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The essence of medical practice

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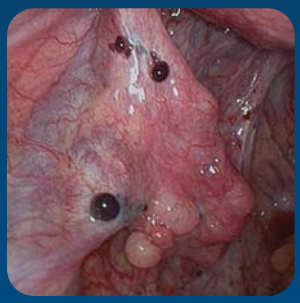

Infertility in women

Contents

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Editorial

Dear Doctor

We appreciate your continuous support, which has been very encouraging for us. The comments and queries from you regarding previous issues and the enthusiastic participation have brightened the overall scenario of Info Medicus!

We have tinted a budding issue "Infertility in women" as a review article. Down syndrome is common genetic disorder and it has been discussed in clinicians corner. In this issue we have also included Cystectomy with orthotopic neobladder; an option for giant leiomyoma of urinary bladder in case review.

Perioperative management of patients taking treatment for chronic pain we have selected for clinical review. Also we have other usual topics like clinical method where we have discussed emergency pericardiocentesis and in clinical focus we have stable angina.

We are looking ahead to your interpretation to help us improve our publication.

That's all for now and we would expect your cooperation as always.

Thanks and best regards,

(Dr. S. M. Saidur Rahman)
Medical Services Manager

(Dr. Rumana Dowla)
Manager, Medical Information & Research

Infertility in women

Female infertility

Infertility is the failure of a couple to become pregnant after one year of regular, unprotected intercourse. In both men and women the fertility process is complex.

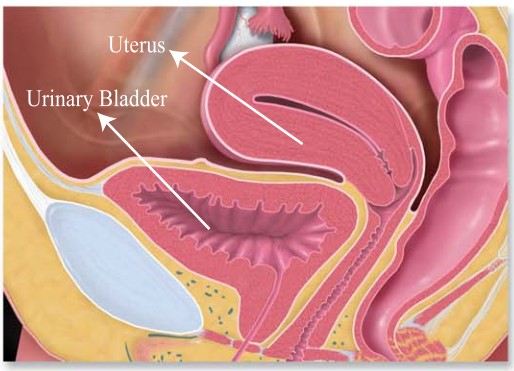
Although this report specifically addresses infertility in women, it is equally important for the male partner to be tested at the same time

Males and females each account for 40% of infertility. In the remaining 20%, either both partners are responsible or the cause is unclear. Although this report specifically addresses infertility in women, it is equally important for the male partner to be tested at the same time.

The female reproductive system

The primary structures in the reproductive system are as follows:

- The uterus is a pear shaped organ located between the bladder and lower intestine. It consists of two parts, the body and the cervix.
- When a woman is not pregnant the body of the uterus is about the size of a fist. During pregnancy the walls of the uterus are pushed apart as the fetus grows.
- The cervix is the lower portion of the uterus. It has a canal opening into the vagina with an opening called the os, which allows menstrual blood to flow out of the uterus into the vagina.



The female reporductive system

- Leading off each side of the body of the uterus are two tubes known as the fallopian tubes. Near the end of each tube is an ovary.
- Ovaries are egg producing organs that hold between 200,000 and 400,000 follicles. These cellular sacks contain the materials needed to produce ripened eggs, or ova.
- The inner lining of the uterus is called the endometrium, and during pregnancy it thickens and becomes enriched with blood vessels to house and support the growing fetus. If pregnancy does not occur, the endometrium is shed as part of the menstrual flow.

Reproductive hormones: The hypothalamus (an area in the brain) and the pituitary gland regulate the reproductive hormones. In women, following hormones serve as chemical messengers that regulate the reproductive system:

- Gonadotropin releasing hormone (GnRH)
- Follicle stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Estrogen, progesterone, and the male hormone testosterone are secreted by the ovaries at the command of FSH and LH

Risk factors

Age: As a woman ages, her chances for fertility decline. Infertility in older women appears to be mostly due to a higher risk for chromosomal abnormalities that occur in her eggs as they age.

Chances for pregnancy by age	
Age	*Fertility %*
Up until 34	90%
By age 40	Declining to 67%
By age 45	Declining to 15%

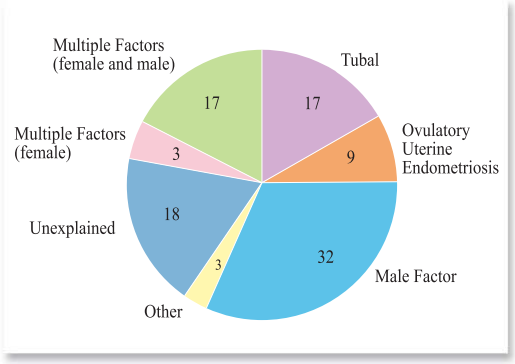
Weight factors and excessive exercise: Although most of a woman's estrogen is manufactured in her ovaries, 30% is produced in fat cells. Because a normal hormonal balance is essential for the process of conception, it is not surprising that extreme weight levels, either high or low, can contribute to infertility.

Being underweight: Body fat levels 10% to 15% below normal can completely shut down the reproductive process. Women at risk include the following:

- Women with eating disorders, such as anorexia or bulimia
- Women on very low calorie or restrictive diets are at risk, especially if their periods are irregular
- Strict vegetarians, if they lack important nutrients, such as vitamin B_{12}, zinc, iron, and folic acid
- Marathon runners, dancers, and others who exercise very intensely

Lifestyle factors

Smoking: Women who smoke one or more packs a day and those who started smoking before the age of 18 are at greater risk for infertility.



Risk factors for infertility

Caffeine: A correlation has been found between caffeine consumption and infertility, possibly because it has estrogen like effects. Caffeine is found not only in coffee but also in tea, many soft drinks, chocolate, and a number of common medications.

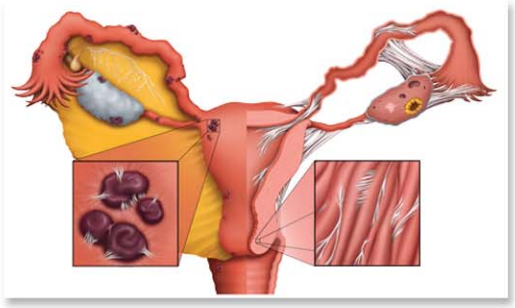
Alcohol: Even moderate alcohol intake (as little as five drinks a week) can impair conception and also have adverse effects on the developing fetus.

Sexual practices: Sexual practices such as having multiple partners, not using condoms, and having intercourse during a period increase the risk for sexually transmitted organisms that can cause pelvic inflammatory disease leading to infertility.

Stress: There is some modest evidence that stress can affect the outcome of fertility treatments. One interesting small study reported a significantly higher incidence of pregnancy loss in women who experienced both high stress and prolonged menstrual cycles.

Causes

Causes of infertility can be found in about 90% of infertility cases, but despite extensive tests, about 10% of couples will never know why they cannot conceive. Between 10% and 30% of cases of infertility have more than one cause. Male or female infertility each account for about 30% to 40% of cases.



Pelvic inflammatory disease (PID) is the major cause of infertility worldwide

Pelvic inflammatory disease: Pelvic inflammatory disease (PID) is the major cause of infertility worldwide. PID comprises a variety of infections caused by different bacteria that affect the reproductive organs, appendix and parts of the intestine that lie in the pelvic area. The sites of infection most often implicated in infertility are in the fallopian tubes, a specific condition referred to as salpingitis. PID may result from many different conditions that cause infections. Among them are the following:

- Sexually transmitted diseases (cause of most PIDs). Chlamydia trachomatis is an infectious organism that causes 75% of infertility in the fallopian tubes. Gonorrhea is responsible for most of the remaining cases.
- Pelvic tuberculosis
- Nonsterile abortions
- Ruptured appendix
- Herpes virus

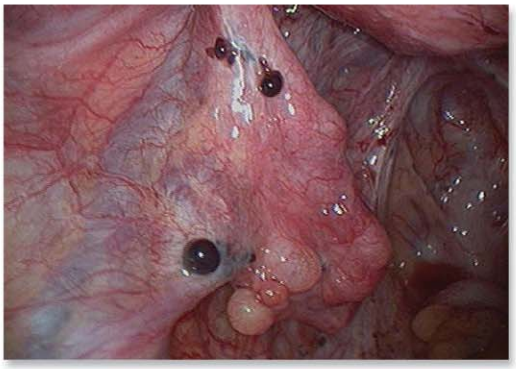
Premature ovarian failure: Premature ovarian failure (POF) is the early depletion of follicles before age 40, which, in most cases, leads to premature menopause.

The following conditions may produce POF:

- Adrenal, pituitary or thyroid gland deficiencies.
- Genetic factors related to the X chromosome. A woman needs two functioning X chromosomes for normal reproduction. When one is abnormal, ovarian function fails. The most severe example is Turner's syndrome, a genetic condition, in which one of the two X chromosomes is missing or malfunctioning. Milder cases of ovarian failure can occur in fragile X syndrome and other rare inherited conditions that cause partial X chromosome abnormalities.
- Autoimmune diseases including diabetes type 1, systemic lupus erythematosus, autoimmune hypothyroidism and autoimmune Addison's disease, are associated with a higher risk for early menopause.

Idiopathic hypogonadotropic hypogonadism: Idiopathic hypogonadotropic hypogonadism is a rare condition in which follicle stimulating hormone (FSH) and luteinizing hormone (LH) are underproduced and prevent the development of functional ovaries. There are no other abnormalities in the hypothalamus pituitary axis (such as tumors or abnormal stress hormones or prolactin). In most cases, the causes of hypergonadotropic hypogonadism are unknown. Genetic factors, including Kallman's syndrome, have been identified in about 20% of these cases.

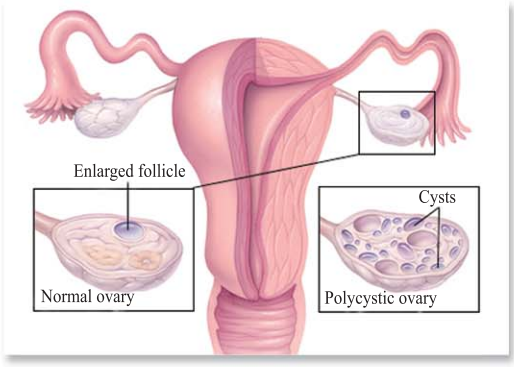
Endometriosis: The medical literature indicates that endometriosis may account for as many as 30% of infertility cases. Some evidence suggests that between 30% and 50% of women with endometriosis are infertile. Often, however, it is difficult to determine if endometriosis is the primary cause of infertility, particularly in women who have mild endometriosis. In an attempt to determine the chances for infertility with endometriosis, researchers have come up with a staging system based on findings during diagnostic surgery. Endometrial cysts may directly prevent infertility in a number of ways.



It is difficult to determine if endometriosis is the primary cause of infertility

- If implants occur in the fallopian tubes, they may block the egg's passage
- Implants that occur in the ovaries prevent the release of the egg
- Severe endometriosis can eventually form rigid webs of scar tissue (adhesions) between the uterus, ovaries and fallopian tubes, thereby preventing the transfer of the egg to the tube.

Polycystic ovarian syndrome: Polycystic ovarian syndrome (PCOS) is a condition in which the ovaries produce high amounts of androgens (male hormones), particularly testosterone. In PCOS, increased androgen production produces high LH levels and low FSH levels, so that follicles are prevented from producing a mature egg. Without egg production, the follicles swell with fluid and form into cysts. Every time an egg is trapped within the follicle, another cyst forms, so the ovary swells, sometimes reaching the size of a grapefruit. Without ovulation, progesterone is no longer produced, whereas estrogen levels remain normal.



Polycystic ovarian syndrome (PCOS) is a condition in which the ovaries produce high amounts of androgens

Functional hypothalamic amenorrhea and eating disorders: Functional hypothalamic amenorrhea (FHA) is the absence of menstruation due to disturbances in the thyroid gland and hypothalamus pituitary adrenal (HPA) system, which regulates reproduction and other important functions. The eating disorders anorexia and bulimia are most often associated with FHA.

Luteal phase defect: Luteal phase defect is a general term referring to problems in the corpus luteum that result in inadequate production of progesterone. Because progesterone is necessary for thickening and preparing the uterine lining, the ovum fails to successfully implant in the endometrium. Between 25% and 60% of women who experience recurrent miscarriages may have a luteal phase defect. A luteal phase defect, however, can also occur in fertile women, so other factors may be responsible for implantation failure.

Benign uterine fibroids: Benign fibroid tumors in the uterus are extremely common in women in their 30s. Large fibroids may cause infertility impairing the uterine lining, by blocking the fallopian tube or by distorting the shape of the uterine cavity or altering the position of the cervix. Some evidence suggests that even small fibroids may reduce the chances of pregnancy in women who are undergoing assisted reproductive techniques.

Elevated prolactin levels: Prolactin is a hormone produced in the pituitary gland that stimulates breast development and milk production in association with pregnancy. High levels of prolactin reduce gonadotropin hormones and inhibit ovulation. Hyperprolactinemia in women who are not pregnant or nursing can be caused by hypothyroidism or pituitary adenomas. These are benign tumors that secrete prolactin can cause headache and visual problems as well as breast secretions. Some drugs, including oral contraceptives and some antipsychotic drugs can also elevate levels of prolactin.

Structural problems causing obstruction: Inborn genital tract abnormalities may cause infertility. Mullerian agenesis is a specific malformation in which no vagina or uterus develops. Even in these cases, some women can become mothers by undergoing in vitro fertilization and having the fertilized egg implanted in another woman who is willing and able to carry the pregnancy. Uterine or Abdominal Scarring Bands of scar tissue that bind together after abdominal or pelvic surgery or infection (called adhesions) can restrict the movement of ovaries and fallopian tubes and may cause infertility.

Other causes

- Ectopic pregnancies
- Cancer treatments
- Medications
- Celiac sprue disease
- Epilepsy
- Thyroid problems
- Metabolic Syndrome, also called Syndrome X

Confirmation of diagnosis

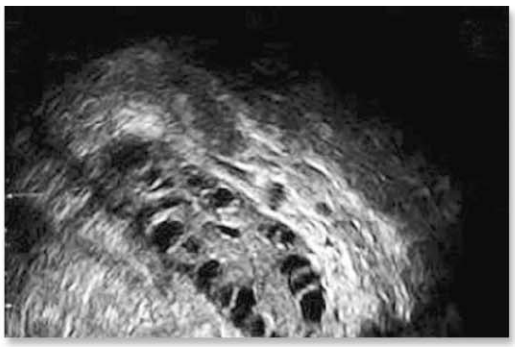
In any fertility work up, both male and female partners are tested if pregnancy fails to occur after a year of regular unprotected sexual intercourse. Fertility testing should be done earlier if a woman is over 35 years old or if either has known risk factors for infertility.

Medical history and physical examination: The first step in any infertility work up is a complete medical history and physical examination. Sexual technique and timing, menstrual history, lifestyle issues, any medications being taken and a profile of the patient's general medical and emotional health can help the physician decide on appropriate tests.

Imaging and other procedures

- Ultrasound and Sonohysterography
- Transvaginal sonohysterography
- Magnetic resonance imaging
- Hysteroscopy
- Hysterosalpingography
- Investigative tests to determine remaining eggs
- Genetic testing

Easy preliminary steps



Ultrasound of ovary

Before embarking on an expensive fertility work up, the following steps are free or low cost and can be helpful:

- Monitor basal body temperature. This is accurate in determining if ovulation is actually taking place.
- Take an over the counter urine test for detecting LH surges. This helps determine the day of ovulation.

Laboratory tests

A number of laboratory tests may be used for detecting the cause of infertility and for monitoring treatments:

Hormonal levels: Blood and urine tests are taken to evaluate hormone levels. Hormonal tests for ovarian reserve are especially important for older women. Examples of possible results include the following:

- High FSH and LH levels and low estrogen levels suggest premature ovarian failure or hypogonadotropic hypogonadism.
- High LH and low FSH may suggest polycystic ovary syndrome or luteal phase defect.
- High FSH and high estrogen levels on the third day of the cycle predicts poor success rates in older women trying fertility treatments.
- LH surges indicate ovulation.
- Blood tests for prolactin levels and thyroid function are also measured. These are hormones that may indirectly affect fertility.

Clomiphene challenge test: Clomiphene citrate (Clomid, Serophene), a standard fertility agent, may be used to test for ovarian reserve. With this test, the physician measures FSH on day 3 of the cycle. The woman takes clomiphene orally on the fifth and ninth days of the cycle. The physician measures FSH on the tenth day. High levels of FSH either on day three or day ten indicate a poor chance for a successful outcome.

Tissue samples: To rule out luteal phase defect, premature ovarian failure and absence of ovulation, tissue samples of the uterus can be taken one or two days before a period to determine if the corpus luteum is adequately producing progesterone.

Tests for autoimmune disease: Tests for autoimmune disease, such as hypothyroidism and diabetes, should be considered in women with recent ovarian failure that is not caused by genetic abnormalities.

General guidelines for treatments

Some authorities recommend that if a couple fails to conceive after one to two years during which unprotected sex has been sufficiently frequent, then they should consult a fertility expert. Women who are 35 or older, however, may want to begin exploring their options if they do not become pregnant within six months to a year.

Treatments by causes

Endometriosis treatments: Conservative surgery (typically laparoscopy) is the appropriate approach for restoring fertility. Assisted reproductive technologies (ART) may be helpful for women with late stage endometriosis.

Hyperprolactinemia treatments: Dopamine agonists, including bromocriptine or cabergoline. Surgery in some cases.

Luteal phase defect treatment: Clomiphene or superovulation agents (FSH agents or hMG).

Hypogonadotropic hypogonadism treatment: Fertility drugs (hMG preferable to FSH alone) with or without assisted reproductive technologies.

Pelvic inflammatory disease treatment: Screening high risk women for the presence of Chlamydia trachomatis and treating the organism before it causes symptoms could reduce the risk of PID by almost 60%. If any sexually transmitted infection is detected, both partners should receive antibiotics.

Polycystic ovarian syndrome treatment

- Lifestyle changes e.g. weight loss and exercise in women who are overweight.
- Metformin (Glucophage), a diabetes agents used to restore insulin response. This agent and similar ones used in diabetes are showing great promise in reversing symptoms, reducing male hormones and restoring regular menstrual cycles and ovulation in some women with PCOS.
- Clomiphene or superovulation agents (FSH agents or hMG) with or without assisted reproductive technologies (ART).
- Ovarian surgery e.g. a procedure called ovarian drilling, in which the surgeon opens 6 to 12 small holes in the ovary, is showing promise and reduces the risk for multiple pregnancies compared to fertility treatments.

Premature ovarian failure treatment: Assisted reproductive technologies with donor eggs.

Preserving fertility after cancer treatments: Removal and freezing (called cryopreservation) of ovarian tissue containing embryos or freezing immature and unfertilized eggs to use for later reimplantation.

Fallopian tubal blockage treatment: Surgical procedures like laparoscopy or salpingostomy to clear the tubes. Average pregnancy rate after salpingostomy is about 30% but they can vary widely.

Fertility drugs: Fertility drugs are often used alone as initial treatment to induce ovulation. If they fail as sole therapy, then they may be used with assisted reproductive procedures or artificial insemination to produce multiple eggs, a process called superovulation. There are drugs like:

- Clomiphene
- Gonadotropins and GnRH agonists
- Human menopausal gonadotropins (hMG)
- FSH
- Urofollitropin
- Human Chorionic gonadotropin (hCG)
- GnRH analogs (Agonists or Antagonists)

Assisted reproductive technologies (ART)

Assisted reproductive technologies (ART) are procedures that either place sperm inside the woman or uses donated eggs or employ techniques that retrieve eggs from the ovary and reimplant them. Fertilization may occur either in the laboratory or in the uterus. The standard ART procedures are generally called artificial insemination (AI) and in vitro fertilization (IVF).

Artificial insemination

Artificial insemination (AI) it is the least complex of the assisted reproductive technologies and is often tried first in uncomplicated cases of infertility. AI either involves placing the sperm directly in the cervix (called intracervical insemination) or into the uterus (called intrauterine insemination, or IUI). IUI is the standard AI procedure.

It is useful under the following circumstances

- When the woman's cervical mucus is unreceptive
- When donor sperm are required
- If the man's sperm count is very low
- When unexplained infertility exists in both partners

Those in whom AI fails, couples with specific fertility defects, or when the woman is older may be candidates for more advanced reproductive technologies.

Standard in vitro fertilization (IVF)

The best candidates for IVF are women with damaged fallopian tubes and some experts believe it is a better option than attempting surgical repair. IVF is also used when infertility is unexplained or when the male partner has the infertility problem. A typical IVF procedure is as follows:

- At first superovulation is induced using fertility drugs so that several eggs can be harvested from the ovary before they have been released from the follicles.
- To harvest eggs, the physician generally inserts a probe into the vagina and is guided by ultrasound. A needle is then used to drain the liquid from the follicles, and several eggs are retrieved.
- The eggs and sperm are combined in a Petri dish. Between 48 to 72 hours later the eggs are usually fertilized.
- The resulting embryos are reimplanted into the woman's uterus.
- It takes about two weeks to determine if the process is successful.

Complications of assisted reproductive technologies

- Higher rates of cesarean sections
- Multiple births
- Low birth weight
- Higher mortality rates
- Higher risks for later lung and heart problems
- Higher risk for mental retardation or learning disabilities

Risks to the woman: Studies suggest that there is a significantly higher risk for Caesarean sections (41.9% to 71.4%) after ART. There may also be a higher risk for urinary tract infections before delivery. In women using donor sperm from sperm banks, rare cases of AIDS, hepatitis, and other sexually transmitted diseases from infected sperm have been reported.

Risk for birth and genetic defects in children: Several major studies have now reported a higher risk for low birth weight and birth defects in children born from assisted reproductive technologies. Low birth weight, in any case, is a well known complication of multiple births, which are common with ART. However, even for single newborns delivered at term, 6.5% were underweight, compared to 2.5% in the general population. Another study found that 9% of children conceived with ART had major birth defects, including cleft lip or palate or problems with the feeding tube or windpipe, compared to 4.2% of babies conceived naturally. Birth defect rates were higher for single or multiple births as well as for births that reached term. Still, ART remains a good option for many infertile couples.

Reference

1. American Society for Reproductive Medicine (www.asrm.com)

2. The Endometriosis Association (www.endometriosisassn.org)

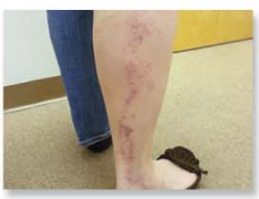
DERM DILEMMA

CASE 1

A 76 year old white woman requests consultation because of a growth on her chin. She states that a dark "spot" had been present at the site for "quite some time," but the duration of the current elevation is only about 2 to 3 months. She denies bleeding or discomfort. She was recently diagnosed with cirrhosis secondary to chronic hepatitis. Examination reveals a crusted nodule abutting a deeply pigmented macule. Gentle removal of the crust yields a smooth, pink surface. No atypical lesions are noted elsewhere. Cervical lymph nodes are nonpalpable.

What is your diagnosis?

CASE 2

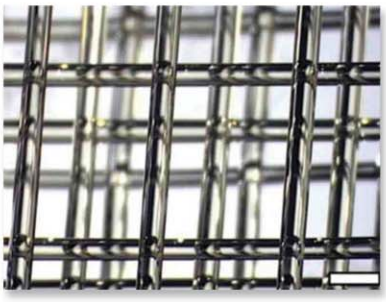


A 38 year old white woman complains of a rash affecting her right leg. The dermatitis first became apparent several months ago and has rapidly progressed. She describes moderate to severe pruritus that has not been relieved by treatment with topical hydrocortisone cream. She denies the presence of systemic disease and is on no medications. Examination reveals a fairly linear dermatitis of the affected leg extending from her ankle to the popliteal fossa. No similar eruption is noted elsewhere.

What is your diagnosis?

Reference: Eme. Med. June 2012, Vol. 44, No.6:11-12

Answers 17

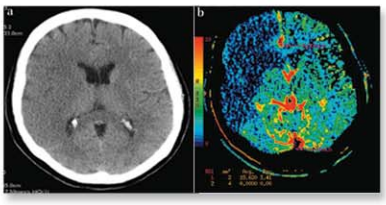


3D printed sugar network to help grow artificial liver

Researchers have moved a step closer to creating a synthetic liver, after a researcher team created a template for blood vessels to grow into, using sugar. Scientists have long been experimenting with the 3D printing of cells and blood vessels, building up tissue structure layer by layer with artificial cells. But the synthetically engineered cells often die before the tissue is formed. The technology, in which a 3D printer uses sugar as its building material, could one day be used for transplants. Sugar is a very nice material that can be dissolved away in the presence of living tissue, it's very friendly to biological tissue. The body's cardiovascular system i.e. blood vessels solves this issue with natural cells and tissues. So a group of scientists are building a synthetic vascular system that would serve the same purpose by creating a place where the future artificial blood vessels would be located. The network is surrounded with the cells that to be fed by the blood vessels when the tissue is implanted and once having this structure of pipes to be and tissue, dissolve away the sugar using water. Although the researches did not do any implantation, they said they had wanted to demonstrate that it was possible to build the thicker tissue that could be fed by this network of pipes and this way, to create a full organ in future.

More genetic links to osteoarthritis uncovered

Osteoarthritis is the most common form of arthritis, affecting about 40% of people over the age of 70. Scientists have discovered another eight pieces of genetic code linked to osteoarthritis, bringing the total number to 11. Inherited factors account for at least half of any individual's chance of developing this common condition that affects the joints. And understanding these factors could offer up new treatments. The research compared the DNA of osteoarthritis patients with that of 11,000 healthy volunteers. This allowed scientists to find the most promising "culprit" regions of the genetic code to study in more detail. Researchers at Newcastle University confirmed the three previously reported gene variants and found a further eight linked to osteoarthritis. The one with the strongest effect was situated in the region of the GNL3 gene which produces a protein with an important role in cell maintenance. Three others were in DNA regions involved in the regulation of cartilage, bone development and body weight. Osteoarthritis runs in families and that this is due to the genes that people pass on, rather than their shared environment. Genetic regions are the major risk factors for developing osteoarthritis.



New brain scanner helps paralyzed people spell words

A new brain scanner has been developed to help people who are completely paralyzed speak by enabling them to spell words using their thoughts. It uses functional magnetic resonance imaging (fMRI) to help patients choose between 27 characters the alphabet and a blank space. Each character produces a different pattern of blood flow in the brain and the device interprets these patterns. The new technology is based on earlier applications of the technique, which used free letter spelling to allow people to answer the equivalent of multiple choice questions with just a few possible answers. British neuroscientist Adrian Owen, for instance, used fMRI to help a man believed to have been in a vegetative state for five years to answer "yes" and "no" questions by interpreting his brain activity. But the new scanner uses the entire English alphabet and the blank space. This novel spelling device constitutes an alternative approach to motor independent communication. This noninvasive device requires only little effort and pretraining, it is immediately operational and possesses high potential for clinical applications, both in terms of diagnostics and establishing short term communication with non-responsive and severely motor impaired patients.

Reference: bbc.co.uk

The triple test as a screening technique for Down syndrome

Introduction

The triple test is one of a range of screening tests that are used to identify pregnant women whose fetus is likely to be affected by trisomy 21 (Down syndrome) and who should then be offered a diagnostic test. All of the tests similar to the triple test are based on the same mathematical principle (Bayes theorem) and work by combining a prior probability derived from maternal age at expected date of delivery with a likelihood ratio usually based on two multivariate Gaussian distribution functions.

Down syndrome facies

This combination results in a reasonably accurate risk estimate of the probability that the fetus has Down syndrome. Women whose risk exceeds a specified cutoff are then offered a diagnostic test (ie, amniocentesis or chorionic villus biopsy), which allows a cytogenetic diagnosis to be determined. This may be done either by cell culture and karyotyping or by fluorescent in situ hybridization (FISH). The triple test is used only in the second trimester of pregnancy and now has a range of competitors (Table 1). As one of the first entrants into the serum screening arena, it is therefore legitimate to question whether it remains relevant more than 20 years after it was developed. There are a number of factors that affect the decision about which screening test to use: screening test effectiveness; coste ffectiveness; cost benefit/cost hazard.

How reliable are screening protocols?

When screening, reliability is measured by assessing the effectiveness of different screening protocols by measuring the detection rate and corresponding screen positive rate.

To allow comparison, it is usual to fix the screen positive rate and assess the detection rate using a computer model rather than gleaning this directly from patient data. Different studies generate different basic data sets and modeling can generate controversy over the value of different protocols. The original description of the triple test estimated that adding unconjugated estriol to a double test increased the detection rate from 55% to approximately 60% for a 5% screen positive rate. A later estimate claimed that for ultrasound-dated pregnancies, the double test had a detection rate of 58% and the triple test 67% for a screen positive rate of 5% and suggested that without ultrasound there was only a 4% difference in detection rates between the two tests. In the early days of Down syndrome screening, it was often felt by laboratory managers that the slight increment in detection was not worth the extra reagent and staff costs, leading them to option for the double test.

Table 2 shows estimates of detection rates at specific screen positive rates for different screening strategies and makes it clear that the triple test is now outclassed by other test variations.

Table 1: Strategies for antenatal Down syndrome screening

Test name	Used in	Analytes
Double test	Second trimester	AFP + hCG (total or free-β)
Triple test	Second trimester	As double test + unconjugated estriol
Quadruple test	Second trimester	As triple test (using free-β hCG) + inhibin-A
Combined test	First trimester	Ultrasound measurement of NT + PAPP-A + free-β hCG
Serum integrated test	Both first and second trimester	PAPP-A (first trimester) + quadruple test (or triple test)
Integrated test	Both first and second trimester	As serum integrated test + NT in first trimester
Contingent test	Both first and second trimester	Dependent on structure of contingent screen chosen

Logical choices and consumer behavior

The triple test is, thus, no longer the most effective screening test for antenatal Down syndrome and consequently many national guidelines recommend other screening tests instead. In practice, however, it is still in common use, at least in the United Kingdom (UK). There must, therefore, be other factors that influence choice of screening tests to use.

Table 2: Detection rates for different antenatal Down syndrome screening strategies from the SURUSS study

Test name	DR @ SPR = 1%	DR @ SPR = 3%	DR @ SPR = 5%
Double test (using free-β hCG)	46%	63%	71%
Triple test (using free-β hCG)	56%	70%	77%
Quadruple test (using free-β hCG)	66%	79%	84%
Combined test	66%	78%	83%
Serum integrated test	77%	86%	90%
Integrated test	84%	91%	93%

Over the last 10 years in the UK, the triple test was the test routinely offered. It would be logical to expect there would be a move to the quadruple test because this would allow improved detection and lower screen positive rates without the need to redesign the way in which patient services were provided. This did not occur, partly because the only commercially available assay for inhibin-A (the fourth analyte in the quadruple test) was not suitable for use in a routine laboratory because it was insufficiently stable and the intrabatch assay variation was excessive (coefficient of variation [CV], 17%). This lead to an excessively high screen positive rate when compared with the computer simulation models of quadruple screening. Consequently, although superior in a research setting, the quadruple test was not practical for use in a routine laboratory. More recently, the inhibin assay has been automated, leading to substantial improvement in performance. In the UK, this has not resulted in wide uptake of the extra test. Another reason for the reluctance to add extra tests is the law of diminishing returns meaning as each extra analyte is added to the basic double test the incremental improvement in detection rate is less. Furthermore, there is a tendency for the newer tests to be more expensive so the cost benefit equation becomes harder to justify. In the UK National Health Service (NHS) centrally funded health service model, it is difficult to persuade the commissioners to pay yet more for a tiny improvement in a screening program when there are pressing health needs that must be addressed elsewhere. Yet another factor was consumer behavior. In the UK, the standard service provided by the NHS was the second trimester triple test.

One of my roles is the Director of Prenatal Screening for the South Yorkshire Sub regional Down's Screening Program run by the laboratory of the Northern General Hospital, Sheffield. It was obvious from the pattern of cytogenetic reports in our regular audit meetings that a significant proportion of patients were exercising their consumer choice and paying for private first trimester screening because they wanted to know the result earlier than would be possible under the NHS scheme. This trend is reversing, as first trimester screening is now provided in the Sheffield NHS screening program. Since patients wanted earlier screening, it was clear that first trimester screening had to be made available with all of the consequent changes to the antenatal care package that this introduction process entailed.

Clearly, women did not choose the first trimester test on the basis of effectiveness, cost effectiveness, and cost benefit/ hazard ratios. Rather, an ultrasound test is far more personally interactive and, in addition to allowing the first view of the baby, gives an immediate answer as to whether the baby has any major problems. It is, therefore, entirely understandable that first trimester testing was popular with patients.

Here, there were good practical reasons why the integrated test was not introduced. For instance, the integrated test uses information collected in both trimesters of pregnancy and requires a wait until all of that data has been collected before calculating the risk estimate.

This means there is the need to ensure that women attend on more than one occasion for the screening test to be performed, increasing the risk of drop out when appointments are missed. Furthermore, there is a delay during which information that may allow an early diagnostic test to be carried out is withheld. This delay has been criticized as being ethically unacceptable. An alternative method that was suggested to avoid the ethical objections to the integrated test was the contingent screen. In this test, the first trimester screening results were revealed and those at very low risk were excluded from the next stage while those at very high risk were offered a diagnostic test. Those in the middle were offered a second stage test in the second trimester and, depending on the result, were offered a diagnostic test. A trial of the acceptability and effectiveness of a contingent screen found that 16.7% of women booked too late to be offered the first trimester stage of the process, but the majority of women entering the screening process completed it, thereby proving that fears of high dropout rates were unfounded Most women were happy to be offered contingent screening.

Alternative screening tests

Fetal cells in maternal blood

Many years before the introduction of Down syndrome screening, it was discovered that fetal cells could be identified in the maternal circulation and used to identify fetal gender. After the introduction of Down syndrome screening, a great amount of effort was made to develop extraction methods that would allow fetal cells to be purified from maternal blood, which would allow noninvasive prenatal diagnosis. As a result, dozens of research teams worked on projects to extract erythroblasts, leukocytes, trophoblasts, etc. Unfortunately, while fetal cells have been successfully extracted in a research setting, this process has not been introduced into routine practice.

Cell free DNA in maternal serum

In 1997, the presence of cell free fetal DNA in maternal serum was identified. This was thought to offer another prospect for noninvasive prenatal testing. Thirteen years later, methods for antenatal rhesus typing and fetal gender have been described. A routine application for RhD typing has been tested and proven to be effective. Experimental methods for using this technology for Down syndrome testing have been reported and include: single nucleotide polymorphism allelic ratios; circulating placental messenger ribonucleic acid (mRNA) analysis and epigenetic-genetic chromosome dosage. It is worth noting that these experimental methods are mostly all described by the same research group, however. Thus, 13 years after this method for screening was developed, no routine application for an euploidy detection has yet been described. Therefore, it only took two years of research indicating that antenatal serum screening for Down syndrome could be effective before the technique was introduced as a routine screening test. Cell free DNA was identified 13 years ago and, although several techniques to allow it to be used for diagnosis have been described, none have been taken into routine use. We cannot, therefore, predict whether serum DNA will ever become a routine test: To become accepted, it has to supplant already established tests and the technical difficulties associated with amplification based testing (which makes sample purity/ lack of contamination vital) must be overcome. Finally, there are ethical implications of DNA and RNA testing which must be considered.

Conclusions

As the years have progressed, it has been superseded by newer variations (eg, first trimester combined testing and the quadruple test), which have been recommended in national guidelines, not because the triple test has been unreliable, rather because the other tests have proven more effective in terms of greater detection with lower screen positive rates. The triple test remains relevant because it is the foundation upon which current antenatal screening tests for Down syndrome are rooted. It is also important because of the ethical dilemmas it creates. Most countries currently allow their citizens to have reproductive autonomy but the introduction of Down syndrome screening has lowered the barriers to other forms of genetic screening tests. It becomes possible that reproductive autonomy may be threatened by economic factors that may favor compulsory screening. Thus, Down syndrome screening will continue to be controversial for many years to come.

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Cystectomy with orthotopic neobladder; an option for giant leiomyoma of urinary bladder

A 47 year old female presented with obstructive and irritative voiding symptoms and hematuria for last 3 years. On examination the patient had gross pallor and palpable suprapubic lump. Ultrasonography revealed a large hyperechoic mass with bilateral hydroureteronephrosis. There were multiple echogenic masses in uterus suggestive of fibroids. CT scan revealed heterogeneously enchancing polypoidal soft tissue mass inside the bladder lumen with diffuse thickening of bladder wall with an exophytic component which was inseparable from the uterus and extending into the left adnexa with dilated uterine cervix [Figure - 1], [Figure - 2]. On cystoscopy tumor was broad based and was arising from the trigone and the posterior wall of bladder but ureteric orifices were free of tumor. TUR biopsy was done which showed features of Leiomyoma. Patient underwent cystectomy and hysterectomy with orthotopic neobladder using ileum. Postoperative course of the patient was uneventful and she was discharged on CIC. Patient is doing fine and voiding on her own eight months postoperatively.

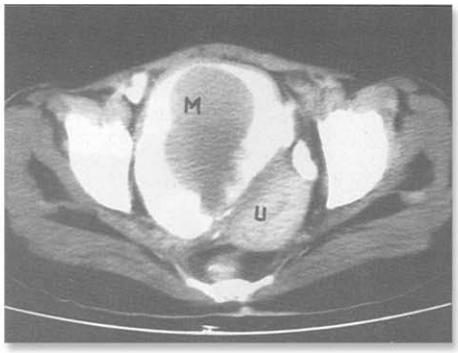

Fig 1: CT section showing enlarged uterus with fibroid (UF) with loss of planes between it and bladder

Comments

Leiomyoma of urinary bladder though rare, yet is the most common benign mesenchymal tumor of the urinary bladder and accounts for less than 0.43% of all bladder tumors. Though most common site is kidney capsule, it can occur anywhere in the genitourinary system.

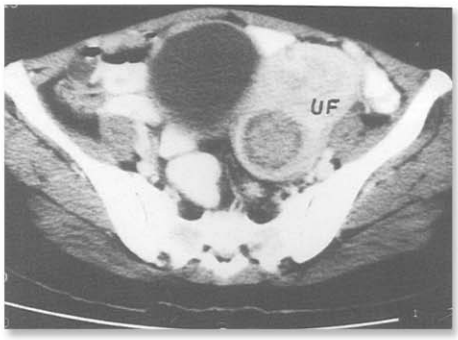

Fig 2: CT section showing broad base intraluminal mass (M) in urinary bladder with adjacent uterus (U). Fat plane between two is not well appreciated

Clinical Presentation and Diagnosis

Most of leiomyomas are asymptomatic and incidentally detected on routine gynaecological examination. Patients with leiomyoma present with variety of symptoms depending upon location of the tumor. Hematuria is not a common symptom but occurs when tumor outgrows the blood supply as in present case. 39% patients have concomitant uterine fibroids and 50% of these tumors were palpable on bimanual examination. On ultrasonography, leiomyoma appears smooth walled lesion with numerous internal echoes and homogenous echotexture. There can be presence of concomitant fibroids uterus and when these tumors are obstructive, hydro-ureteronephrosis may be seen. Ultrasonography has been found to be superior than IVU in diagnosis, localization and measurement of leiomyomas.

On CT scan, these tumors appear smooth filling defect with attenuation values of 25-50 Hounsfield units. On MRI, leiomyomas give an intermediate intensity on T1 weighted images giving good contrast between it and low intensity of the urine. On T2 weighted images it gives foci of high and low intensity along with good contrast between the tumor and intermediate bladder muscle making extravesical spread determination easy.

Treatment

Growth of leiomyoma is not an indication for surgery as risk of developing leiomyosarcoma is only 0.27% as compared to a risk of 0.23% in leiomyoma of stable size. Various parameters are used in determining the type of surgery like size, site, extent of lesion and involvement of sphincters or ureters. In general smaller lesions are managed by transurethral resection (TUR) with low re-operation rates while larger lesions require open surgery, varing from a simple enucleation, partial cystectomy to cystoprostatectomy with reconstruction of bladder. Enucleation of large trigonal leiomyomas is described which gives a good surgical outcome but tumor involving full thickness of bladder wall are not suitable for transurethral resection even if they are small. More so, even after complete enucleation, tumor recurrence has been reported with this concern and presence of deep seeded broad base tumor at the trigone in the present case, decision of cystectomy with orthotopic continent diversion was taken. On 8 months of follow up the patient is doing fine, who otherwise would have had uncertain outcome with conservative treatment.

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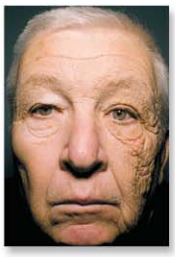
2. Arch Esp Urol 1995;48:987-90

Digital Mucous Cyst

A 37 year old man presented with an 8 month history of a solitary, round, asymptomatic nodule on his second toe. The dome shaped, fluctuant nodule measured 6 mm in diameter and was located off the midline on the dorsal side of the second toe, between the interphalangeal joint and the proximal nail fold (Panel A). Polarized light dermoscopy without compression (Panel B) revealed a flesh colored lesion with superficial telangiectasias. The lesion turned more translucent with compression (Panel C), and bright white structures, characteristic of lesions with increased collagen when viewed under polarized light could be visualized. The appearance was consistent with a digital mucous cyst. Digital mucous cysts are benign ganglion cysts of the digits, typically located at the distal interphalangeal joints or in the proximal nail fold. They may be associated with osteoarthritis, but this was not present in this patient. The cysts usually occur on the hands, although they have also been noted on the toes, as in this case. The cause of these cysts is uncertain but may involve mucoid degeneration of connective tissue. Often, as in this case, such cysts are asymptomatic and do not require treatment.

Reference: N Engl J Med April 5, 2012; 366;14: 1335

Unilateral Dermatoheliosis



A 69 year old man presented with a 25 year history of gradual, asymptomatic thickening and wrinkling of the skin on the left side of his face. The physical examination showed hyperkeratosis with accentuated ridging, multiple open comedones and areas of nodular elastosis. Histopathological analysis showed an accumulation of elastolytic material in the dermis and the formation of milia within the vellus hair follicles. Findings were consistent with the Favre Racouchot syndrome of photodamaged skin, known as dermatoheliosis. The patient reported that he had driven a delivery truck for 28 years. Ultraviolet A (UVA) rays transmit through window glass, penetrating the epidermis and upper layers of dermis. Chronic UVA exposure can result in thickening of the epidermis and stratum corneum as well as destruction of elastic fibers. This photoaging effect of UVA is contrasted with photocarcinogenesis. Although exposure to ultraviolet B (UVB) rays is linked to a higher rate of photocarcinogenesis, UVA has also been shown to induce substantial DNA mutations and direct toxicity, leading to the formation of skin cancer. The use of sun protection and topical retinoids and periodic monitoring for skin cancer were recommended for the patient.

Reference: N Engl J Med April 19, 2012; 366; 16:e25

Info Quiz Participants

- Have you selected the correct answer (s) You still have time to put your entry submission together for Info Quiz Prize
- The closing date for entries is 15 November 2012
- We look forward to receiving your winning entry

Info Quiz Answers
July-September 2012

1. e	2. c	3. b	4. c	5. c
6. b	7. b	8. c	9. c	10. d

Perioperative management of patients taking treatment for chronic pain

The British Pain Society defines chronic pain as pain that is continuous for more than 12 weeks or (if the pain followed trauma or surgery) is longer than the time the healing would have been expected to take. The presence of preoperative pain and high anxiety have been validated as predictors for early postoperative severe pain. Therefore, an inadequately managed patient with chronic pain risks experiencing severe postoperative pain. Providing effective analgesia is complicated by omission of regular medications owing to preoperative fasting, potentially leading to worsening of symptoms or development of withdrawal syndromes, while the prescription of additional medications perioperatively can increase the likelihood of side effects and drug interactions. We discuss the management of the drug and interventional treatments for chronic pain syndromes that the nonspecialist may encounter in the perioperative hospital setting.

What should a preoperative assessment cover?

A preoperative assessment is an opportunity to evaluate the patient and develop a perioperative management plan (box 1). The fundamentals are the same for any preoperative assessment, but some areas specific to the patient with chronic pain need a more focused approach. In this article we discuss the management of the following patient groups who may attend a preoperative assessment clinic:

- Patients taking regular potent analgesics, antidepressants, or antiepileptics who will be fasting for more than 24 hours
- All patients taking oral ketamine or methadone
- Patients with an implanted drug delivery system or spinal cord stimulator
- Patients anxious about the postoperative control of their acute surgical and background chronic pain
- Patients with a history of opioid addiction

Box 1 | Treatments for managing patients with chronic pain

Drugs

- Analgesics: paracetamol, non-steroidal anti-inflammatory drugs, opioids, methadone, ketamine, tramadol
- Antidepressants: Tricyclics, selective serotonin reuptake inhibitors, and selective noradrenaline reuptake inhibitors
- Anticonvulsants: Gabapentin, pregabalin, carbamazepine, oxcarbazepine, sodium valproate, lamotrigine, phenytoin
- Others: Baclofen, cannabinoids, lidocaine 5% patch, capsaicin cream

Interventional techniques

- Intrathecal drug delivery system
- Spinal cord stimulator

Other treatments

- Physiotherapy
- Psychology (cognitive behaviour therapy)
- TENS (transcutaneous electrical nerve stimulation)
- Acupuncture

To understand a person's chronic pain it is necessary to take a history of the pain, in particular recording the patient's current medications used for pain control and the daily intake of opioids or other drugs used. This questioning enables assessment of the patient's potential tolerance to opioids and allows drug interactions or side effects to be anticipated. Identify exacerbating and/or relieving factors for the pain and the use of adjunctive therapies, so that they can be avoided or used perioperatively. It is important to involve patients in management decisions.

How do we manage patients with chronic pain who are taking regular opioids?

A patient's routine opioid regimen will not provide sufficient analgesia for acute postoperative pain. In such patients, a doubling or quadrupling of the morphine dose appropriate for an opioid naive patient having the same procedure may be needed. Although potential complications, such as sedation and respiratory depression, are indeed dose dependent, long term users of opioids are often tolerant to such effects. Recent reviews show that patients using transdermal pain patches (such as fentanyl or buprenorphine) can continue with these throughout the perioperative period.

Box 2 | Strong opioids available and used in patients with chronic pain

Oral
- Morphine: Solutions, tablets, modified 12 hour release, modified 24 hour release
- Oxycodone: Also modified release, modified release with naloxone
- Tramadol: Also 12 and 24 hour modified release
- Fentanyl: Tablets, lozenges
- Methadone: Liquid and tablets
- Ketamine

Transdermal
- Fentanyl patches
- Buprenorphine

Sublingual
- Fentanyl
- Buprenorphine

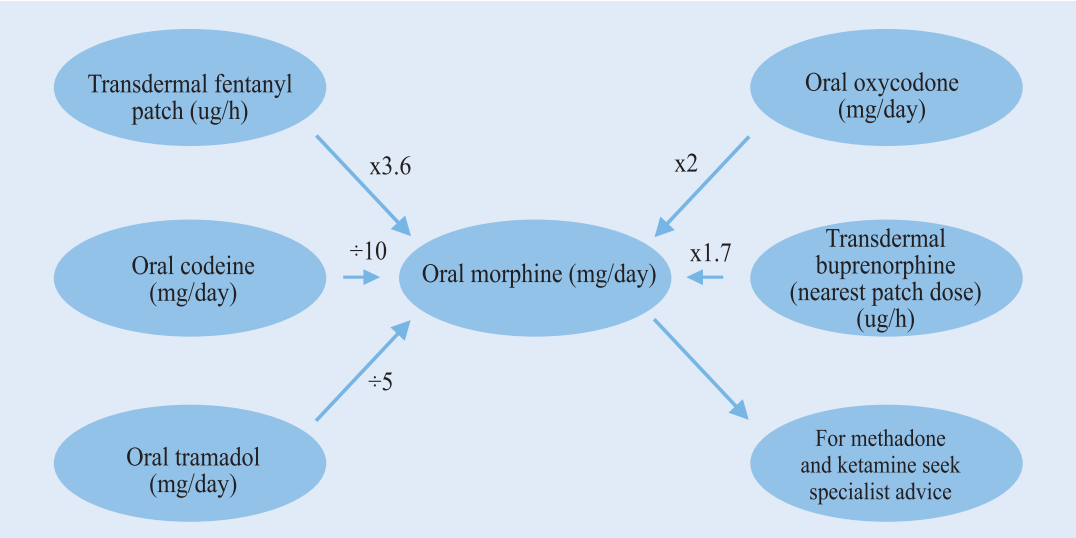
Intranasal
- Fentanyl

Intrathecal (via implanted pump reservoir)
- Morphine
- Fentanyl
- Hydromorphone
- Diamorphine (usually in combination with local anaesthetic)

However, opioid patches are not licensed for acute post operative pain and should not be titrated in an effort to achieve this. Pharmacokinetic models have shown that drug absorption increases with a rise in skin temperature, so monitor patients with fever for side effects from opioids. Patients taking long acting oral opioids can continue taking them up to and including the morning of surgery, restarting them as soon as possible after surgery. Certain circumstances, commonly perioperative fasting, necessitate prolonged cessation of patients' usual oral medication, with opioid medication having to be continued parenterally. This can be complex but is manageable using dose conversion charts: the patient's regular opioid medications are converted into a single total daily oral morphine equivalent dose. This equivalent dose can then be converted to a daily parenteral dose. Equivalent doses of strong opioids cannot be exact and are therefore only a guide; because of cross tolerance, published recommendations suggest starting at 50% of the equianalgesic dose when moving from one opioid to another.

How do we manage antidepressants?

Thirty five percent of adults who present for surgery are taking antidepressants and although most are being treated for mental health disorders. Pain practitioners use low dose tricyclic antidepressants, selective serotonin reuptake inhibitors and selective noradrenaline reuptake inhibitors as first line treatment in many neuropathic pain conditions. Although newer antidepressants reportedly have better side effect profiles and tolerability, a clinical review highlighted a potential association between selective serotonin reuptake inhibitors and perioperative bleeding. Also, patients receiving serotoninergic antidepressants risk developing serotonin syndrome, with the risk increasing when co-administered with tramadol.



Clinical features may not present until after surgery and include tremor, agitation, myoclonus, hyperthermia and hypertension. With these concerns, it could be argued that antidepressants should be stopped perioperatively. However, Kudoh et al showed in a randomised study that the perioperative cessation of selective serotonin reuptake inhibitors leads to a statistically significant postoperative increase in depressive symptoms, delirium and confusion.

How do we manage anticonvulsants?

Anticonvulsants are used as a treatment of chronic neuropathic pain and although overlap exists with anticonvulsants used for seizures. This review deals only with the management of those being treated for chronic pain. Long term users of anticonvulsants can develop biochemical and haematological abnormalities and it is advisable to arrange a full blood count and electrolyte testing preoperatively; in the case of sodium valproate, the manufacturer advises a full blood count.

A systematic review of gabapentinoids in 2006 supports the continuation of anticonvulsants perioperatively; the authors concluded that they are safe perioperatively and are associated with reduced pain scores and lower opioid requirements postoperatively. It is prudent to avoid abrupt cessation, which can lead to withdrawal symptoms, including rebound status epilepticus. Consequently, if withdrawal of these drugs is necessary, manufacturers recommend gradual withdrawal over seven to 10 days.

Conclusion

Many of the 19% of adults in Europe who have chronic pain will need surgery at some point. Although our understanding of pain syndromes has increased, so too has the range of drug and interventional techniques available for treating them, making the perioperative management of patients with chronic pain more challenging. The main principles of good perioperative management include the provision of pain control and avoidance of withdrawal symptoms, while being aware of the risk of side effects and drug interactions. Several strategies can achieve these goals, with each tailored to the needs of the individual patient.

Reference

1. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. 2. Eur J Pain 2006;10:287-333

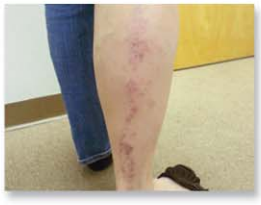
DERM DILEMMA

ANSWER

CASE 1

A shave biopsy provided the diagnosis of vertically invasive lentigo maligna melanoma with a depth of at least 0.6 cm. The dermatopathologist noted ulceration and a high mitotic index, both poor prognostic indicators. The patient was referred to a surgical oncologist for wide excision and sentinel lymph node biopsy. The latter revealed lymph node metastasis and a modified radical neck dissection was subsequently performed. Adjuvant interferon was withheld due to the liver cirrhosis. Several months later, a hyperpigmented nodule was noted in proximity to the excision site, and histopathologic findings are pending.

CASE 2



Lichen striatus (LS) is a unilateral, self-limited eruption that follows the lines of Blaschko. The condition most commonly occurs in preteen and adolescent females and may involve either the trunk or extremities. The onset is heralded by the appearance of red to flesh-colored papules with scale that rapidly extend in a band-like pattern. In many individuals, LS is asymptomatic and of cosmetic concern only; however, some experience intense pruritus. The eruption spontaneously involutes, usually within 18 months. Potent topical steroids and tacrolimus may relieve the pruritus and hasten resolution.

Emergency pericardiocentesis

Overview

This supplement provides a summary of the teaching points which demonstrates the equipment and techniques used to perform emergency pericardiocentesis in adults.

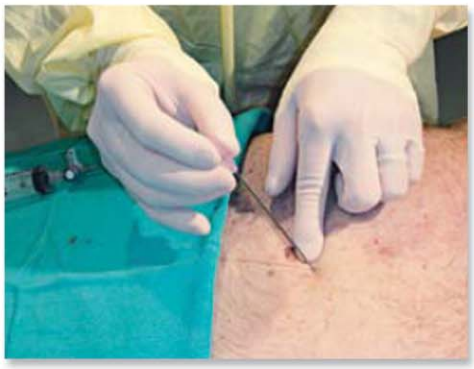


Fig 1 : Insertion of the spinal needle in the subxiphoid approach

Indications

Pericardiocentesis is indicated as an emergency procedure in patients with cardiac tamponade. Accumulation of fluid in the pericardial sac can increase the pressure around the heart. The intrapericardial pressure then increases until it equals the right ventricular diastolic pressure and then the left ventricular diastolic pressure, which leads to impaired cardiac filling and decreased cardiac output. Because of the distensibility of the pericardial sac, large amounts of fluid can accumulate gradually without hemodynamic effects. However, rapid accumulation of a small amount of fluid may overwhelm the distensibility of the pericardium with a rapid increase in intrapericardial pressure, leading to hemodynamic compromise.

The classic presentation of patients with pericardial tamponade includes Beck's triad of jugular venous distention from elevated systemic venous pressure, distant heart sounds, and hypotension. Most patients will have at least one of these signs; all three rarely appear simultaneously, and then only briefly before cardiac arrest. Jugular venous distention can be difficult to assess in obese or hypovolumic patients. Distant heart sounds may signify a pericardial effusion but can also occur in response to obesity or chronic obstructive pulmonary disease. Tachypnoea is a common clinical finding in patients with cardiac tamponade and dyspnea is the most frequently reported symptom on presentation with a sensitivity of about 87% to 88% for cardiac tamponade. In most cases, acute pericardial fluid collection is not detected on chest radiography unless more than 200 ml of fluid has accumulated.

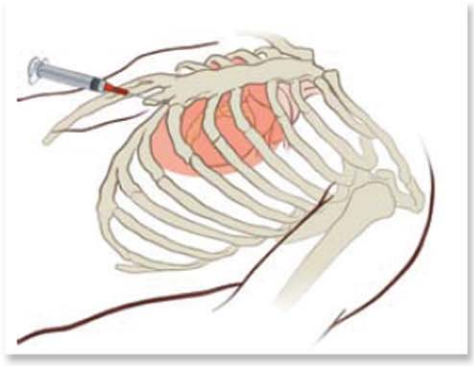


Fig 2 : Advancement of the needle toward the left shoulder

Pericardial tamponade can result from the accumulation of effusion fluids, blood, infectious purulent material or gas within the pericardial space. Simple pericardial effusions with a single collection of serous fluid may be amenable to uncomplicated pericardiocentesis, but drainage of more complex effusions, such as loculated collections of infectious material, may be more difficult.

Patients at risk for pericardial tamponade include those with metastatic cancer, a history of mediastinal radiation, end stage renal disease, recent cardiac surgery or traumatic injury. Other causes of pericardial tamponade may include pericarditis, myocardial infarction, congestive heart failure, collagen vascular disease and tuberculosis. Pericardial tamponade should be considered as a possible cause of cardiac arrest with pulseless electrical activity. Bedside ultrasonography can be used to detect the presence of pericardial fluid and features of pericardial tamponade. The presence of pericardial fluid and the diastolic collapse of the right atrium or ventricle are diagnostic of pericardial tamponade. Other findings that may further support this diagnosis include a dilated inferior vena cava without respiratory variations in size or changes in flow velocities across the tricuspid and mitral valves. In patients with pericardial tamponade, emergency pericardiocentesis to aspirate pericardial fluid can restore normal cardiac function and peripheral perfusion. It can be a life saving procedure.

Contraindications

Emergency pericardiocentesis is not indicated for a patient with a pericardial effusion and stable vital signs.

The combination of a traumatic pericardial effusion and unstable vital signs is a relative contraindication to emergency pericardiocentesis, since these circumstances are an indication for emergency thoracotomy. Although pericardiocentesis can be used as a temporizing measure, the patient will still require an urgent thoracotomy or creation of a pericardial window, since ongoing bleeding can cause a rapid reaccumulation of blood within the pericardium. Other relative contraindications to emergency pericardiocentesis include myocardial rupture, aortic dissection, and a severe bleeding disorder.

Severe bleeding disorders will predispose patients to continued bleeding and a rapid reaccumulation of pericardial fluid; they require coordinated medical and surgical efforts. However, in a patient whose condition is unstable and in whom emergency pericardiocentesis could be used to relieve a life-threatening pericardial tamponade, there are no absolute contraindications for the procedure.

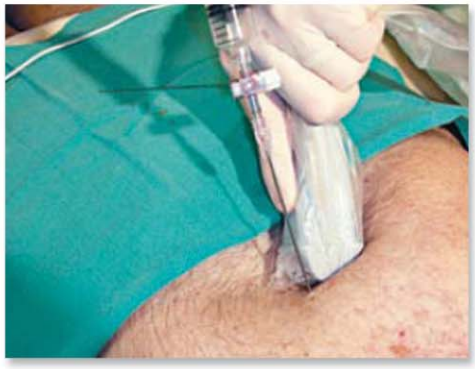


Fig 3 : Emergency pericardiocentesis performed with real time ultrasound guidance

Equipment

Appropriate universal precautions for potential exposure to body fluids should be used when performing this invasive procedure. Hand washing before beginning patient care is an important part of every procedure. The physician should wear a gown, gloves, and a face mask with shield. Sterile technique should be observed as time allows, including the use of an antibacterial skin cleanser. Hemodynamic monitoring is warranted. Because the procedure is being performed in emergency conditions, there may be a need for cardiac resuscitation; therefore, a code cart, resuscitation equipment, and appropriate medications, including atropine, should be immediately available. Pericardiocentesis should be performed with ultrasound guidance whenever a bedside ultrasound machine is available. Otherwise, a wire with alligator clips and an electrocardiograph machine can be used to watch for the pattern of ST-segment injury that occurs when the myocardium is contacted. Materials needed for the actual emergency pericardiocentesis procedure include an 18-gauge spinal needle, a polytef-sheathed needle or another suitable needle, a three-way stopcock and a 20 ml syringe.

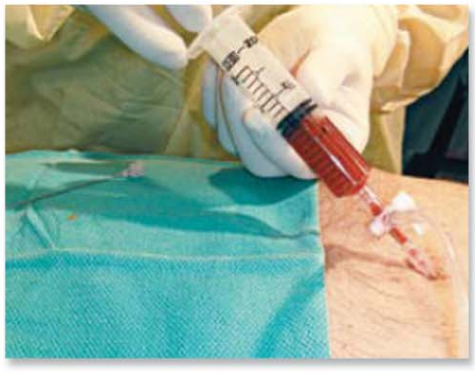


Fig 4 :Tubing attached to a three-way stopcock for continued drainage of the pericardial effusion

Preparation

Rapidly assemble the materials needed for pericardiocentesis and place them within easy reach at the bedside. Continuous hemodynamic monitoring should be used to watch for signs of decompensation during pericardiocentesis. Before beginning the procedure, locate the appropriate surface landmark by palpating the xiphoid process. After donning sterile gloves, quickly wash a wide area of the patient's anterior chest wall and upper abdominal area with an antibacterial skin cleanser. If the patient's clinical condition allows, raise the head of the bed 30 to 45 degrees, which will give more direct access to the pericardial fluid collection. Drape the area with sterile towels. Because of the time-sensitive nature of this procedure during an emergency, local anesthesia is not typically used. Local anesthetic is appropriate when the patient is awake and alert and emergency pericardiocentesis is not required.

Procedure

Three options for performing emergency pericardiocentesis are presented here. Ultrasoundguided pericardiocentesis is recommended, since it allows direct visualization of the needle as it enters the pericardial effusion and can assist the practitioner in determining which approach is most likely to successfully drain the pericardial fluid. Regardless of fluid location as visualized on ultrasonography, a subxiphoid or apical approach may be required if ongoing resuscitation efforts include cardiopulmonary resuscitation.

If an ultrasound machine is not available, electrocardiographic monitoring is recommended to indicate when the needle makes contact with the myocardium. A blind approach can be attempted if neither electrocardiographic monitoring nor an ultrasound machine is immediately available, but this method is often associated with unacceptably high morbidity and mortality as compared with a method involving electrocardiographic or ultrasonographic monitoring. The subxiphoid approach to emergency pericardiocentesis begins just below the xiphoid process and the left costal margin. Insert the spinal needle with the stylet in place to prevent dermal tissue from plugging the needle (Fig.1). Other needles with a steel core, such as a 16 to 18 gauge polytef sheathed needle, may also be used. If a needle with stylet is not available, an alternative technique is to nick the skin with a scalpel before inserting the needle. Once the needle has punctured the skin, remove the stylet and attach a three way stopcock and 20 ml syringe. Advance the needle toward the left shoulder while aspirating continuously (Fig. 2).

Fig 5 : The parasternal approach to pericardiocentesis, in which the needle is inserted in the fifth Intercostal space, just lateral to the sternum

Using real time ultrasound imaging, guide the needle toward the largest collection of pericardial fluid while watching the ultrasound screen and simultaneously recording video clips (Fig. 3). Withdraw fluid from the pericardial effusion by aspirating with the syringe. Removing even a small amount of fluid can lead to dramatic improvements in cardiac output and blood pressure. Once the needle is properly oriented to remove fluid easily, empty fluid from the syringe by attaching tubing to the three way stopcock (Fig. 4), which will allow continued drainage of the pericardial effusion with no movement of the needle. Continue to remove pericardial fluid until vital signs normalize and no further fluid can be removed from the pericardium. If the removal of a small amount of pericardial fluid has the effect of stabilizing the patient's condition, drainage tubing may not be required. The parasternal approach is an alternative method of performing emergency pericardiocentesis. Insert the needle perpendicular to the chest wall in the fifth intercostal space, just lateral to the sternum (Fig. 5). Use ultrasonography to locate the largest portion of the effusion that is close to the body surface, and guide the needle into the pericardial sac to aspirate fluid. Another ultrasound guided technique that is not described here is the apical approach, in which the needle is inserted in the intercostal space below and 1 cm lateral to the apical beat, aimed toward the right shoulder. If ultrasonographic guidance is not available, attach a sterile alligator clip and wire to the spinal needle and connect the wire to a precordial lead on a continuous electrocardiographic monitor (Fig. 6). As you advance the needle, monitor the electrocardiographic tracing for ST-segment elevation, which indicates that the needle has been advanced too far and is in contact with the myocardial surface. If this occurs, withdraw the needle until ST-segment elevation resolves, then redirect the needle to obtain pericardial fluid. Blind pericardiocentesis can be performed by entering the skin just below the xiphoid process and the left costal margin at a 45 degree angle and advancing the needle toward the left shoulder. This blind technique is associated with a higher rate of complications than the techniques guided by ultrasonography or electrocardiography and therefore should be performed only in an emergency, when neither of these two forms of monitoring is immediately available.

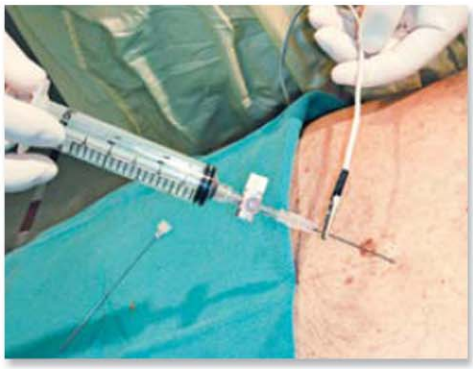


Fig 6 : Pericardiocentesis performed with electrocardiographic guidance, recommended when ultrasound guidance is not available.

Aftercare

After pericardiocentesis is complete, visualize the heart with ultrasonography to confirm the removal of the pericardial fluid and adequate cardiac function. Continue resuscitation as needed, depending on the patient's hemodynamic response to the procedure. Obtain a chest film after completing the procedure to assess for complications such as a pleural effusion or pneumothorax. Continue to monitor the patient for signs of hemodynamic instability and for physical findings that suggest fluid is continuing to accumulate in the pericardial sac. Definitive care may include placement of a soft catheter in the pericardial space or surgical placement of a pericardial window to allow for continuous drainage.

Complications

As with any invasive procedure, complications may occur. Those most often associated with this lifesaving procedure are cardiac dysrhythmias, cardiac puncture, pneumothorax, and coronary-vessel injury. Other complications associated with pericardiocentesis include peritoneal puncture (with the subxiphoid approach), liver or stomach injury (also with the subxiphoid approach), puncture of the internal thoracic artery (with the parasternal approach), and diaphragmatic injury (with the subxiphoid approach). Pericardiocentesis can also result in death.

Summary

Emergency pericardiocentesis can be a lifesaving procedure when pericardial tamponade is present. Ultrasound guidance is recommended to minimize the potential complications of this procedure. After completing the procedure, continue to monitor the patient for signs or symptoms of recurrent tamponade until definitive care can be provided.

References: JAMA 2007;297:1810-8

Stable angina

Stable angina occurs when coronary blood flow is impaired by fixed or stable atheroma of the coronary arteries. During exertion, an imbalance between myocardial oxygen supply and demand causes transient myocardial ischaemia. Coronary atheroma is by far the most common cause of angina; however, the symptom may also be a manifestation of other forms of heart disease such as aortic valve disease, hypertrophic cardiomyopathy or coronary vasopasm (Prinzmetal's angina). Occasionally, the coronary arteries are involved in other disorders such as polyarteritis and other connective tissue disorders.

Clinical features

The history is by far the most important factor in making the diagnosis of stable angina. The condition is characterised by central chest pain, discomfort or breathlessness that is precipitated by exertion or other forms of stress, and is promptly relieved by rest. Physical examination is frequently negative but may reveal evidence of:

- Aortic stenosis (an occasional cause of angina)
- CHD risk factors (e.g. hypertension, diabetes)
- LV dysfunction (e.g. cardiomegaly)
- Other arterial disease (e.g. carotid bruits, peripheral vascular disease)
- Conditions that exacerbate angina (e.g. anaemia, thyrotoxicosis)
- Retinopathy (diabetic or hypertensive)

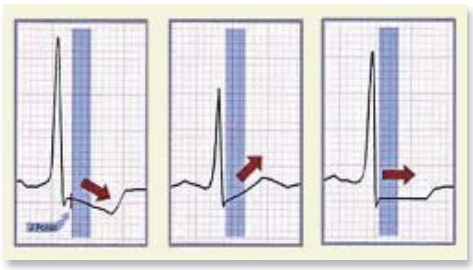


Fig: ST segment Depression

Investigations

Resting ECG: May show evidence of previous MI but is often normal even in patients with left main or severe three-vessel coronary artery disease. The most convincing ECG evidence of myocardial ischaemia is obtained by demonstrating reversible ST segment depression or elevation, with or without T wave inversion, during symptoms.

Exercise ECG: The patient's ECG and BP are monitored during exercise to a standard treadmill or bicycle ergometer protocol. Planar or down-sloping ST segment depression of ≥1 mm is indicative of ischaemia; up-sloping ST depression is less specific. Exercise testing can provide objective evidence of myocardial ischaemia and is also a useful means of assessing the severity of coronary disease and identifying high-risk individuals. However, false negatives and positives do occur and the predictive accuracy of exercise testing is lower in women than men.

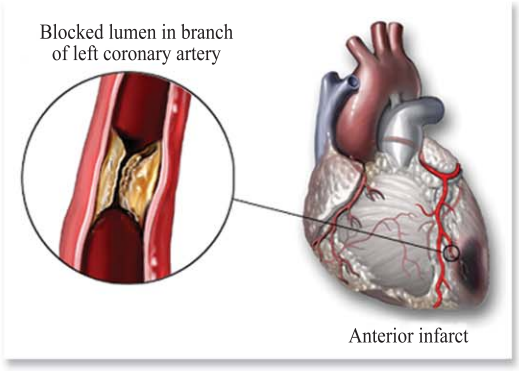
Myocardial perfusion scanning: Has a higher predictive accuracy than exercise ECG and is particularly helpful in patients who are unable to exercise or who have an equivocal or uninterruptable exercise test, Scinti-scans of the myocardium are obtained at rest and during stress (exercise or pharmacological, e.g. dobutamine) after i.v. administration of a radioactive isotope that is taken up by viable perused myocardium. A perfusion defect present during stress but not at rest indicates reversible myocardial ischaemia; a persistent defect suggests previous MI.

Stress echocardiography: An alternative to myocardial perfusion scanning with similar predictive accuracy (superior to exercise ECG). Ischaemic segments of myocardium exhibit reversible defects in contractility (visualised by echocardiography) during exercise or pharmacological stress; areas of infarction do not contract at rest or during stress. The technique is particularly useful for identifying areas of viable 'hibernating' myocardium in patients with heart failure and CHD being considered for revascularisation.

Coronary arteriography: Provides detailed anatomical information about the extent and nature of coronary artery disease. It may be indicated when non-invasive tests have failed to elucidate the cause of atypical chest pain but is usually performed with a view to revascularisation.

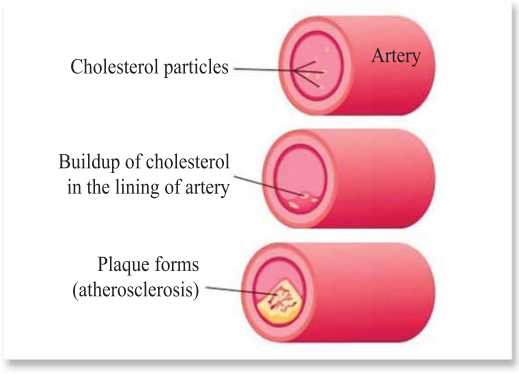
Management

Secondary prevention: In all forms of atheromatous vascular disease including angina, patients are at increased risk of major vascular events such as MI or stroke and can be offered a variety of treatments and measures to improve their outlook.



- The most important lifestyle modification is smoking cessation but other steps include regular exercise and aiming for ideal body weight.
- Total cholesterol should be lowered to <5 mmol/1 but all patients with CHD should receive statin therapy, irrespective of serum cholesterol concentration.
- BP should be treated to a target of <130/80 mmHg, although ACE inhibitors (unless contraindicated) are of benefit in all patients with vascular disease.
- Aspirin reduces the risk of adverse events such as MI and should be prescribed indefinitely for all patients with CHD; clopidogrel is an equally effective alternative in patients intolerant of aspirin.

Relief of symptoms: Patients should be advised to avoid vigorous exertion after a heavy meal or in cold weather. Sublingual glyceryl trinitrate (GTN) in spray or tablet form will usually relieve an attack of angina in 2-3 mins. Patients should be encouraged to use GTN prophylactically before engaging in exercise that is liable to provoke symptoms. Four groups of drugs are used to prevent the symptoms of angina:



- Nitrates
- β-blockers
- Calcium antagonists
- Potassium channel activators (nicorandil)

The goal is control of angina with minimum side effects and the simplest possible drug regimen. Revascularisation should be considered if symptoms persist despite the use of two drugs.

Percutaneous coronary intervention (PCI): This is performed by passing a fine guidewire across a coronary stenosis under radiographic control and using it to position a balloon which is then inflated to dilate the stenosis. A coronary stent is a piece of coated metallic 'scaffolding' that can be deployed on a balloon and used to maximise and maintain dilatation of a stenosed vessel. PCI is an effective symptomatic treatment but has not been shown to improve survival in patients with stable angina. It is mainly used in single or two vessel disease; coronary artery bypass graft (CABG) surgery is usually the preferred option in patients with three vessel or left main disease. The main acute complication is vessel occlusion by thrombus or dissection, which may lead to acute MI (2%) or the need for emergency CABG. The overall mortality risk is <0.5%. The main long term complication is restenosis. The routine use of stents in appropriate vessels reduces both acute complications and the incidence of restenosis. Drug-eluting stents can reduce this risk even further but their use is currently controversial owing to a possible increased risk of stent thrombosis. In combination with aspirin and heparin, adjunctive therapy with potent platelet inhibitors, such as clopidogrel or glycoprotein IIb/IIIa receptor antagonists, improves the outcome of PCI, with lower short and long term rates of death and MI.

Coronary artery bypass grafting (CABG): The internal mammary arteries, radial arteries or reversed segments of saphenous vein can be used to bypass coronary artery stenosis, usually under cardiopulmonary bypass. The operative mortality is 1.5% but higher in elderly patients and those with poor LV function or significant comorbidity (e.g. renal failure). There is a 1-5% risk of perioperative stroke. CABG improves survival in patients with left main coronary stenosis and those with symptomatic three vessel coronary disease; the benefit is greatest in those with impaired LV function or positive stress testing prior to surgery. Approximately 90% of patients are free of angina 1 yr after surgery, but <60% of patients are asymptomatic >5 yrs after CABG. Arterial grafts have much better long term patency rates than vein grafts. Treatment with aspirin or clopidogrel improves graft patency, while intensive lipid lowering therapy slows progression of disease in the native coronary arteries and grafts. Persistent smokers are twice as likely to die in the 10 yrs following surgery compared with those who give up at surgery.

Reference: Davidson's Essentials of Medicine

Jog your memory

Please select the correct answer by (√) against a, b, c, d of each questions in the Business Reply Card and send it through our colleagues or mail within 15 November 2012; this will ensure eligibility for the Raffle Draw and the lucky winners will get attractive prizes!

1. **Diaphragmatic hernia can occur through all the following, except**
   a. Oesophageal opening
   b. Costovertebral triangle
   c. Costal and sternal attachment of the diaphragm
   d. Inferior vena caval opening

2. **The treatment of choice for recurrent transient ischemic attacks in a patient on aspirin with new onset atrial fibrillation**
   a. Anticoagulation
   b. Carotid endarterectomy
   c. Clopidogrel
   d. Carotid stent

3. **The Cells belonging to the following type of epithelium are provided with extra reserve of cell membrane**
   a. Transitional
   b. Stratified Squamous
   c. Stratified Cuboidal
   d. Stratified Columnar

4. **Women receiving Oestrogen therapy have increased risk of developing all of the following cancers, except**
   a. Breast Cancer
   b. Endometrial Carcinoma
   c. Carcinoma of gall bladder
   d. Hepatocellular Carcinoma

5. **A 16year old girl failed in her final examination. Disgusted with her life, she cut across the front of her wrist at the flexor retinaculum. She was rushed to the hospital. The surgeon noticed that the cut was superficial. The structure that would not have been damaged**
   a. Ulnar Nerve
   b. Median Nerve
   c. Palmar cutaneous branch of median nerve
   d. Superficial branch of radial nerve

6. **A man with alcoholic liver failure requires general anaesthesia for surgery. Anaesthetic agent of choice is**
   a. Ether
   b. Halothane
   c. Methoxyflurane
   d. Isoflurane

7. **Physiological Gastrectomy is**
   a. Ligation of all major arteries
   b. Antrectomy
   c. Upper 1/3 of stoma resected
   d. Ligation of 4 out of 5 arteries

8. **After 5 days of fasting, a man undergoes oral GTT. True is all except**
   a. Growth hormone levels are increased
   b. Increased glucose tolerance
   c. Decreased insulin levels
   d. Glucagon levels are increased

9. **A patient with pneumonia for 5 days is admitted to the hospital. He suddenly ceases to recognize the doctor and staff. He thinks that he is in jail and complains of scorpions attacking him. He is in an altered sensorium. This condition is most likely**
   a. Acute delirium
   b. Acute schizophrenia
   c. Acute dementia
   d. Acute paranoia

10. **Chandu, aged 32 years presents with abdominal pain and vomiting. He also complains of some psychiatric symptoms and visual hallucinations. Most likely diagnosis is**
    a. Intermittent Porphyria
    b. Hypothyroidism
    c. Hyperthyroidism
    d. Hysteria

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