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The HEALTHY MALE

Newsletter of Andrology Australia - Australian Centre of Excellence in Male Reproductive Health

CONTENTS:

Andrology

An-drol'-uh-jee

The study of the functions and diseases specific to males, especially of the reproductive organs

FROM THE DIRECTOR

The most common genetic condition affecting males, Klinefelter's Syndrome, is significantly under-diagnosed in Australia. This disorder is one cause of male hypogonadism, a condition where men fail to produce the male hormone, testosterone.

Due to the lack of recognition of Klinefelter's, many men with low testosterone are not receiving hormone treatment known to improve their health and quality of life. This has implications for the development of male physical characteristics and fertility.

Klinefelter's Syndrome is just one of the genetic conditions that can cause infertility in men. There are other genetic problems that can affect sperm and cause infertility, but reasons as to why these occur is unknown.

By supporting research into genetics, scientists can discover more about the genetic causes of infertility and develop other methods to enable infertile men to father children.

This issue of *the Healthy Male* is dedicated to the genetic aspects of reproduction in men, most notably Klinefelter's Syndrome.

Professor David de Kretser

A Hidden Problem

Raising GP awareness of Klinefelter's Syndrome and encouraging checks of testes on prepubescent boys, will enable males with Klinefelter's to be diagnosed and the syndrome to be recognised as a common genetic problem.

A recent paper[1] revealed that Klinefelter's Syndrome is severely under-diagnosed in Denmark, which also implies under-diagnosis in Australia and around the world.

The study found that only one in four adult men in Denmark with the syndrome, are being diagnosed. The authors of the paper used the Danish Cytogenic Central Registry, which has been recording karyotyping results (karyotype is a test that assesses the number and features of the chromosomes in a sample of cells from blood), since 1961 to describe the prenatal and postnatal prevalence of Klinefelter's Syndrome.

Surveys of karyotypes of male infants at birth, has estimated a prevalence of 1/650 in live-born males. Postnatally, the rate of diagnosis was much lower than anticipated with only 25% of the expected number diagnosed. Only 10% of the expected diagnoses were made in boys in the peri-pubertal period when testosterone plays an essential role in the development of secondary sexual characteristics. Advancing maternal age was found to be associated with a greater likelihood of Klinefelter's syndrome.

As seventy-five percent of adult Danish males with Klinefelter's are never diagnosed, they are denied treatment with testosterone or other health care appropriate to this condition.

The typical male suffering from Klinefelter's Syndrome is characterised by abnormally long legs and arms, feminine distribution of body fat, decreased body hair, small testes and penis, a verbal IQ below normal and learning difficulties. The majority of these men are infertile with low or absent sperm production. If Klinefelter's is detected and testosterone therapy started early enough, proper development of sexual characteristics and bone and muscle mass can occur. The treatment will also assist not only the physical, but emotional and mental aspects of life.

[1] Bojesen A, Juul S, Gravholt CH, (2003): Prenatal and Postnatal Prevalence of Klinefelter Syndrome: A National Registry Study. J Clin Endocrinol Metab 88(2):622-6

Andrology Australia is supported by a grant from the Federal Department of Health and Ageing

>> PROFESSIONAL EDUCATION

International Guest Speaker

Professor Niels Skakkebaek from University of Copenhagen in Denmark recently visited Australia as part of Andrology Australia's support of the Annual Fertility Society of Australia (FSA) meeting in Perth.

A renowned international expert on testicular histology as a tool in early detection of carcinoma in situ and testicular dysgenesis syndrome, Professor Skakkebaek spoke at the FSA meeting about testicular dysgenesis syndrome and the possible emerging environmental relationship.

During his visit to Australia he also spoke at an informal round table discussion with a group of interested health professionals at the Baker Institute in Melbourne. The afternoon included a short presentation by Professor Skakkebaek followed by a review and discussion of case material.

Andrology Australia's testicular cancer consumer guide was completed during Prof. Skakkebaek's stay and he provided comment to media endorsing the guide.

"It is very important for men to have reliable and up to date information about testicular cancer as they can then understand what is happening to their bodies and the treatment that is needed," said Professor Skakkebaek.

"In many countries around the world, including Australia, the number of men with testicular cancer is increasing every year, so they need to be aware of the signs".

Professor Skakkebaek has been awarded a number of prizes and awards for his work including, most recently, the W. Nielsen's Award (2001) and the Svend Andersen's Award (2001).

>> RESEARCH ROUNDUP

Genetic Database

For approximately 40% of men with an unknown cause of infertility, it is expected that the cause is genetic. To further research into genetic causes of male infertility, Andrology Australia is supporting the DNA Repository based at Monash Institute of Reproduction and Development (MIRD).

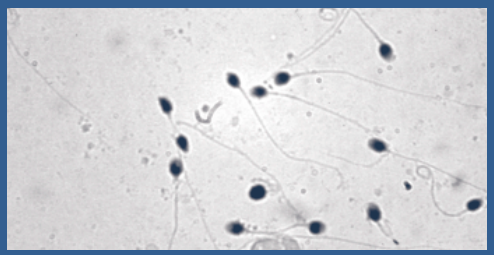
The DNA Repository is a database made up of blood samples from 2500 infertile men and 400 control men who have children and high quality sperm. Prince Henry's Institute of Medical Research (PHIMR) and the Royal Women's Hospital in Melbourne also provide samples. The database is important for research into the genetic basis of male infertility and is also being used in the process of developing contraceptives for men and women.

When blood samples are collected, the DNA is purified and stored. All the clinical and genetic data for each sample is kept on computer database allowing specific requests to be easily accessed. When necessary, the database allows for samples to be analysed for recognised mutations or problems with androgen receptors, DNA packaging, gene imprinting, Y chromosome deletions, sperm tail genes and spermatogonia.

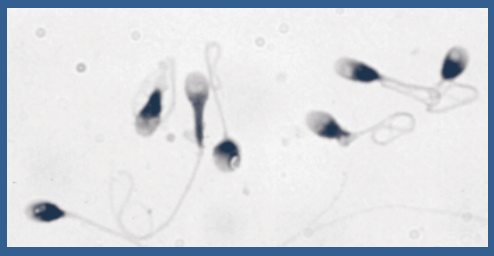
A number of collaborations have formed with other institutions and scientists through use of the database, including overseas collaborations. Professor Yoshitake Nishimune from Osaka in Japan is collaborating with scientists at MIRD and PHIMR to use the database to identify new genetic causes of infertility. Other research collaborations include those with Melbourne's Prince Henry's Institute of Medical Research and the Walter and Eliza Hall Institute of Medical Research. A number of studies are underway using the database and some have already been published in respected journals.

Research in genetics has contributed to the development of technology and allowed the possibility of some infertile men to father a child. If a man can produce some sperm but not enough to achieve a natural pregnancy because of a genetic condition, it may be possible to produce a child through Assisted Reproductive Technologies (ART) such as intra-cytoplasmic sperm injection (ICSI). It is important for couples with a genetic problem to receive counselling before and during the ART process particularly if the genetic change is unknown or likely to affect the children born using these procedures.

For more information on the DNA Repository, please contact Dr. Moira O'Bryan at Monash Institute of Reproduction and Development. Telephone: 03 9594 7127.



Normal Sperm



Abnormal Sperm

Author: Associate Professor Rob McLachlan

Focus on KLINEFELTER'S SYNDROME

What is Klinefelter's Syndrome?

Klinefelter's Syndrome is a genetic condition that only affects males. It is congenital, which means that the condition is present from birth.

What causes Klinefelter's Syndrome?

Men with Klinefelter's Syndrome have an extra X chromosome. Chromosomes are found in each cell of the human body. They carry the genetic material that determines all human characteristics, including hair colour, eye colour, height, and gender. In total, each cell has 23 pairs of chromosomes (or a total of 46).

Of the 23 pairs of chromosomes, one pair are sex chromosomes. These determine a person's gender. One sex chromosome is inherited from the mother and the other from the father. Females always pass on an X chromosome, but males can pass on an X or a Y chromosome. The normal male chromosome arrangement is 46XY, but men with Klinefelter's Syndrome have 47XXY. The extra X chromosome can come from either parent.

The exact reason men with this condition receive an extra X chromosome is not known. However, some researchers believe that increased maternal age significantly affects the prevalence of Klinefelter's Syndrome[1].

What are the effects of Klinefelter's Syndrome?

Klinefelter's Syndrome is the most common cause of male hypogonadism, a condition where men are unable to produce both sperm and enough of the male hormone testosterone for the body's needs.

Testosterone is the most important androgen in men. Androgens are hormones responsible for the development of male characteristics such as hair and beard growth, penile growth, muscle gain bone strength and fat distribution. Testosterone plays an essential role in reproductive and sexual function in men.

The inadequate production of testosterone in men with Klinefelter's Syndrome affects the development of these male characteristics. The extra X chromosome also affects the ability to produce sperm. Men with this condition are infertile as they almost always have no sperm in their ejaculate (azoospermia).

How common is Klinefelter's Syndrome?

Klinefelter's Syndrome affects about one in 650 men. It is one of the most common genetic disorders. However, it is believed that many men with Klinefelter's Syndrome are never diagnosed[1].

How is Klinefelter's Syndrome diagnosed?

Small testes (1 - 4 ml, about the size of a sultana grape) after puberty are an indication of Klinefelter's Syndrome in 99% of cases. Diagnosis is confirmed using a blood test called a karyotype. This test assesses the number and features of the chromosomes in a sample of cells from blood.

A blood test is also carried out to determine levels of testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH). Luteinizing hormone stimulates the production of testosterone. In many men with Klinefelter's Syndrome, levels of LH are raised, but testosterone levels are borderline or below normal. FSH levels are also raised indicating damage to the sperm producing tubes in the testes.

With the increase in prenatal testing such as amniocentesis or chorionic villus sampling (CVS), Klinefelter's Syndrome may be diagnosed before birth, or by pediatricians immediately after birth (postnatally). In other cases it is not identified until around the time of puberty when expected physical changes are delayed or do not occur. However, symptoms are not always very obvious and the diagnosis is not made until the man seeks medical help for infertility or for a loss of sex drive or bone fracture.

Why is Klinefelter's Syndrome under-diagnosed?

It is suspected that as many as three quarters of the men with Klinefelter's Syndrome are not diagnosed and so remain untreated for life[1].

The reasons for the under-diagnosis of this condition vary. Doctors may not routinely check testicular size. Also, some signs and symptoms of this condition during childhood and puberty, such as learning difficulties and behavioural problems, can be due to other medical conditions. As a result, doctors may not consider Klinefelter's Syndrome in these cases.

A lack of knowledge about their own body is another reason that men with undiagnosed Klinefelter's Syndrome may not visit a doctor. These men may be unaware of how small their testes are and they may not think anything is wrong. Other men may be too shy or embarrassed to approach a doctor if concerned about the size of their testes.

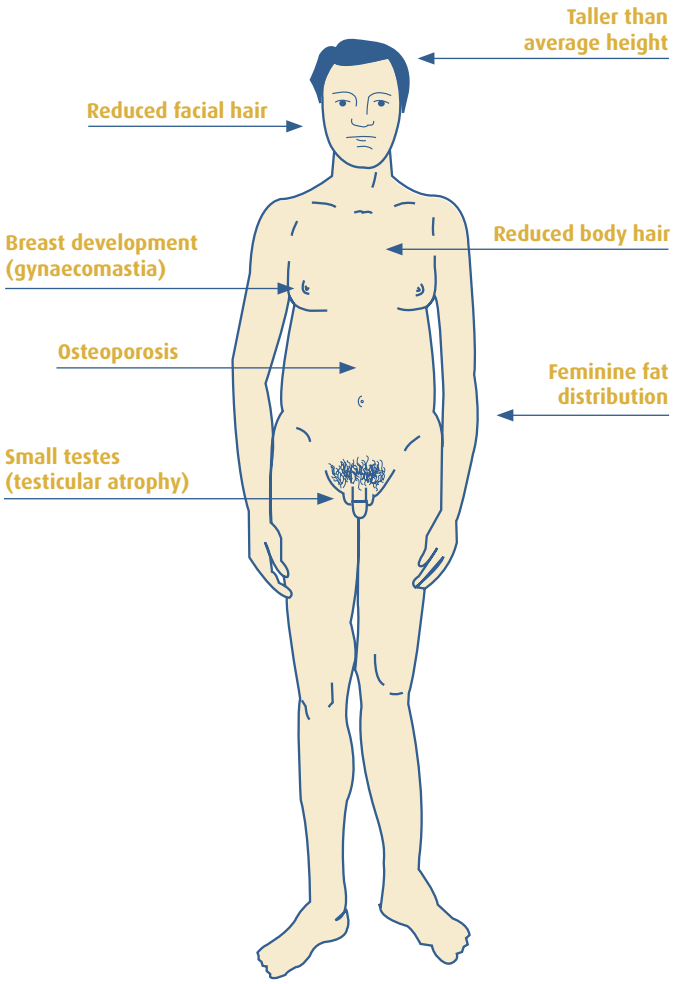
What are the signs and symptoms before puberty?

Klinefelter's Syndrome is not usually diagnosed in newborn boys as they usually appear to be normal. In young boys with the condition, the following problems may occur:

- Difficulties with speech and reading;
- Delayed motor development;
- Reduced attention span;
- Poor muscle tone;
- Behavioural problems;

However, these signs and symptoms may also occur in other medical conditions.

Focus on KLINEFELTER'S SYNDROME



What are the signs and symptoms from puberty onwards?

The signs and symptoms of Klinefelter's Syndrome during puberty and adulthood include:

- Small testes;
- Breast enlargement (gynaecomastia);
- Taller than average height;
- Fat accumulation on abdomen and hips;
- Reduced facial and body hair and decreased shaving frequency;
- Reduced libido;
- Poor erections;
- Fatigue;
- Infertility;
- Osteoporosis;
- Depression.

How is Klinefelter's Syndrome treated?

Klinefelter's Syndrome cannot be cured, but men with the condition require life-long testosterone therapy to maintain general well-being.

What is testosterone therapy?

Replacement of testosterone may be given to men who are not producing high enough levels of testosterone.

Testosterone therapy comes in a number of forms. These include:

- Intramuscular injections;
- Patches applied on the skin;
- Implants;
- Oral capsules.

Patient convenience and familiarity, cost and availability will depend on the type of treatment prescribed.

A general practitioner or endocrinologist supervises testosterone therapy in men with Klinefelter's Syndrome.

When should testosterone therapy start in men with Klinefelter's Syndrome?

Testosterone therapy in males with Klinefelter's Syndrome should be started from puberty. Teenage boys with the condition should start off on a lower dose of testosterone than adult men, and build up to the full dose as puberty progresses.

Management of Klinefelter's Syndrome in teenage boys may need school involvement. For boys who have learning difficulties, they may benefit from extra assistance at school.

How is infertility treated in men with Klinefelter's Syndrome?

Infertility is a major implication of Klinefelter's Syndrome. Infertility counselling is available for men coming to terms with childlessness and its effect on them and their partner.

In some cases, sperm can be found in the ejaculate of men with Klinefelter's Syndrome or may be found in the testes by biopsy. In these cases, assisted reproductive technologies such as Intracytoplasmic Sperm Injection (ICSI) can be accessed to achieve pregnancy. ICSI involves injecting a single sperm into the egg by piercing the outer covering of the egg. At this time, it is still unclear in what percentage of Klinefelter's men sperm can be found.

For most men who wish to have children with their partner, the best option is donor insemination. Donor insemination involves implanting donated sperm into a woman to achieve pregnancy.

What other treatments are available for men with Klinefelter's Syndrome?

Men who develop gynaecomastia can have their breasts removed surgically (mastectomy). A plastic surgeon specialising in cosmetic surgery can perform this procedure.

References

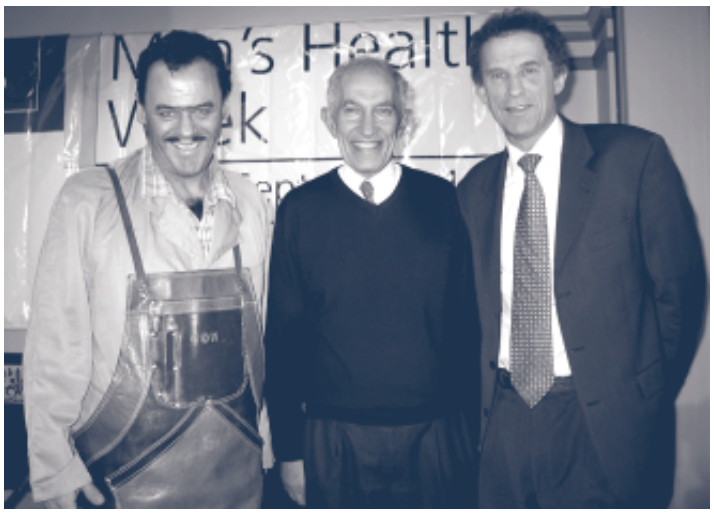
[1] Bojesen A, Juul S, Gravholt CH *Prenatal and postnatal prevalence of Klinefelter Syndrome: A national registry study.* J Clin Endocrinol Metab 88(2): 622-626 (2003).

For more information on **Klinefelter's Syndrome** visit: **www.genetic.org/ks/**

Bendigo Men's Health Week

Professor David de Kretser, Andrology Australia Director, was recently invited to speak at a seminar during Bendigo Men's Health Week (1st to 7th September) to educate men on male reproductive health. Professor de Kretser spoke on the functions of the male reproductive system, as well as explaining statistics and treatments for erectile dysfunction, androgen deficiency and testicular cancer. Mark Mitchell as Con the Fruiterer and Dr John Tickell were also guest speakers at the seminar that attracted around 400 men from Bendigo and the surrounding region.

The week is now in its third year and is organised by a large number of Bendigo community groups and organisations. The evening health seminar is sponsored by Bendigo Rotary Club and Bendigo Community Health Services. The event normally involves over 1000 men and includes activities such as barbecues, walks around the lake and Men in Sheds (open day and displays). This year the program focused on men in mid life, raising children and grandchildren, sexual and physical health and men's health through the decades.



From left: Mark Mitchell aka Con the Fruiterer, Professor David de Kretser, Dr John Tickell at the Bendigo Men's Health Week seminar.

Spreading the Word

Andrology Australia's 'Men's Health Matters' community education strategy has increased in scope and now a large number of libraries and community health centres around Australia are subscribing to *the Healthy Male* newsletter.

The aim of the strategy is to increase awareness of the Andrology Australia program as a source of quality and authenticated information on male reproductive health issues.

Broadening the availability of the newsletter and developing the consumer guides creates more opportunities for people to access information on male reproductive health issues, especially those that do not have access to the Internet.

Andrology Australia is also being called upon to disseminate health information through seminars and workplace information sessions.

If you are part of an organisation and would like to hold a men's health seminar, or make available copies of *the Healthy Male* and other educational resources at no charge, then please contact us. We are happy to provide information and assist you in raising the awareness of men's health issues in the community.

INTERNET UPDATE

Quality Online Information: Internet Study Complete

When searching for health information on the Internet, it is difficult for users to identify quality health information from the millions of health sites available. As part of the Andrology Australia website development, support was provided to the Monash Institute for Health Services Research for a study to identify and characterise Internet sites that provide information on androgen deficiency. This study assessed the nature, quality and accessibility of the information provided on the Internet.

The results of this review have been published and are being used to develop a consumer guide for exploring the Internet for health information on androgen deficiency. The consumer guide will also be applied to the Andrology Australia website. An extension of this project is undertaking a similar evaluation of Internet sites with information on prostate cancer.

Klinefelter's Information Available

A new section of information on Klinefelter's Syndrome will be included on the Andrology Australia website from mid November. The information will include diagnosis, signs and symptoms before and after puberty, and treatment of Klinefelter's Syndrome.

PROFILE

Mr Ben Harris

Ben is the Executive Director of the Optometrists Association Victoria. An economist by training, he is also Vice President of the Australian Federation of AIDS Organisations and Advisory Board Member for Andrology Australia.

Ben has a history in health workforce, financing and public health. He began his career with the Commonwealth Health Department, before being appointed adviser to the Federal Health Minister from 1997 to 1999. He has also worked on legislation review at the National Competition Council. Now at the Optometrists Association Victoria, Ben has continued his work in health promotion and management.

Ben and his wife Sharon live in Elsternwick in Victoria. Ben enjoys the Melbourne lifestyle, being a member of the North Melbourne Football Club and a subscriber to theatre and arts bodies. Ben is active in his community and in his career.

Ben is a firm advocate for a partnership approach to health care, combining the talents of local expertise, government, researchers and educators to ensure the best outcome for the community. While lacking the subject expertise of others on the Andrology Australia board, he enjoys the challenge of supporting the good work and knowledge of Australian researchers and clinicians into a program to promote excellence in male reproductive health for all Australians.

IN BRIEF

1300 number

Andrology Australia has registered a 1300 number to make access to our information services even easier. At the cost of a local call, you can contact us from anywhere around Australia on 1300 303 878.

Testicular Cancer guide available

The next 'Men's Health Matters' consumer guide on testicular cancer endorsed by the Urological Society of Australasia, is now available. For a free copy please call 1300 303 878 or email info@andrologyaustralia.org.

Testosterone testing standardised

A benchmark for accurate measurement of testosterone levels in men that will standardise testosterone level testing across Australia and improve delivery of health care services has recently been determined by Andrology Australia.

The results of the study were made available at the Australasian Association of Clinical Biochemists (AACB) 41st Annual Scientific meeting on the Gold Coast, September 2003.

Localised Prostate Cancer guide available

The Australian Prostate Cancer Collaboration (APCC) and the Australian Cancer Network (ACN) have partnered with Andrology Australia to reprint the 'Localised Prostate Cancer Consumer Guide', after extremely high demand caused the first print run of 28,000 to run out in 12 months.

To obtain a copy of the Guide, ring the national Cancer Help-line on 13 11 20 or access www.prostatehealth.org.au

International guest speaker

Professor Frederick Wu (Manchester, UK) visited Australia in September as part of Andrology Australia's support of the Annual meeting of the Endocrine Society of Australia (ESA).

Professor Wu spoke at both the ESA clinical weekend workshop and main meeting on Androgens and the Ageing Male.

Newsletter of Andrology Australia
Australian Centre of Excellence in Male Reproductive Health

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