemia status is tested first and if he is a carrier, the woman's sample is tested. If both are carriers they are referred to a local designated health post for genetic counselling. The counselling team consists of a doctor and a professional with a degree in health studies. Those who marry after counselling are referred to their local health post or health house in rural areas for follow up until they have completed their family. Couples pay for their own screening test at a cost in 2004 of around US\$5. Over 90% of the population has governmental health insurance which covers the cost of prenatal testing and diagnosis.

The Government funds the planning and audit of the service and an extensive education programme. Classes about thalassaemia are held for high school students and young men doing military service and the judiciary is linked to the programme through annual meetings for marriage registrars.

By the end of 2001 over 2.7 million prospective couples had been screened and 10,298 at risk couples had been identified. After counselling about half went on to get married to each other. Preliminary data suggested a 70% reduction in the thalassaemia birth rate.

Another consequence of the programme was pressure for a change in legislation on abortion. A fatwah was given that allowed abortion before 18 weeks gestation when a fetus was diagnosed with thalassaemia and in 1998 there was a governmental decision to allow this, legalised through the Abortion Act in 2005.

In the evaluation of the thalassaemia screening programme in Iran, the most difficult, expensive and time consuming component of the programme was identified as the education of health workers and the community.

Targeted thalassaemia screening in Pakistan

Thalassaemias are the most common inherited single gene disorder in Pakistan, with about 5,250 infants being born with β thalassaemia major each year. The cost of treating one annual birth cohort of affected children for one year amounts to more than 4% of the health related expenditure of the government. As treated children

survive longer this could absorb almost half of the health expenditure. Although first trimester prenatal diagnosis is acceptable to many families at risk, access to prenatal diagnosis and termination of affected pregnancies is problematic.

The weak health care infrastructure of Pakistan does not allow population screening for thalassaemia and so an alternative approach has been suggested, based on the premise that gene variants are trapped within extended families, including the biradari (the tribe or sub-division of a tribe). The identification of an affected child is a marker of a group at high genetic risk.

In a study of 15 large families, 10 with a history of haemoglobin disorder and 5 without any history who acted as controls, screening for thalassaemia and abnormal haemoglobins was undertaken in 1,455 family members. In the control families, no carrier was found among the 397 individuals tested, while in the 10 families with an index case 183 of 591 people tested were carriers – 31%. 17 of the 214 married couples (8%) consisted of 2 carriers. All carriers reported that they had used the information provided in the testing and counselling process. Couples where both partners were carriers and who had 2 or more healthy children avoided further pregnancies and most couples with 1 or no healthy child used prenatal diagnosis. The results of this study suggest that targeted carrier screening may be a successful strategy to help families avoid the birth of affected children.

Six families who had an index case of a haemoglobin disorder declined testing to identify carriers. The reasons given were the difficulty in getting family members together for testing, a desire to avoid testing because the individuals were apparently healthy, and concern about possible stigma attached to being a carrier and potential problems in arranging marriages.

Targeted screening in India

It has been estimated that there are about 45 million carriers of β thalassaemia in India and about 15,000 infants affected by β thalassaemia are born every year, constituting about 10% of all those affected by thalassaemia worldwide. A study of premarital carrier screening in extended families where there was an index case of thalassaemia examined the carrier identification yield from three screening strategies: screening couples who had a family member affected by a haemoglobin disorder, testing individuals referred for anaemia investigation, and population based college student screening in a district with known high levels of thalassaemia carriers and cases. The yield of carriers from the extended family method was 78.2% of those tested, 19.5% of the anaemia patients tested and 4.0% of college students. The study also found that very few of the carrier couples did not go ahead with marriage plans, that couples subsequently presented earlier for prenatal diagnosis and that all couples who underwent prenatal diagnosis and had an affected fetus terminated the pregnancy.

Saudi Arabia

In Saudi Arabia a royal decree passed in 2003 requires that prospective marriage partners undergo screening for haemoglobin disorders followed by non-directive genetic counselling. The couple can then decide whether to marry. In 1990 a fatwa allowed the termination of pregnancy up to 120 days after conception if the fetus is

shown beyond doubt to be affected by a severe congenital abnormality that cannot be treated. Similar programmes exist in Bahrain, Jordan, the UAE and Tunisia.

Sardinia and Cyprus

Programmes in Sardinia have included a marked and extensive involvement of the population at large which has included mass media activities, posters, information booklets and lectures directed to community leaders as well as the general population. Meetings were held with physicians, especially paediatricians and obstetricians, family planning associations, nurses and social workers to inform them of the disease and the characteristics of the programme. Formal education on inherited anaemias has been introduced into the school curriculum. In Cyprus, the Orthodox Church contributed to the overall success of the programme by encouraging premarital carrier screening. In contrast, in Italy, the Catholic Church did not engage with the preventive campaign.

Evaluation of the programmes showed that it was important to organise adequate facilities for screening and prenatal diagnosis before the initiation of the educational campaign, so that demand for services can be met. Although carrier screening is voluntary, demand among young unmarried individuals is growing, suggesting increasing knowledge of how thalassaemia can be prevented. In Cyprus and Italy, screening of adolescent school children has been introduced.

For programmes in the Mediterranean regions where screening and counselling have been introduced, there has been a marked decline in the incidence of thalassaemia major. For example in Sardinia the incidence has declined from 1 in 250 live births to 1 in 4,000, corresponding to prevention of 94% of cases. When reasons for the residual cases were investigated, absence of information/misinformation was the reason for 67% of cases, false paternity for 13% and unacceptability of prenatal diagnosis of termination of pregnancy for 20%. An important factor in the success of the programme is that those being screened are informed of risks to relatives so that they too can be offered testing. This family based 'cascade' approach has led to the screening of 90% of the couples at risk in the population. This coverage has been achieved by screening only 11% of the population of child-bearing age.

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