# The KS Story
## You are not alone

### AN INFORMATIVE GUIDE & FURTHER STUDY

***The KS Story*** is the culmination of twelve years ongoing study and an emotional journey through the workings of the congenital chromosome condition Klinefelter's Syndrome (KS).

The book was created primarily as a conduit to respected support groups, medical specialists and research units, with a chapter devoted to further study, including a comprehensive support address and online section and a selection of books, research papers, medical journals and scientific magazines.

The book also offers a glimpse into the various aspects of Klinefelter's Syndrome; showing how it affects individuals and those who love, care and treat them.

***The KS Story*** has been compiled by a person with Klinefelter's Syndrome (karyotype: 47,XXY), from reputable medical, research and support group sources, and with the help and support of several UK and international scientists in the fields of biology, cytogenetics, endocrinology, neuroscience and sexology.

To balance the overwhelming amount of data there is a degree of comic relief in the writing, with a sprinkling of cartoons.

All that is asked, is that you please put aside any preconceived ideas or stereotypes and view the guide with a respectful and open mind.

## The KS Diaries
### LIVING WITH KLINEFELTER'S SYNDROME

*Sensitive, fearful, powerful, touching, forgiving, loving...*

A planned second book (pdf) will present personal histories of childhood, adolescence and adulthood titled: ***The KS Diaries*** and will give you a glimpse through the eyes of those who live and cope with Klinefelter's Syndrome every day.

However, this book is subject to you and people like you. If you wish to contribute your own KS story, please see page 80.

**WARNING**

***The KS Story***
***You are not alone***

**contains frank and sensitive information of a gender & sexual nature, relating to Klinefelter's Syndrome and the effects it has on an individual**

***The KS Story***
***You are not alone***



**First edition 2010**
Self-published as a pdf.



# The KS Story
## You are not alone

An introduction to a *"common genetic condition"* and a reference book for those seeking research & support group information advice and lifelong support

# Klinefelter's Syndrome

### AN INFORMATIVE GUIDE & FURTHER STUDY

Compiler: **Iain W McKinlay** 47,XXY

Foreword by:
**Prof Milton Diamond Ph.D.**

To inform individuals with Klinefelter's Syndrome parents, family members partners and the general public

A reference book for healthcare professionals, counsellors and anyone who works with children and young people

# The KS Story

## You are not alone

"It is strange to think that a condition which was discovered in 1942 is still basically unknown to the general population, even though it is now classed as a "common genetic condition" in males (1:750-1000).

And the reason? It comes down to ***Invisibility*** and ***Complexity***. 'Invisibility,' in that generally no characteristics (phenotype) are present at birth, so diagnosis is not usually made at this time, unless the mother has undergone specific karyotype tests, possibly for aneuploidy conditions in older mothers; generally over 35 years old, examples: trisomy 13, 18, 21 (Down's Syndrome), or X & Y (Klinefelter's Syndrome).

'Complexity' also plays a part, as those with Klinefelter's Syndrome can also be diagnosed at any time after birth, generally because of a lack of academic or social skills pre-puberty, including physical aspects at around puberty and through the teenage years, to infertility problems as adults, or as a result of obesity, osteoporosis, diabetes, or other possible linked conditions in later life.

To those with KS, there will be some with mild implications while there will be others who suffer in silence, aware that they are different but oblivious to the condition and support networks and afraid to openly discuss their feelings with their parents, Spouse/partner or doctor.

Commenting purely on the UK, I am unaware of any national figure of diagnosed individuals, however, given the current estimate for annual live births of between 400 and 500 for the more frequent 47,XXY karyotype and an upper age of 80, there is a potential for around 40,000 people in the UK walking around with Klinefelter's Syndrome.

Add to that the rarer male karyotypes and mosaics (please see p23); parents & family members; spouses/partners; relatives... and you have a substantial number of people involved with Klinefelter's Syndrome.

With only a few hundred registered with UK support groups, I believe there is a need for more education. However, knowing where to look for reputable sources of information is another story.

For the many individuals who know there is something not quite right about themselves and who may feel confused or alone.

For those who have just been diagnosed, feel fine, but want to understand the mechanisms behind their traits and symptoms.

For the aforementioned people and with respect, to doctors & medical staff, health workers, teachers and anyone who works with children and young people – and for society in general, I offer this informative guide to Klinefelter's Syndrome.

If ***The KS Story*** can help just one person take those first steps to finding the truth about themselves and seeking any appropriate treatment, or give a parent, spouse or partner who has noticed changes in their loved one vital information, then the guide will have made a difference and I'll be more than satisfied."

Iain W McKinlay 2010.

**Phenotype** n. The observable characteristics of an individual...

**Karyotype** n. The chromosome set of an individual...

**Aneuploidy** n. The condition in which a chromosome number of a cell is not an exact multiple... (e.g. X or XXY).

**Trisomy** n. An aneuploidy condition where there is an extra chromosome present within each cell of the body... (e.g. XXY).

*(Please look at a medical dictionary or online for a full description of the above terms.*

*See page 13 / M2 in margin, for two online encyclopedia examples you could try. There are a load out there, so find the one that suits you best).*

**Harry Fitch Klinefelter Jr**

Klinefelter, Harry F. Jr., MD; Reifenstein, Edward C. Jr., MD; Albright, Fuller MD,
*'Syndrome characterised by Gynaecomastia, Aspermatogenesis without A-Leydigism and increased excretion of Follicle Stimulating Hormone'*,
The Journal of Clinical Endocrinology & Metabolism, **2**:615-27, 1942.

*Image courtesy of*
*The Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institutions.*

**Patricia A Jacobs OBE**

Jacobs, P. A. and Strong, J. A.
*'A case of human intersexuality having a possible sex-determining mechanism'*,
Nature, Lond. **183**:302-303, 1959.

*Image kindly supplied by Prof P A Jacobs.*

*for their love, support and understanding*
*The KS Story guide is dedicated to:*

*my family*

*x x x*

The KS Story
You are not alone

***The KS Story***
*has been compiled from medical papers, journals, books and the Internet, from respected research & medical specialists and support groups, by an individual with Klinefelter's Syndrome (XXY).*

***The KS Story*** *is not mine alone, but a fusion of knowledge and experience offered by the latter dedicated and compassionate people who have contributed to its content.*

*This informative guide is offered primarily as a conduit to the above people, to whom you should direct all enquiries for the most appropriate support, advice and literature.*

*All that I ask, is that you please put aside any preconceived ideas or stereotypes and view the following pages with an open and respectful mind.*

# Foreword

## XXY The Most Common Genetic Difference

**Milton Diamond Ph.D.**
University of Hawaii John A. Burns School of Medicine USA

*Image kindly supplied by Prof M Diamond.*

*When Iain McKinlay approached me with questions about Klinefelter's syndrome for a book he was writing on the subject I was surprised. As one of the more common atypical genetic conditions I thought a book on the subject would have been done several times over from not only scientific and medical perspectives but also from different personal points of view. I was quite mistaken. There were none to be found. Certainly many scientific, medical and informative articles covered the topic but nothing existed that attempted to gather all aspects of the subject for the average reader. There was especially nothing generally readily and in detail available for those individuals with the condition or for their family and friends, or even for those just interested or curious who wanted more information.*

*In this volume you will find exactly that. Iain McKinlay presents, in a candid and direct way, those things he had found useful in his quest to understand his own XXY situation and aspects of himself. Here he presents his findings so both he and the reader become fairly current in ability to answer many personal questions that occur to those living with this circumstance and others trying to come to terms with it.*

*Despite the relative widespread occurrence of the XXY combination in people the condition has only come out of the medical and scientific community to common attention about a decade or so ago. And the way it has become understood has varied greatly. Some concentrate attention on the genetics involved and others attend more to behavioural or potential medical concerns or consequences of having any of the Klinefelter's combinations e.g., XXY, XXXY, XXYY. Some consider Klinefelter's syndrome and its many variations as intersex conditions, others don't. In any case it is a uniting of typical X and Y chromosomes to form different combinations. This fusion occurs naturally and in different forms for the same reasons that there is variation in just about everything in nature. We all develop with different hair, eye and complexion colors, of different height and weight and variation in all other characteristics. It is no different in regard to sex and sexuality and genetics. I summarize this by saying "Nature loves variety" we see it everywhere. Variety is one of the mechanisms of evolution. From these differences the fittest characteristics compete to survive. Unfortunately, society often doesn't appreciate variety. It expects everyone to be the same. This often leads these common differences of development to be hidden. And like many other matters related to our lives, especially those of a personal nature, one's Klinefelter's condition is most often kept private even from those close to us. Physicians and others dealing with these conditions as medical phenomena usually maintain a public quietness about it since having an XXY or analogous chromosome combination has often been accompanied by stigma or shame. It emphatically deserves neither. Klinefelter's condition is a spontaneous genetic occurrence. And, the variability in how it will effect or manifest in any one individual is so large that many clinicians do not even assign the condition name unless a host of nonchromosomal features exist.*

*Without doubt this book can and will serve as a starting place from which many readers will go further. There are all sorts of resources listed.*

*The book is unique for several reasons in addition to the subject matter covered. It is the product of Iain's individual labor of intense curiosity and creativity, it is a work of Iain's talent as a book designer, and the contained drawings and art work are testament to his artistic abilities. His generosity in offering this book to the public is another mark of this special individual. I think many owe him great and heartfelt THANKS.*



## Furthering knowledge of Klinefelter's Syndrome

It was never my intention to profit from this book, merely to 'do my bit' and to stop going stir-crazy while undergoing extensive medical treatment.

However, while I am delighted to offer ***The KS Story*** to you as a gift, may I ask one favour? That you please *consider* a donation to help support the organisation where you obtained the pdf with their educational projects. The amount is your choice; whatever you feel is appropriate.

You will be contributing towards valuable work and furthering the knowledge of Klinefelter's Syndrome in your own country and around the world.

Most support groups have secure payment methods online, or you can send them a cheque or postal order. If you're not sure, just ask them.

That said, there's absolutely no arm-twisting and I'm not expecting anyone on pocket money to contribute!

If you are a professional who has obtained the pdf, then your interest is a donation in itself and I would not expect researchers, consultants and other healthcare professionals to contribute – *unless you wish to of course*.

Alternatively, you might like to donate your own KS story for the second book (pdf), ***The KS Diaries*** (*please see p80*).

*Humongous thanks.*

*Iain W McKinlay 2010*

**Endocrinology**
HORMONES

**Gender**

**Genetics**

**Intersex**

**Medicine**
CLINICAL & SURGICAL

**Orthopaedics**
SURGERY

**Rheumatology**
OSTEOPOROSIS
AVASCULAR NECROSIS

# Important Information

## PLEASE READ

## WARNING

***The KS Story – You are not alone***

**contains frank and sensitive information of a gender & sexual nature, relating to Klinefelter's Syndrome and the effects it has on an individual**

## The Book (pdf)

### NOT TAKING ADVANTAGE

The purpose of creating this book is to supply pure information about Klinefelter's Syndrome and to point you in the right direction to reputable information, advice and support resources.

Other than specific contributors, credited and referenced within *The KS Story* and links to two free search engines (included for the convenience of the reader), this has been done without commercialism or personal gain.

To this end, no named products will be associated with, or promoted within *The KS Story*.

If you wish specific information on a product, please contact an advice or support group, or search for specific products online.

***Disclaimer*** *Please see page 86.*

## Further Study (contact listings)

### CONTACT DETAILS

Please be assured that within the *Further Study* chapter all contributors have supplied up-to-date [2010] contact information.

Some contact details, email or web addresses are likely to change before the book pdf is updated in November 2012.

### DIFFERING VIEWPOINTS

While there may be differing views within the general population and some support groups, in what Klinefelter's Syndrome is, or isn't, (e.g. Intersex), all contributors have approved (in writing) their contact details under a specific category heading.



# Contents

# Acknowledgments

## Family, Friends & Contributors


### *Family & Friends*

Chauffeur, welfare visits, food parcels and family gatherings. Just a few of the unselfish acts my **mother, sister and brother-in-law** have provided in order to ease my passage through the last 14 years of pain, stress and uncertainty. But of course their love and support runs far deeper.

There are no words to express what they mean to me, no words to thank them for their continuing support and understanding. That said, if I can help just one child with Klinefelter's Syndrome, or the parents of a child or teenager with this condition, perhaps that would go some way.

Family acknowledgments would not be complete without mentioning my **father**. He died in 1980 after many years of heart disease and 17 years before I was diagnosed with Klinefelter's Syndrome. With only the traits & symptoms of KS apparent to him our relationship was 'strained' at times, but despite our differences I think of him with love.

I am rich in relatives and delight in our evolving love and friendship. I am also grateful for their support during recent cancer treatment (2009/10).

I am fortunate to have many good friends, evolving from holidays on the white stuff, Munro-bagging, camping trips and annual BBQs of note.

Of very close friends, I am privileged to have four. I continue to have a unique friendship with my x-wife. Of male friends, two are lifelong. Like brothers, during our early teens my cousin and I went through the tentative actions of girl-chasing, but with shyness rarely caught any! At secondary school my second male friendship developed. He is now 3000 miles away, yet we're closer than ever. 26 years ago, the third friendship started as graphic designer and client. We thought alike and through many projects, and now frequent visits, a great friendship developed.

Only the aforementioned know of my struggles to come to terms with who I am. They don't all fully understand my situation but they accept that which they know. *What more can anyone ask.*

### *'The KS Story' Advisors*

My sincere thanks to the following research advisors for their invaluable and enthusiastic assistance, user-friendliness *and* patience:
**Prof Milton Diamond,** University of Hawaii, John A Burns School of Medicine, USA;
**Prof Patricia A Jacobs OBE,** Wessex Regional Genetics Laboratory, UK;
**Dr Shirley G Ratcliffe,** *Consultant Paediatrician (Retired)*, UK;
**Prof Anne Fausto-Sterling,** Biology & Gender Studies, Brown University, USA ;
**Prof Dick F Swaab,** The Netherlands Institute for Neuroscience, NL.

### *Unsung Heroes & Heroines*

A huge THANK YOU to the numerous Klinefelter's Syndrome information and support groups and individuals, and allied organisations in the UK and worldwide who have assisted me with facts and figures for the book. They truly are the heroes & heroines of this book.

### *Healthcare Professionals*

Very special thanks to the following healthcare professionals who have treated me over the last 14 years. Also for reviewing *The KS Story*; making valuable suggestions and pleasing noises.

Staff at the former Princess Margaret Rose Orthopaedic Hospital and the New Royal Infirmary of Edinburgh. 2001 & 2003. Staff at Hay Lodge Health Centre *(The Practice)*: for allowing me to freely moon once a month (Male HRT). Hay Lodge Hospital *(NHS Trust)*, for 6 years of care; on the couch and scraped off the ceiling! Ward 1 for their healing hands and unique humour. Medical & surgical staff at Borders General Hospital and the Borders Macmillan Centre (BGH), for their outstanding bedside manner and interest in *The KS Story*. 2007-08 & 2009-10.

### *Last and never least*

My GP, **Dr P T Young**, for helping me get through the pain and stress of the last decade and for his faith and support in my efforts to create ***The KS Story***.




## References within text

Throughout this guide there are Acknowledgments to the many contributors who have taken time out from their furious schedules to substantially assist a mere mortal with his studies. These people have been referenced within the specific chapter margins. References for main advisors are shown below, with small red initials within the appropriate chapter text (e.g.[PJ]).

If appropriate, contact details and published work for the following people can be found within the ***Further Study*** chapter *(p74-79)*.

**I would never knowingly plagiarise someone else's work.** With such a large body of information and with an appaling memory, despite making every effort to check my work, there may be information taken from a source from which I have forgotten to reference/credit. To those concerned I sincerely apologise and thank them for their wisdom.

| | | |
|---|---|---|
| **MC** | **Cull, M** | *(AHN Founder)*, Adrenal Hyperplasia Network, UK. |
| **MD** | **Diamond, M** | *(Professor)*, University of Hawaii, John A Burns School of Medicine, USA. |
| **AF-S** | **Fausto-Sterling, A** | *(Professor of Biology & Gender Studies)*, Brown University, Rhode Island, USA. |
| **LG** | **Gooren, L J G** | *(Professor)*, Free University Hospital, Amsterdam, NL. |
| **PJ** | **Jacobs, P A** | *(Professor)*, Wessex Regional Genetics Laboratory, Salisbury, UK. |
| **NCBI** | **(Website)** | National Center for Biotechnology Information, part of NLM/NIH, USA. (Used in this book: **PubMed** & **MedlinePlus**). |
| **SR** | **Ratcliffe, S G** | *(Consultant Paediatrician)* retired. Previously at MRC Genetics Unit, Edinburgh, UK. |
| **MS** | **Simmonds, M** | Androgen Insensitivity Syndrome Support Group, Banbury, UK. |
| **DS** | **Swaab, D F** | *(Professor)*, Netherlands Institute for Neuroscience, Amsterdam, NL. |

### Steroid Hormones

The mass of the steroid hormones are sufficiently small enough (lipophilic) to pass easily from blood to brain tissue.

Steroid hormones bind with steroid receptors in the cytoplasm of cells in order to regulate gene expression (switch-on). The resultant processes translocate to the cell nucleus **Kawata, CF.** (1995).

Cholesterol is the precursor for the five major steroid hormones: Androgens, Oestrogens, Progestins, Glucocorticoids and Mineralocorticoids.

The testes secretes three gonadal steroid hormones known collectively as Androgens, including Testosterone, Dihydrotestosterone (DHT) and Androsterone – testosterone being the most important.

There are also three Oestrogens: Oestradiol, Oestrone and Oestriol. By far the most important of these is oestradiol, the oestragenic potency of which is 12 times oestrone and 80 times oestriol. Oestradiol is also the female equivalent of testosterone in males.

(Androgens are also secreted in small amounts by the ovaries and adrenal cortex, and oestrogens by the latter, testes and placenta).

Recent studies show sex hormones & receptors exert many actions beyond reproduction, such as: areas of the brain to do with learning and memory, emotions, motor coordination and pain sensitivity. **McEwan,** (1999), *Behaviour, mood, cognitive function*. Also functions which could have important neuropsychiatric and neurodegenerative diseases. (**Swaab, DF.** (2002); **Swaab, et al.** (2003).

**Direct Links**

**M1**
You can access email and websites directly from this pdf [Just click on the address.]

**ADDRESS LINKS IN TWO OR MORE LINES**
Due to technical aspects beyond my comprehension (grrr), website links in two or more lines, will not function. For these links, take a note of the address then manually add the additional lines of text to your browser's website field.

**DID YOU KNOW?**
Additional information can be found in these yellow background 'Did you know' boxes, scattered throughout the guide...

...and very important information, on these green backgrounds. Sometimes with a red border.

**PLEASE DON'T SCREAM AT ME!**
I would like to apologise in advance for the appaling spelling and punctuation within this book – but grammar in particular.

I have no idea what a *past participle* is or an *inflexion*, or really when to include a semicolon or a coma (limitations of spellchecker when you can't spell).

This is due in part to years of looking out of classroom windows as a child; for doodling inside my desk (can't touch you for it); for getting regular verbal tellings off for grammar *and* 6 of the belt for spelling (oh yes, Human Rights and litigation would have a field-day nowadays); for taking 'O' level English at night-school and still failing; for... well, you get the picture.

# About this book

## Information overload! – just dabble

***The KS Story*** is two things. Primarily it is a conduit to the various support and scientific experts, but to get you started it also offers an overview of both Klinefelter's Syndrome and conditions associated with it. Within these pages there is a great deal of information to take in, but the book isn't a novel; you don't have to read it from cover to cover. Treat it as a reference book, just taking what you need, that way hopefully you'll retain more information and you won't get bogged down in chapters that don't interest you. You can then contact those groups within the ***Further Study*** chapter which can assist with your specific needs.[M1]

**Please read the margin box on the opposite page, titled 'Important'.**

## Complexity and Study

Klinefelter's Syndrome is a highly complex condition and cannot be generalised – ***everyone is different***. As too are the different characteristics of a person (phenotypes/karyotypes), which are also complex and varied. (*Further details see p22-23*).

***The KS Story*** deals with Klinefelter's Syndrome generally as a whole entity, though there is a bias towards 47,XXY in some chapters; basically because it's my own karyotype and the one I studied the most. As mentioned, this book is an overview of KS, so if you have another karyotype it should still be of interest to you.

You can also go to the ***Further Study*** chapter, where you will find contacts and websites to support and research groups who can offer you a tremendous amount of information, on ALL karyotypes. These specialists will help you to understand more fully your own particular condition, your symptoms and your feelings, and if you wish, will put you in touch with other KS individuals or families.

## Copyright and Copying 'The KS Story'





## Unpronounceable mouthfuls

Throughout the guide you will come across new and unfamiliar names and procedures. Don't be put off by them. If you wish to know more about your condition it will help if you can understand the meaning behind these unpronounceable mouthfuls. And it's amazing how quickly they just roll of the tongue – *honest!*

If you plan to study your condition more fully, then I highly recommend the purchase of a good concise general and medical dictionary. Believe me, they are invaluable. If you can't stretch to the latter, your local library should be able to loan you the books. Alternatively, you could check out any definitions online.[M2]

## Little red references

Throughout this guide you will see a few little red letters and numbers within the text, which relate to additional information, or to original source references. For example:

[M5] additional information found within page margins;
[MD] reference (*see p11*).

## We live by words

Dictionaries and many medical papers continue to use the words 'normal', 'disorder', 'defective', 'abnormal'. ***I'm not abnormal or defective!*** Within the context of describing Klinefelter's Syndrome, I have tried to use certain guidelines, laid out to eliminate some of these offensive words.[M3] For example, for the word 'normal' the words 'typical', 'usual' or 'most frequent' have been used, and 'condition' rather than 'disorder'. Of course there are times when this is not possible, e.g. within a support group name, or when quoting someone.

## Who comes first?

So as not to offend anyone; wherever possible, alphabetical order has been employed.

## Who does what?

To differentiate between medical investigation and an individual looking for information on their condition, throughout this book the word **'research'** is used for the former, and **'study'** for the latter.

## Last but not least

Despite the serious nature of this condition, I have tried to maintain a degree of humour within the writing and graphically with a sprinkling of cartoons. With such a lot of information to take in, it can be quite daunting, so I feel a comic turn here and there is no bad thing. Even for those with Klinefelter's Syndrome, life's not all doom and gloom! *Trust me – a smile will lift your day!*

**M2**
Try some of the free online dictionaries or encyclopedias, such as:
**w:** http://en.wikipedia.org/
**w:** www.encylco.co.uk/

*Oh – and someone who knows how to spell the word, would be an advantage!*

Or, get yourself a phonetic dictionary or a basic electronic spelling corrector with a phonetic feature.

**M3**
Taken from a paper: by **Prof Milton Diamond** (University of Hawaii, John A Burns School of Medicine) & **Dr H Keith Sigmundson** (Canada), *Management of Intersexuality*.

**Double Page Spreads**
This pdf is laid out like an open book (2 pages), so please remember, if you are looking for a particular page (e.g. 51), you will have to go to page 26 on the pdf reader's page number field or thumbnail.

**Important**
*The KS Story* is written with many people in mind.

Apart from those associated with KS and the general public the guide also informs healthcare professionals and is therefore technical in places, so not all the information will be understood by all – or for that matter desired or required by all. But there should be sufficient to help you understand the basics and point you in the right direction for further study.

*"Klinefelter's Syndrome is a highly variable condition and although some people are seriously affected others may have mild implications."* SR

# Who should read this book?

## There are six groups who hopefully will benefit from reading and using this book.

1 ***One*** Typical kids can seem unwilling to listen and learn and to parents may be seen as simply bone idle. But in some the cause is genetic and is not a fault of the child.

Everyone's situation is different and sometimes due to embarrassment or a lack of knowledge, there may be an unwillingness by some parents to offer sex education and advice to their children; leaving it primarily in the hands of schools and peer groups. It then becomes doubly difficult for both sides to communicate about the symptoms and feelings of typical teenagers—never mind those with Klinefelter's Syndrome (KS). With the result that those individuals with KS can go through their adolescence and early adulthood feeling alone and confused; not knowing who to turn to for support.

This guide is primarily offered to those individuals who exhibit some of the KS traits shown on page 22, but who are perhaps too shy to express their concerns and feelings to parents, spouse/partner, or to their GP. From experience, being a generally shy child and teenager, I was unwilling to share my sexual feelings and physical lackings with anyone, particularly to my parents, and certainly not to a family doctor. But then attitudes change with the generations; today's parents are far more open-minded and knowledgeable of some genetic conditions and GPs too are much more approachable.

2 ***Two*** Following on closely to the latter are those individuals who have just been diagnosed with Klinefelter's Syndrome and are interested in knowing more about their condition.

It is often the case that if you know that there are others out there with the same condition; who have gone through the same experiences as yourself, it somehow eases the loneliness. And when you discover that these people are willing to listen to you and offer support and guidance; and these are individuals with KS, as well as parents of KS children, it can really lift your spirits.

3 ***Three*** Those with KS will have their own set of circumstances regarding the 'telling' of their physical differences and emotions.

The third group who should benefit from reading this book are therefore the parents, family members spouse or partner of individuals with KS. Hopefully it will help them to understand a little better what's going on in the mind and body of their loved ones.



Of course, there will also be those who never tell. But it should be remembered that none of us have any say in how our blueprint creates us. So why should anyone suffer for a condition over which they have no control?

Within the research statistics and complex medical data lies someone's child. Above all else, don't they deserve the same love and support as any person? Klinefelter's Syndrome, though genetic, is not hereditary, so can't be predetermined, but if something doesn't seem right, perhaps for an older couple trying for a family, or to parents worried about their son, knowing some of the KS symptoms might just be beneficial.

4 ***Four*** I have tremendous respect for the work all medical personnel do. All of us know the pressures that our local frontline doctors and medical staff are under. It must be hard enough keeping up with all the usual diseases and conditions, and while I'm sure a good number of consultants and GPs know about Klinefelter's Syndrome, because of the complex nature of KS, (from experience), I have come across many hospital staff, including those working in associated fields, who had never heard of it, or needed 'reminding' of some of the finer points.

5 ***Five*** This book may also be useful to family planning counsellors, teachers, nursery staff and other people involved with children and young adults. And of course to anyone interested in understanding this ***"common genetic condition"*** in males.

6 ***Six*** **48,XXXY; 49,XXXXY; mosaics...** With such a complex condition, within this guide I generally treat Klinefelter's Syndrome as a whole entity. That said, I do highlight 47,XXY, being the one that most people seem to mention and the one which is perhaps the easiest to explain how it occurs.

Many of the karyotypes that until very recently were considered part of the KS 'family' are now seen as syndromes in their own right. The ***Further Study*** chapter *(p70)* will help you find specific information and support for your particular karyotype, or offer contacts who may be able to direct you. It also includes a range of linked and sex-determining conditions.

Interestingly, Triple X Syndrome, karyotype: 47,XXX (often called the female version of KS) which is also a result of nondisjunction *(see p17);* 47,XYY Syndrome and Klinefelter's Syndrome are often grouped together within research studies. *(Please see **Karyotypes** p23 and **Further Study** for more information).*

***And finally***

If you take only one piece of advice from this book – ***make it a visit to your family doctor, or to an endocrinologist.*** *Why? See p61.*

**Prenatal Diagnosis– continue or terminate?**

A child with Klinefelter's Syndrome deserves a fair chance at life; to be able to fulfil their ambitions and to contribute to the world around them.

KS creates vastly different traits and symptoms, even within the same karyotype. Medically, some do suffer, some have mind implications, while many have no symptoms at all and can go through life unaware that they have KS, only finding out if they have infertility tests or another linked condition. *(See p22 & 58).*

According to one study in 2000[1] there were some obstetric units that had no established protocols for health professionals on how parents should be told about prenatal diagnosis. There were also some obstetric staff who knew very little about the effects of sex chromosome anomalies and when first informed, some parents were given misleading information. Of course this situation may have changed since 2000 – ***but I can't stress enough how vital it is that you should NOT consider termination until you have talked to a specialist genetic counsellor and ideally a Klinefelter's Syndrome support group; who can give you advice, support and firsthand knowledge of growing up with this condition.***

At the end of the day, having knowledgeable parents who can love, encourage and support their child through the difficult years of life; such as puberty and adolescence, will make a difference beyond measure.

[1] **Abramsky, L. et al.** (2000). *What parents are told after prenatal diagnosis of sex chromosome abnormality: interview & questionnaire study.* North Thames Perinatal Health Unit, Imperial College of Science, Technology & Medicine, Harrow and Psychology & Genetics Research Group, Guy's, King's College and St Thomas's Hospital School of Medicine, London.



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Endocrinology
HORMONES

Genetics

# What is Klinefelter's Syndrome?

## The basics

Every human adult contains more than one hundred million million cells (each averaging one hundredth of a millimetre in diameter). The cells vary enormously in shape and size depending on their job within the body, e.g. muscle, nerve, organ, blood etc.

However, they all have the same basic content *(see cell diagram on p40)*. Within the wall of the cell is the cytoplasm, a jelly-like substance and embedded in this is the nucleus. Think of the cytoplasm as the factory floor, producing products for the body, and the components of the nucleus as the managers; issuing instructions to the workforce.

The blueprints relating to specific products are stored within the nucleus in a chemical form (or code), called Deoxyribonucleic Acid (DNA). Organised into groups along a ladder-shaped structure, it makes up the majority of each chromosome *(see p41)*.

The total blueprint to create a typical human are stored on 46 such chromosomes, arranged in 23 pairs, in each cell of the body.

A typical female and male have 46 chromosomes; 23 maternal and 23 paternal (paired), with the last pair (X and Y) determining the sex of the individual, written as: 46,XX and 46,XY respectively.

### *What causes Klinefelter's Syndrome?*

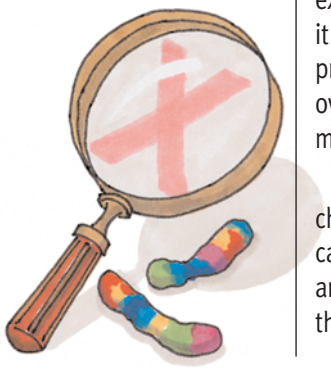
In life variations happen and sometimes an egg cell (ovum) or sperm cell (spermatozoon) develops which carries one or more extra X chromosomes. Although the cause is currently unknown, it results primarily in a change occurring during meiosis; a process which is undertaken by all cells destined to be sperm or ovum. In this process the 46 chromosomes in the cell divide to make four new cells with 23 chromosomes each.[M1]

During meiosis chromosomes pair with their corresponding chromosomes and exchange bits of genetic information; this is called 'Crossing over.' In males, the X and Y chromosomes pair and in females, the X chromosomes from each parent pair. After the exchange the chromosomes separate and meiosis continues.

**M1**
The process of *Meiosis* is quite involved to include within this book. However, if you are interested in understanding it's function, I suggest that you take out an illustrated children's book on higher human biology, from your local library. *(From experience, school books are technically easier to understand).*

**Meiosis description**
This information was obtained on:
**w:** www.medicinenet.com/

That text was in turn based on information from **NICHD** (part of NIH), **Dr Robinson, A.** University of Colorado, USA.





In some cases the X and Y chromosomes or the two X chromosomes fail to pair and exchange genetic material, resulting in them moving independently to the same cell; producing a sperm with both an X and Y chromosome or an ovum with two Xs. This is called 'Nondisjunction.' *(See table to right)*.

When a sperm with an X and Y chromosome fertilises an ovum with a single X chromosome, or a typical sperm with a Y chromosome fertilises an ovum with two Xs, an XXY child is conceived. So instead of 46,XY a male with Klinefelter's Syndrome has 47,XXY. *(See diagram on p41)*.

An extra X can also occur in females – 47,XXX ('Triple X Syndrome'), or an extra Y in boys (i.e. 47,XYY). Additional Xs and Ys and combinations of the two can also occur. (*See karyotype table on p23 and* ***Human Reproduction*** *on p42*).

Klinefelter's Syndrome (karyotype: 47,XXY) is classed as a ***"common genetic condition"*** in males. A study in 2007 now shows KS at 1.72 per 1000 male infants (previously 1.3).[M2]

It has also been shown that there are 400-500 live male KS births in Britain each year, ***"though many will not be recognised until adulthood."***[SR]

As mentioned previously, because of the variable nature of KS, some individuals may go through life blissfully unaware of their condition, others may suffer in silence; never knowing why they are that way, or to frightened to seek help. Many only find out they have KS if they have medical tests; such as for infertility or associated conditions such as osteoporosis.

It is preconceived by many parents that their son is gay, because he is not interested in girls, when often it is shyness and possible rejection. Research currently shows no more links to homosexuality than is in the general population.

### *And finally*

Amongst other vital components, such as proteins and ATP, chromosomes carry our DNA, which passes on hereditary traits and controls how our body is made and how it functions.

**Although classed as a 'genetic' condition; because of the additional chromosome(s), KS itself is not an hereditary condition. KS is not passed down from previous generations.**

## Nondisjunction

**IN OVUM CELL FORMATION**
**Parent's Genotype:**

| XX | XY |
|---|---|
| XX O | X Y |

**The Gametes**

**Possible Male Gametes**

| Possible Female Gametes | X | Y |
|---|---|---|
| XX | XXX Triple X Syndrome | XXY Klinefelter's Syndrome |
| O | XO Turner's Syndrome | YO Will not survive* |

* A Zygote would die without the vital genes within an X chromosome

**IN SPERM CELL FORMATION**
**Parent's Genotype:**

| XX | XY |
|---|---|
| X X | XY O |

**The Gametes**

**Possible Male Gametes**

| Possible Female Gametes | XY | O |
|---|---|---|
| X | XXY Klinefelter's Syndrome | XO Turner's Syndrome |
| X | XXY Klinefelter's Syndrome | XO Turner's Syndrome |

**Above:**
Adapted from *Teach Yourself Genetics* by **Morton Jenkins.** Copyright © 28.01.2005 Morton Jenkins. Published by **Hodder and Stoughton Limited / Edward Arnold (Publishers) Limited / Hodder Education.** Reproduced by permission of **Hodder Education / Hodder & Stoughton /.**

**M2**
**Prof Jacobs, P A. et al.** (2007), *Is the prevalence of Klinefelter's syndrome increasing?* Division of Human Genetics, University of Southampton Medical School, Wessex Regional Genetics Laboratory, Salisbury, UK.



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AGTC Genetics

That said, although a large percentage of XXY males do not produce enough sperm to allow them to become fathers, you should not automatically assume you are infertile without further testing. There is evidence which points to a substantial number of XXY males having the ability to father a child.

It should also be noted that a father with Klinefelter's Syndrome *may* transfer his 47,XXY karyotype to his naturally conceived offspring. If this course of action is chosen, like Intracytoplasmic Sperm Injection (ICSI); counselling should be seriously considered.[M4]

*(See the **ICSI** chapter p48, which also includes information on specific prenatal diagnosis and screening procedures.*

**M4**
Whether naturally conceived or by ICSI, there is substantial research evidence to support both the transfer of non-mosaic Klinefelter's Syndrome from father to offspring and of producing a typical 46,XY or 46,XX birth.

Check out the various papers at the **NCBI/PubMed** website:
**w:** www.ncbi.nlm.nih.gov/pubmed

**DID YOU KNOW?**

**ICD-10: Q98**

**WORLD HEALTH ORGANISATION**

*International Statistical Classification of Diseases, 10th Revision (2007).*

Klinefelter's Syndrome and other male chromosome conditions cover: Q98.0-9.

*KS examples:*
47,XXY karyotype: Q98.0
Additional Xs: Q98.1
Male 46,XX karyotype: Q98.2
Unspecified: Q98.4
Mosaicism: Q98.7.

### KS or not KS – that is the question

**It seems that karyotype 47,XXY isn't necessarily Klinefelter's Syndrome!**

Up to now all support and research groups have acknowledged 47,XXY as Klinefelter's Syndrome. In fact some include XXYY & XXXY to XXXXY.

Now there are some people in the USA that have proposed to call the most common karyotype (47,XXY) ***'Klinefelter Disease'*** and all the other variants: ***'Klinefelter Syndrome.'***

However, other scientists including **Prof M Diamond,** *(John A Burns School of Medicine, University of Hawaii)* strongly discourage the use of the word 'disease' as ***"it just adds to the stigma."***

According to a Canadian KS website, if an individual has been diagnosed with an additional X chromosome, but exhibits none of the symptoms, then they do not have Klinefelter Syndrome.

***"I never refer to newborn babies as having Klinefelter's, because they do not have the syndrome."***

**Dr Robinson, A. MD,** *Paediatrician,* University of Colorado Medical School, USA, and the director of the NICHD-sponsored study into 47,XXY.

The latter quote is mentioned in a paper written by **Bock, R.** *(1993),* National Institute of Child Health & Human Development (NICHD).

The paper (13 pages long), does offer a good deal of useful information on KS, however, it is written for an American reader.

It also mentions that there is very little information on adults with KS. Perhaps that was true in '93, but not now. You will find many papers on the American NCBI website:
**w:** www.ncbi.nlm.nih.gov/pubmed

I suggest that you read other papers in conjunction with this one to obtain a balanced view.

***The above relates to the USA and so far all UK support and research sources continue to call 47,XXY Klinefelter's Syndrome.***

*(Please see table on p23 for additional karyotype information).*





## A brief history of the people behind the syndrome

**1942**

### *Harry Fitch Klinefelter Jr (1912-1990)*

*'Syndrome characterised by Gynaecomastia, Aspermatogenesis without A-Leydigism and increased excretion of Follicle Stimulating Hormone.'*

Harry Klinefelter Jr. was born on the 20th March 1912 in Baltimore, Maryland, USA.

After premedical training at the University of Virginia, he received his medical degree from the Johns Hopkins Medical School in 1937.

In 1942, as a 'travelling fellow' at the Harvard Medical School in Boston, he was allowed to move to another department; having broken several pieces of expensive laboratory equipment. He was assigned to follow patients at the famous 'Saturday morning clinic' at the Massachusetts General Hospital, under the direction of Dr Fuller Albright, 'the father of [American] endocrinology research.'

Shortly after commencing his studies he saw a man with enlarged breasts (gynaecomastia), and small testes.

Dr Klinefelter was very interested in this case, and as Dr Albright had seen similar cases in the past, but was unsure of the cause, he asked Dr Klinefelter to set up a study of this man and other similar cases.

During his research, Dr Klinefelter found that these individuals were very tall, had small hard testes, were infertile and had elevated levels of Gonadotrophin Releasing Hormone (GnRH), Follicle Stimulating Hormone (FSH), and Lutenising Hormone (LH). These raised levels of hormones indicated that the initial problem was in the testes.

The above titled paper was published in the Journal of Clinical Endocrinology & Metabolism (1942; **2:** 615-27), by Harry F Klinefelter, Jr., MD; Edward C Reifenstein, Jr., MD; Fuller Albright, MD.

As was customary, the senior author always came last, but the media of the day were already calling it ***'Klinefelter Syndrome.'***

Dr Klinefelter said that, *"this was really another of Dr Albright's diseases. He unselfishly allowed my name to come first on the list of authors."*

Following his time with Prof Albright, Dr Klinefelter served 3 years in the US army during WW2, advancing from First Lieutenant to Major. He then returned to private practice and a member of the faculty at Johns Hopkins University, becoming Associate Professor of Medicine in 1965.

He devoted the rest of his life to studying alcoholism, endocrinology and clinical research in rheumatology, retiring in 1988 at the age of 76. He died in 1990.

*Professor Fuller Albright...*



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## Fuller Albright (1900-1969)

Fuller Albright graduated from Harvard Medical School in 1924. In the late 20s he worked with Dr Ellsworth at Johns Hopkins University, before moving to Berlin to work with Dr Zondek, mostly in pituitary gland research.

On returning to the States he set up a kidney stone clinic, and an endocrinology clinic at the Massachusetts General Hospital, specialising in ovarian dysfunction.

Dr Albright discovered many mechanisms of endocrine diseases; mostly in calcium metabolism.

He developed Parkinson's Disease around 1946 and although he continued to work, in his last years each month a medical student was assigned to him, to take him around the hospital and to learn from him.

He died in 1969 following a neurosurgical attempt to correct the Parkinson's Disease in 1956.

## 1949
## M L Barr (1908-1995)

Murray L Barr was born in Belmont, Ontario, Canada. He gained his BA in 1930 and MD in 1933 from the University of Western Ontario.

After working as a GP for two years, he returned to the Anatomy Department, specialising in Neurology.

After the Second World War Dr Barr returned to the same university were in 1949 he and a graduate student, Ewart G Bertram began a study into the process of fatigue in the cells of the nervous system.

While examining the sample brain cells (neurons) of their animal specimens, they discovered dark blotches, which looked like a drumstick. It was later discovered that the marks were 'clumps' of chromatin.

More surprising, was that when Bertam's detailed notes were examined they discovered that all the marks came from females.

In 1949 they published their work in a magazine publication of the Royal Canadian Air Force (their funding partners), on the sex chromatin, which later became known as 'Bertram & Barr Bodies' or just 'Barr Bodies'.

In 1951 Dr Barr became Professor of Anatomy.

The Klinefelter's Syndrome connection came in 1956. Buccal smear tests of men with Congenital Testicular Hypoplasia were reported as having a positive X-chromatin Barr Body.

Under typical circumstances, if an individual has an XX karyotype, one X is put to work while the other is put aside as a clump of chromatin. A woman therefore has a positive X-chromatin, or Barr Body, while a man; who typically has an XY karyotype, does not.

Therefore, the conclusion was, to theorise, that there was an extra X chromosome present in individuals that exhibited the symptoms of Klinefelter's Syndrome.[M1]

**M1**
The aforementioned text was based on information written by **Haché D**, which was supplied to the support group **Klinefelter Syndrome and Associates, USA.**

*The original Bertram & Barr paper was published in a Royal Canadian Air Force magazine.*

Additional information from: **Amory, John K. et al.** (2000, p356: 333-35), *Klinefelter's syndrome*, The Lancet, supplied by **Dr S G Ratcliffe.**





## 1959
## Patricia A Jacobs OBE (1934-)

*'A CASE OF HUMAN INTERSEXUALITY HAVING A POSSIBLE SEX-DETERMINING MECHANISM.'*

Professor Patricia A Jacobs' first exposure to cytogenetics was in 1955, and except for a brief time studying the Praying Mantis and a goat-sheep hybrid; called a 'Greep', she has spent her entire career in the study of the human chromosome.

In 1957 Dr Jacobs was appointed to the scientific staff of the newly created Medical Research Council's group in Edinburgh, by the director Michael Court Brown, for research into general effects of radiation; to study the chromosomes of leukemic cells.

Dr Jacobs spent 4 months at Harwell and Oxford learning techniques of mammalian cytogenetics and culturing human bone marrow, from Dr Charles Ford and Dr Lazlo Lajtha respectively.

With few leukemic patients back in Edinburgh, in 1958, fired up with enthusiasm Dr Jacobs looked for ways to use her newly acquired skills for examining human chromosomes. It was then that she was offered a marrow sample from Dr John Strong, a local endocrinologist. The sample was from a chromatin-positive man with Klinefelter's Syndrome, and in 1959, with the technical assistance of Miss Muriel Brunton, went on to describe her first sex-chromosome abnormality in humans.

Immediately recognising the importance of their observations Dr Court Brown encouraged Dr Jacobs to publish a note in Nature (1959; **183:** 302-03), *(as title)*, by Patricia A Jacobs and Dr J A Strong. Dr Jacobs was 24.

1959 continued to be an outstanding year with the published work of J Lejeune et al., of an additional chromosome 21 (Down's Syndrome), and C E Ford et al., regarding the chromatin-negative female; karyotype 45,X (Turner's Syndrome). That year Dr Jacobs also described the first female with a 47,XXX karyotype. And in 1964 karyotype 48,XXYY was described.

In 1965, following a controversial period regarding studies of XYY patients, both in the UK and US, Dr Jacobs left Edinburgh to be with her American husband and to start a new chapter in her life; taking up an appointment at the newly established John A Burns School of Medicine, in the Department of Anatomy & Reproductive Biology, in Honolulu, Hawaii, studying spontaneous abortions linked to chromosome abnormalities, employing the previously unused, and more precise banding techniques.

Back in Britain, Prof Patricia Jacobs was made a Fellow of the Royal Society in 1993 and was awarded the OBE in 1999.

She continues to work with her beloved chromosomes and with the same enthusiasm for cytogenetics as she had back in the late 50s.[M2]

*These are just some of the people who pioneered cytogenetics in the 20th Century, and the story continues today, with new advances in the understanding of human chromosomes and their function and effect within the body.*

**M2**
The aforementioned text was kindly supplied by **Prof PA Jacobs.**

Personal text is based on reprints from **Nature**, Vol. 183, pp 302 & 303, Jan 31 1959 and **Prof Jacobs'** speech, *William Allan Memorial Award, from the American Society of Human Genetics*, in 1982.



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**Symptom** n.
*an indication of a disease or disorder noticed by the patient.*

**Trait** n.
*typical, distinctive, characteristic feature or quality.*

# KS Traits & Symptoms

**Klinefelter's Syndrome is a variable condition. Some people are seriously affected, while others have mild symptoms.**

## Behavioural & Personality traits seen more in individuals with Klinefelter's Syndrome (KS):

- Concentration difficulties
- Delayed speech development
- Emotional immaturity
- Impaired gross motor coordination in early childhood
- Impaired memory, particularly short-term
- Increased dependency
- Increased frequency of speech disorders
- Lack of self-assertion in early childhood
- Lack of self-confidence
- Low self-esteem
- Lowered endurance
- Lowered IQ, particularly verbal
- Lowered level of attention
- Lowered vigour and drive
- Mood swings
- Passivity
- Poor auditory discrimination
- Poor contact ability and loneliness
- Preference for quiet games
- Shyness & reticence

**PLEASE NOTE:**
The information on this page has been obtained from various support and research groups and from various countries.

Please remember that one KS individual will be very different from another. These are ***possible*** associated conditions only.

Some people will have a lot of these traits and symptoms, some very little, while others will have no perception of them at all — even those who have the same karyotype.

It should therefore be noted that a person with KS will not fit neatly into any particular pigeon-hole or exhibit a specific phenotype. ***"Stereotyping those who have KS into homogeneous profiles should be resisted."*** MD

## Psychological & Physiological symptoms seen more in individuals with KS:

- Autoimmune conditions
- Disproportionately long legs, compared to body
- Increased need for sleep
- Lack of facial and body hair at puberty
- Low or no testosterone production
- Poor muscle tone
- Possible breast tissue (*Gynaecomastia*) at puberty
- Possible gender dysphoria
- Possible oestrogen production with or in place of testosterone *(Caused by ovotestis ie. ovary and testis in one or separate organs)*
- Possible osteoporosis in later life
- Small hard testes
- Small penis
- Sterility*

* Sperm analysis is required before infertility is predicted, as there have been documented cases of paternity.

e.g. **Laron, Z. et al.** (1982; 8(2): 149-51 *Paternity in Klinefelter's Syndrome – a case report.* Arch Androl.





# Karyotypes

**Typical Male:** 46,XY.
**Typical Female:** 46,XX

**Figures taken from various respected UK and International sources**
(Approximate rate per 1000. Example: 47,XXY has 1.72 live births per thousand)

### Klinefelter's Syndrome
47,XXY (1.72) M1
48,XXXY*
48,XXYY*
49,XXXXY*
49,XXXYY*
50,XXXYY*

***Mosaics***
46,XY/47,XXY
46,XX/47,XXY
46,XY/48,XXXY*
47,XXY/49,XXXXY*

### Triple X Syndrome
47,XXX

### XYY Syndrome
47,XYY (1.00) M2
47,XYY,q+ • 47,XYY,16qh+
48,XYYY

***Mosaics*** 46,XY/47,XYY

### Other Karyotypes
46,XX (Male) (1.87) */M3/M6
47,XXX (Male) M4
47,XXY (Female) **/M5
48,XXXX • 49,XXXXX

***Mosaics***
46,XX/47,XX,del(Y)(q11)
46,XX/46,XY

### Turner's Syndrome
45,X (0.2) M3
***Mosaics*** 45,X/46,XX
45,X/46,XY (Male)
45,X/47,XXX
45,X/46,X,r(X)
45,X/46,X,i(Xq)/
47,X,i(Xq),i(Xq)
45,X,inv(q)/46,XX,inv(q)

**del** = deletion **i** = inversion **p** = short arm of chromosome **q** = long arm of chromosome. **r** = a ring chromosome

This table shows only a sample of the karyotypes which I have found to date. Be aware that some lesser known support websites can show correct karyotypes, but incorrectly written, while other karyotypes are definitely iffy or just plain wrong. Please contact a respected support group for general karyotype information. For information of your own karyotype you should talk to your GP or an endocrinologist. In the UK the latter are referred through a GP only.

* Karyotype information will vary depending on the country of origin or the organisation. For example, over the last few years there has been a shift in opinion regarding the rarer KS karyotypes (e.g. 48,XXXY; 48,XXYY; 49,XXXXY). With their own distinct phenotype and clinical presentation an increasing number of endocrinology, research and support organisations now view them as separate sex chromosome variations, in the USA some have their own support groups.

While this opinion exists in many countries, including the UK, there are other organisations and individuals worldwide who continue to view the rarer karyotypes as Klinefelter's Syndrome and continue to support them, though some KS groups may recommend a more appropriate support organisation for the very rare karyotypes.

### * 46,XX Male (De La Chapelle Syndrome)
Sometimes at early egg formation the SRY genes (Sex determining Region of the Y chromosome) attach themselves to an X chromosome, creating an XX male. 46,XX Males have a similar phenotype to 47,XXY (KS) but there is no increase in height as appears with the latter.

### ** 47,XXY Female
There has been a case in Germany of an SRY-negative 47,XXY woman, with a son and two daughters (one daughter also has the 47,XXY karyotype).

### Mosaic M7
In a Mosaic person different cells have different sex chromosomes; ie. 46,XY/47,XXY has typical male sex chromosomes in one cell but in another, KS chromosomes. There are some extremely complex mosaic karyotypes, such as 45,X/46,X,i(Xq)/47,X,i(Xq),i(Xq), (i.e. Turner's Syndrome/typical female/Triple X Syndrome).

M1
**Prof Jacobs, P A. et al.** (2007), *Is the prevalence of Klinefelter's syndrome increasing?* Division of Human Genetics, University of Southampton Medical School, Wessex Regional Genetics Laboratory, Salisbury, UK.

M2 **Prof Jacobs, P A.**

M3
**Intersex Society of North America (ISNA),** paper supplied by **The Gender Trust.**

M4
**Borghi, A. et al.** (1980; 3(2): 163-8 *Endocrinol Invest.* Found on **NCBI (Entrez PubMed)** website USA.

M5
**Rottger, S. et al.** (2001), Germany. Found on **NCBI/MedlinePlus.**

M6/M7
Explained by **Dr Ratcliffe, SG.** *Consultant Paediatrician* Retired).



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Endocrinology
HORMONES

# Endocrinology

## Hormone replacement therapy

At your first endocrine appointment you will be examined and the consultant will discuss your particular treatment. Everyone will be different in how they are looked after.

The consultant will probably suggest that you obtain a density scan, to evaluate the condition of your bones. The DEXA scan is a simple, non-invasive procedure, similar to a film-producing x-ray, i.e. no tunnels, *and you even get to laze for 15 minutes while it checks you out!*

Following that, you may be placed on an osteoporosis therapy to boost your bone density. This consists of a course of tablets, taken daily for a minimum of three years, possibly indefinitely. However, as it becomes part of your daily routine you will not find it a chore. The tablets periodically stop bone breakdown, as well as increase your calcium intake. You may be offered some other treatment.

Next comes the hormone replacement therapy. There are several ways to administer the treatment nowadays, and your GP or endocrinologist will advise you on this, as some will not be suitable for everyone.

**Please note.** The following therapies should only be taken with a diagnosis and support from your endocrinologist or doctor, who will be able to offer you more details and suitability for these and newer methods of treatment. For instance, some products have not been tested on males less than 18, or limited testing on older males (e.g. 65 upwards).

Additionally, some therapy products are only licensed for certain countries.

There are other serious health issues to consider before treatment begins, which will be outlined to you by your GP (MD) or endocrinologist. You also have to 'work' with your healthcare professional; keeping them informed of initial and later side effects.

**Development is ongoing and there are new products appearing, so check with your GP, endocrinology consultant or a KS support group for up to date product information.**

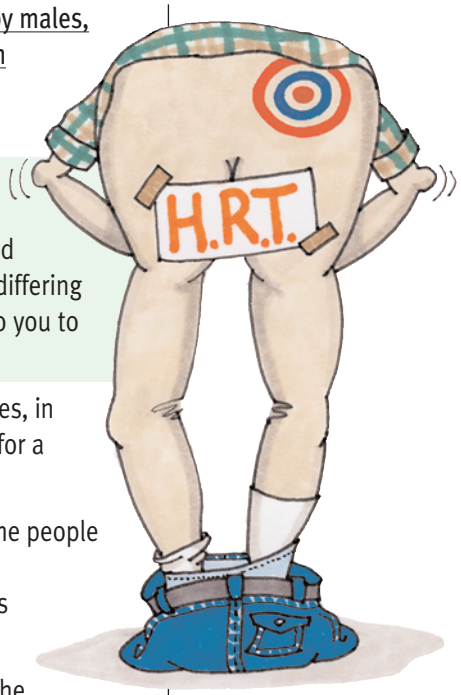
**Methods shown here are relevant to the UK, so may not be available in your own country.**

Take a look at product information at the USA website:
**w:** www.medicinenet.com

There is also product information to be found on some of the major pharmaceutical company websites. Just type the product name into your search engine.



Additionally, testosterone should only be used by males, as masculising will result in women, with changes in menstrual cycles. It will also seriously affect the foetus of pregnant women.




I have included here **support group reports**[M1/M2] on each item's effectiveness, including my own experiences *(italics)*, but at the end of the day everyone is different and will experience differing results. In discussion with your consultant, it's up to you to find what suits you best.

Check out the KSA and KO support group websites, in the UK and KS support groups in your own country, for a full list of products and information relating to each.

**Gel:** This method is set to revolutionise the way some people take testosterone and one which will delight many who miss treatment, or have never begun it, perhaps because they dislike the needle.

Supplied in a pump canister, sachets or a tube, the gel is rubbed into the skin of the upper arm or belly, waiting a few minutes until absorbed before dressing.

**Important information to remember:**

- wash hands thoroughly with soap and water after applying the gel as it can be transferred to others.
- if having sexual intercourse within a few hours of applying the gel, then you are advised to wear a t-shirt, to protect your partner.

**SG report:** Because it is so new there is little feedback on use. Like patches the gel may cause aggravation to your skin.[M2]

**Implant:** This consists of a visit to an out-patients clinic every 6 months, for this gradual release alternative. If you prefer this option talk to your consultant who will give you all the facts.

**SG report:** one person reported that the implant forced its way back out, causing round scars.[M2]

*Contd.*

**M1 Support Group (SG) report**
Based on information from the **Klinefelter's Syndrome Association** website.
**w:** www.ksa-uk.co.uk
*(See p74 for contact details).*

**M2 Support Group report**
Based on information from the **Klinefelter Organisation**
**w:** www.klinefelter.org.uk
*(See p74 for contact details).*



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**M3**
Injections are supplied in the form of Testosterone 'salts' (100mg or 250mg), each being absorbed at a different rate throughout the month.

The way testosterone treatment works was described to me as a series of overlapping bells; with each slow-release salt smoothly linking into the next.

However, in many cases, including myself, it seems that the release is either *not* smooth or one or more of the salts are causing additional reaction in some people.

In the highest dose (250mg), there are four salts (active ingredients), which your body converts into testosterone:
*Testosterone propionate*
*Testosterone phenylpropionate*
*Testosterone isocaproate*
*Testosterone decanoate*

**DID YOU KNOW?**
Although testosterone is secreted in very small quantities, its affect on the body is profound and long lasting.

At the onset of hormone replacement therapy, it is vitally important that you, at least, consider counselling.

One common remark from individuals taking male HRT is the problem of peaks within their prescribed absorption period, which can be quite disruptive for several days – *or more.*

Even the introduction of male-pattern hair can cause distress to some individuals; particularly if they have been without body hair, or have had plenty scalp hair for most of their life.

**Injections:** There are now two versions of the deep intramuscular injection. The original jab with an application varying from three weeks to monthly (though it can be more often), and a newer one just taken every three months (10-14 weeks).

Sometimes known as a depot injection, the drug itself is injected into your rump (upper buttocks) and forms a reservoir of testosterone, which will be absorbed over the stated application period. Injections can be given by your GP or practice nurse to ensure you don't forget your dosage. It takes only seconds and you're done. Some GPs offer self injection, while other people prefer the professional touch.

***Trust me—*** *The needles are so sharp nowadays that most times I feel only a little pressure on my rump. Sometimes not even that. Occasionally there is a wee nip, and I mean a* ***wee*** *nip... LOOK, IF A WIMP LIKE ME CAN DO IT, ANYONE CAN!*

There are mixed reports on the monthly/three week distribution. Some groups report good results, while others find horrendous libido peaks.

*For the first few years after commencing hormone treatment I generally found a strong peak about a week after the jab; which resulted in about 7-14 days of hyperactivity (if you get my drift); when the least stimulus set me off...*[M3]

*Then for about a year it very slowly began to level out. 13 years on, throughout the entire month I drift through a kind of generalised medium-grade haze of sexual awareness. Perhaps my brain has got used to the hormone, or perhaps I've finally departed my second puberty, ready to responsibly face society – again!*

**Patch:** This is a transdermal drug delivery system, which you will have to replace daily. It comes in various dose strengths. Higher body weight can also affect daily dose.

This therapy may not have been tested with children. Discuss other options with your doctor or endocrinologist.

**SG report:** Complications usually take the form of skin reactions and difficulty sleeping with the rustling noise it makes.[M1]



*I tried them a few years ago to see if there was a better hormone balance. The spread was good with no recognisable peaks, however there are few places to position the patches and if you get them on a hairy site – well you know what it's like removing a sticky plaster where there are hairs — imagine a three inch square plaster!*

*In my case hairless days are over, 13 years of male HRT have seen to that, so I found I was placing them back on the same place, with resulting irritation to my eczema. Also the patch was made of crackly plastic that drove me nuts; like sleeping on a packet of crisps! And so after 3 weeks of perseverance I gleefully returned to the injections!*

*That said, if you are new to replacement therapy; and are clear of hair, give them a try.*

**Tablet:** You will have to remember to take them as prescribed. Again, this type of therapy may not have been tested with children.

**SG report:** some people have felt a little depressed as the dose wears off.[M1]

**Tablet (buccal sustained release):** A very small tablet-like product is placed between your gum and lip, just above one of your upper front teeth, which then becomes gel-like and sticks to the surrounding tissue. It's called a 'buccal sustained release system', as once placed, the tablet gradually releases testosterone which is absorbed *directly* into your bloodstream. So don't chew or swallow the tablet.

Dosage is twice daily (12 hours apart). You will need to periodically check to make sure the tablet is still in place, such as after eating, brushing your teeth or using a mouthwash.

There are a number of side effects with this method of application, so let your GP know if you experience anything unusual. K

**DID YOU KNOW?**
**40,000 +**
Taking an upper age of 80 and the current estimated annual rate of 400-500 live births which have a 47,XXY karyotype, and you have a potential 36-40,000 individuals with this condition.

Add to that, the other rarer Sex Chromosome Variations, including mosaics and Triple X Syndrome, plus loved ones, healthcare professionals and those working with children & young adults and there is a sizable population who could benefit from reading and utilising this book.

**And that's just in the UK!**



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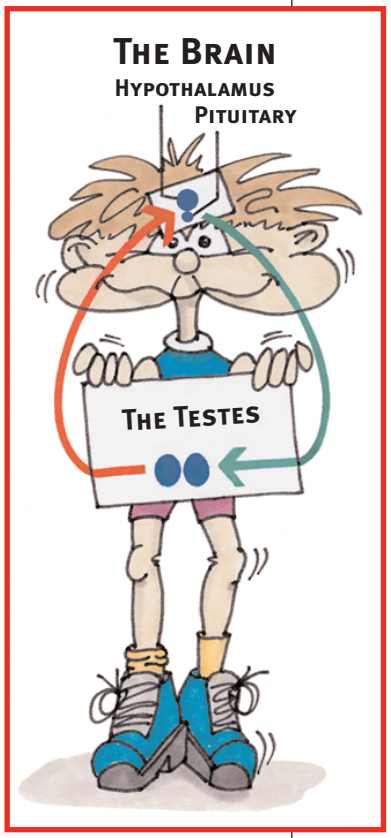
## The Feed-back Response in testosterone & spermatozoa production




THE FEED-BACK LOOP — Stimulate / Feed-back control

# Hormones – the chemical messengers

There are two types of gland within the body. Endocrine glands, which produce (secrete) substances directly into the bloodstream, which then transports them around the body to 'target glands'. These are called 'Ductless Glands.'

The other type is the Exocrine gland: which employs ducts to direct their products into the area where they are required, (i.e. salivary glands).

But for this chapter, and for your understanding (*hopefully*) of Klinefelter's Syndrome it is the secretions of the Endocrine System that are important here.

The latter secretions are called 'Hormones', and can be thought of as chemical messengers; sending instructions all around the body.

Hormones are produced in minute quantities yet their effect on the body can be profound and sometimes long lasting.

A few endocrine glands control themselves, but the majority are controlled by the Pituitary gland; which for this reason is called the 'Master Gland' of the endocrine system. This pea-sized body is located in a bony cavity at the base of the skull, just under the Hypothalamus to which it is connected.

The pituitary gland can regulate the production of hormones within a particular target gland (TG), by producing a 'Stimulating Hormone.' These stimulating hormones are regulated by specific 'Releasing Hormone' which is produced in the Hypothalamus.

The stimulating hormone 'tells' the TG to produce its particular hormone. If too much hormone is produced it sets up a 'negative feed-back response' to the pituitary gland, which produces less of the stimulating hormone, and so the TG produces less of its hormone.

Several glands are controlled in this way, including the testes. *(See diagram)*.





## *The Endocrine glands*

**Adrenal gland:** Situated on top of each kidney and produces the hormone adrenaline. This prepares the body for 'fight or flight' by raising blood pressure; increasing heart-beat and breathing rates; increases the amount of glucose released from the liver and increases the amount of blood to the muscles and reducing the amount to the gut.

**Pancreas:** Situated below the stomach, one part produces digestive juices, while the '*Islets of Langerhans cells*' produce the hormones glucagon, somatostatin and insulin, the latter of which increases the rate that the liver releases glucose into the blood; enabling cells to absorb glucose and stimulates the body to change glucose into fat.

If too little insulin is produced the liver releases too much glucose, causing the condition 'sugar diabetes' (Diabetes Mellitus - type 1 & 2). This causes the glucose in the blood to increase to a dangerous level.

**Parathyroid gland:** Four small glands embedded within the thyroid. Parathyroids are sensitive to calcium levels in the blood. If there is too little, the gland releases the hormone parathormone which increases calcium absorption in the intestine; withdraws calcium from the bones and increases re-absorption of calcium by the kidney tubules.

**Pituitary gland:** Produces hormones which control growth. Other hormones cause the ovaries to release ova (eggs); testes to produce spermatozoa (sperm); the uterus to contract and expel the fetus at birth; and the mammary glands (breasts) to produce milk. Other hormones control the amount of water in urine and the activities of other endocrine glands.

**Placenta:** Apart from its main function within the uterus this organ also acts as an endocrine gland secreting Progesterone, oestrogen and Chorionic Gonadotrophin, which regulates the maintenance of pregnancy.

**Thyroid gland:** Situated in the neck in front of the trachea (wind-pipe). It produces the hormone thyroxine, which has a major influence on the mental and physical development after birth, by controlling the rate of chemical reactions in all body cells.

**Ovaries:** Two organs situated in the lower abdomen, below each kidney. They produce ova (eggs). The ovaries also produce the hormone called Oestrogen which controls the development of female secondary sexual characteristics (breasts, soft skin, female voice); prepares the uterus (womb) to receive a fertilised ovum; stimulates the uterus to protect and nourish a developing baby.

**Testes:** Two organs situated in the groin within the scrotum and produce spermatozoa (sperm). The testes also produce the hormone Testosterone which controls the development of male secondary sexual characteristics (coarse skin, deeper voice and more body hair than in females).

### The Feed-back loop

*(See opposite margin)*
Hypothalamus produces Gonadotrophin Releasing Hormone (GnRH). (Target gland: pituitary gland).

In response to GnRH stimulation the pituitary gland produces Luitenising Hormone (LH); for testosterone production, and Follicle Stimulating Hormone (FSH); for sperm production.

Testicles contain the Leydig cells which produce testosterone and the seminiferous tubules which produce spermatozoa (sperm).

The level of testosterone is controlled by the feed-back loop.

The Pituitary gland and Hypothalamus monitor the amount of testosterone in the blood and control how much is produced; by regulating their own hormones.

**DID YOU KNOW?**
C19, H28, O2 is the element formula for the principal male androgen; testosterone, while – C18, H24,O2 is the formula for the principal oestrogen; oestradiol.

How close we are.



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# A Personal Message

1997 changed the way I viewed my life; past, present *and* future. It put a name to 45 years of fears and embarrassment, and to what I felt but could never tell anyone about. It was the year that I was diagnosed with Klinefelter's Syndrome.

The punchline was somewhat lost on me however, as at the time I was undergoing hospital in-patient tests to discover the cause of acute pain and weakness in the quadriceps of both my legs. And with still no light on the latter problems, I certainly wasn't expecting to be diagnosed with another medical condition.

Some weeks later on leaving my first visit to the endocrine out-patient clinic, having just discovered that a huge chunk of my life had been affected by this condition, I asked a junior doctor if there was any printed information on Klinefelter's Syndrome. He handed me a small pamphlet titled: '*Hypogonadism in Adult Men*', which to be honest confused me even more.

I thought to myself, *call me insensitive, but having just been told I had Klinefelter's Syndrome there was only ONE pamphlet available, amongst the piles of literature on other endocrine conditions – and what the hell was* ***hypogonadism?*** Being my usual non-confrontational self; I thanked the doctor and left.

It wasn't until a few months later; when I began to look into the background to KS that I realised the true extent of what it really means to have Klinefelter's Syndrome.

Amongst the day-to-day business and social struggles and treatment for the crippling leg pain and allied stress, it had not dawned on me at that point, that my search to piece together a clearer picture of my condition had in fact set me on an academic course unparalleled in my life, and one which would last well over eleven years!

It also became clear as I progressed that Klinefelter's Syndrome involved more than just endocrinology. There were many other fields involved, such as: clinical & surgical medicine, genetics, gender issues, rheumatology, orthopaedics and neurology.

You have to understand that much of my academic years were a disaster, so studying was going to create its own degree of challenge. But here I had a quest for information; something vitally important in my life, something that would help me understand my life and enable me to cope more fully with my symptoms.

As usual, my spelling and grammar went out the window and my English and medical dictionaries became constant companions, but it's truly amazing what you can achieve when you're interested in the subject you are learning about.

Of course, while I progressed with my studies into KS the various medical specialists were beavering away trying to discover the original leg condition, with x-rays, electromyography, a nerve induction velocity test and muscle biopsy – joy!

Unfortunately, for the first three years of my study into Klinefelter's Syndrome I had no access to the Internet. I would spend days in feverish letter writing, followed by weeks of non-activity, as I awaited replies. Then in 2001 I discovered that my local library offered Internet access, which transformed the way I studied, and the staff were so helpful. Believe me, the Internet makes a humongous difference to the speed and ease of collecting information.

Eventually, in 2002 with family support I managed to purchase a secondhand computer upgrade — *with a modem!*

I guess there will be many individuals that on leaving the endocrine clinic for the first time will be quite happy to leave it at that. Everyone is different - but some (like myself) *will* want to know more and that is the primary reason for this book.

In my own case, I don't agree with the adage that too much information turns you into some kind of hypochondriac. After so many years in the dark and a general nature for trying to understand how things work, I found that I was drawn to discover more. But again everyone is different.

Everyone will have their own set of circumstances regarding the 'telling' of their physical and/or emotional differences to parents, spouse/partner or to their family doctor. And of course if you have their support, study should be that much easier; as you won't be resorting to covert tactics.

I plunged into my studies with the enquiring mind of a child learning about the world for the first time. After studying cells and chromosomes I found myself delving deeper; trying to understand DNA, then its components, gene replication, protein production, human reproduction, anatomy, orthopaedic surgical techniques...

For weeks I was obsessed with the mind-blowing design *and* beauty of the human body – an enthusiasm that exists to this day. Strangely, I can remember the *'central subdivision of the bed nucleus of the stria terminalis'*, but I keep forgetting to water my plants!

It would be fair to say that my grammar and spelling are appaling and in any other written work it would be strongly suggested that I *"don't give up the day job."* However, Klinefelter's Syndrome can affect academia big time, *(see p22) that's my excuse and I'm sticking to it!* Correcting my scribbles has probably only taken the edge off the worst of it.

Although I have been studying the many facets of Klinefelter's Syndrome for the past 12 years and sound like an expert, I'm not. I have only scratched the surface. It is the research & support groups and medical publications with whom I have obtained study information who are the stars.

Growing out of my own academic flaws and subsequent frustrations in trying to find and understand facts about my condition, my primary objective was to compile a book which would direct the reader to *respected* UK and international research, support and information resources.





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Obviously there are many thousands of websites, papers, journals etc., which I have not yet accessed, but what is important is that with this book you now have a reasonable contact database to commence your own studies.

I have learnt a great deal from my own studies into Klinefelter's Syndrome. It has put names to feelings and removed the fear of uncertainty. It has taught me the value of talking to and working with my GP and in the importance of seeking advice on endocrine and osteoporosis therapy. But above all, it has shown me that I didn't have to suffer in silence; that there are others out there just like me, specialists who are ready to help and support. People who have KS, who know what I'm going through and lift my spirit with their honesty and compassion.

## When no one knows

People see the 'normal' external persona of those with KS and particularly with regard to children, adults may think that their son is just hamming it. They don't sense the physical and psychological maelstrom that some children might feel within.

Some people believe that because the national diagnosis figures are so low that it follows that the majority of males aren't severe enough to warrant them seeking help. While there will be many who are not severe, from personal experience and from talking to individuals and support groups it is clear that from an early age many children with KS hide their physical differences and emotions.

With the hassle of everyday life and the trials and tribulations of all family members, without knowledge of KS, children may close off their feelings to those around them, usually because they think no one will believe them, they may be too embarrassed, or perhaps just don't know how to express their feelings. And so throughout their life they live with their secret – or until they are eventually diagnosed.

Because I felt embarrassed about my chest proportions, since the age of about 10 or 11 I have always worn a top of some kind when in public—*even on the beach*. And no amount of comments such as ***"there are far worse bodies out there than yours"***, would ever convince me to uncover. Stripping to the waist felt unnatural to me; more akin to a female going topless than a male.

From experience, at 10 years old, the thought of surgery (whether or not it was viable), was extremely frightening so I never let on that I had hard lumps beneath my areola, even though they were painful if prodded.

*Quite often diagnoses of Klinefelter's Syndrome is made in childhood or early teens as a result of discovering glandular tissue (gynaecomastia).*

Puberty is a period of extreme physical and emotional change and stress for any child, whether or not they have KS. For some individuals with KS puberty can be a minefield of lies, embarrassment and loneliness. When lumps appear; whether gynaecomastia or fat deposits, or a son's body shape doesn't match up to that of their peers, it is unlikely they will confide in their parents. However, if a parent is overly





concerned about their child, there are non-confrontational ways to discover whether there is an underlying reason; by seeking their GP's advice.

It is important to look out for other traits; such as low self-esteem, passivity, inability to concentrate... (*see p22*).

You could also talk to other parents who have gone through the same thing. *(Please see **Further Study** p74, for family related support groups)*.

## When parents know

The latter family groups are of particular value when the situation arises where a son has been diagnosed in childhood, and it comes to the inevitable point when the parents have to decide how, or if, they should tell their child the truth.

When the truth is withheld, the child may think that their parents are hiding something from them, though sometimes holding back to a later age is more preferable; for instance, if the child is immature.

Some clinicians believe that when a boy is about 10 or 11 years old, parents should inform them that they have body cells which are slightly different from other people, and that is why they are attending hospital clinics. Then around 12-18, more detailed information can be given; including the fact that he *might* be sterile.

That said, parents know their child and at what age they can be told certain aspects of the condition. So it is vitally important that their child's emotional maturity is evaluated before embarking on heavy-duty details. The scenario being that at 12 years old it could be so easy for him to casually pass on his 'secret' to a pal, only for them to thoughtlessly pass it on to someone else, mistaking 'infertility' for a 'sexual disorder', leading ultimately to possible bullying tactics.

So you can see the value of talking to other families and to professionals who can give you help and support.

## Possible gender issues

I would like to say at this point that everyone is different and I talk from my own experience and stress that currently medical research sees no direct link between KS and gender dysphoria, though to gender support groups there are a good many people who exhibit both.

***However, don't automatically assume anything, until you get specialist advice.***

Even having been diagnosed with Klinefelter's Syndrome, there can still be other issues and powerful emotions which some will find hard to express – *to anyone*.

I am blessed with a loving and supportive family, yet through puberty and into adulthood, with no idea of KS, I was unable to open my feelings to them. I had physical differences, but I had something else – something so sensitive I said nothing to anyone until I was in my early fifties.

Since around puberty I have felt *partially* feminine. It's hard to express the amount, but I guess it's around 15%.

I have had no interest in changing sex or gender role; that is there has never been any



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confusion over being anything other than a ***man*/male** and heterosexual.

After 35 years of silence, I really needed to know about my gender issues, but I was embarrassed, unable to talk to anyone and no idea who to contact for information.

Thinking that one of the endocrine doctors would know, I plucked up the courage. Although he made a gallant effort to answer my questions it was an utter disaster, for he knew nothing of this subject and of course it resulted in tangible embarrassment for both of us and inner anger towards myself for having put both of us through that cringing ordeal.

When I eventually contacted one of the gender support groups I was staggered by their vast experience and understanding of emotions such as mine. I can't express in words how I felt that day, listening to the confidential contact on the phone.

Having studied KS for so long I became confident enough to eventually talk to my GP and it was fine, not the big deal I thought it was going to be. And he was so supportive and understanding I wished I had talked to him sooner.

I have recently discovered that I am 'Androgyne.' This is different from being a Transsexual or Transgendered person.
*(See the chapter **The Sex/Gender Spectrum – Terminology & Usage**, 'Androgyne', p67).*

## You are not alone!

From talking to various support groups the most widely felt emotion expressed by those with Klinefelter's Syndrome is the feeling of being alone. Often not aware of what is happening to them, they withdraw into themselves; unable to talk to family members, spouse/partner or to their GP.

And of course nobody around them knows what they are going through, making assumptions – such as that they are gay; because they are not interested in girls/women, or a wimp because they won't participate in physical education or rough competitive contact sports.

Though in general children with KS are passive, there can be mood swings. This is particularly true of adults, with disruptive outbursts, usually due to frustration.

Throughout my life I have been a pussycat— to a point. Then, through building frustration I would suddenly snap, totally losing the plot. Thankfully, it has mostly been inanimate objects that have received my unswerving attention.



Over the years I have learnt to reduce the ferocity of the outbursts; otherwise I would tend to destroy whatever fiddly thing I was trying to create or mend.

Back in 1997, eager to commence my studies into Klinefelter's Syndrome, it seemed then that it was a straightforward and relatively easy to reach goal.
*How wrong I was!*

It would have been a waste to just file away all the knowledge I have collated and learned over the past eleven years, and so I offer it to you, in the hope that it helps you or someone close to you to understand more fully the complex nature of Klinefelter's Syndrome.

**Left:**
***AAAAAAAAAAAAAAAAAAAAAAAAAAAAH!***
One of those fiddly jobs that didn't quite go to plan!
And yes – that might be me!

As I have said, I may not be the world's greatest writer, but the work is – to the best of my ability, honest.

***So please trust me.*** *There is someone out there right now, waiting to hear from you, someone with experience of Klinefelter's Syndrome – and the many other facets that accompany this condition, who is ready to listen, to offer advice, and to ease your mind. And if you're too embarrassed at this stage to talk to someone, go to one of the support group websites.*

*Whatever you decide to do—*
***please remember,***

**You are not alone**



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# The Symptom Story

## The physical and psychological aspects of Klinefelter's Syndrome

### Loneliness and fear

Klinefelter's Syndrome may not be life threatening, but it can cause untold suffering. Many experts will tell you that with early diagnosis and with the appropriate treatment children and later adolescents with Klinefelter's Syndrome can lead a 'normal' life.

On the other hand, researchers will point out that because of the complex nature of Klinefelter's Syndrome the majority of individuals will not be diagnosed until adulthood. So, what happens if you are into your 30s, 40s, or even 70s, and have gone through your life with both the physical and psychological symptoms, but not the diagnosis – how ***'normal'*** a life is that?

There can be the sense of loneliness and fear associated with those symptoms, when you feel you're the only one in the world like that and there is no one to talk to.

For those in their early teens, from experience, it can turn school days; supposedly *'the happiest days of your life'*, into a minefield of lies and deceptions, as a teenager with Klinefelter's Syndrome finds ways not to participate in rough competitive games, or change and shower for physical education.

In sport, often it is a case of having to endure being left as a spectator, or picked last, usually in goal or a place where you don't have major participation. And afterwards in the shower-rooms, it is common for boys of that age to compare genital size, which for those with KS is an absolute no-no.

It is often the case that the teenager will be bullied by boys and ridiculed by the girls for being weak and will cry at the drop of a hat, which also incurs the wrath of their peers.



### Additions and Losses

There is another element to the physical aspects of KS — that of breast tissue *('Gynaecomastia')*. Again this is a point of ridicule and also happens to thousands of typical males. Figures range from 30-60% of the general population, with most cases starting and ending during puberty. Generally, those with breast tissue have hard, often painful lumps behind the areola (the pink or brown area surrounding the nipple).

While many individuals with KS are 'pleasantly plump' to obese, gynaecomastia is not caused by being over-weight, but by glandular tissue surrounded by fat deposits; similar to a woman's breasts and can't be 'cured' by diet or exercise. The cause is generally a hormone imbalance, which is why it can affect those with Klinefelter's Syndrome.

Some males hate their breasts and want them removed. Some tolerate them, while others grow to love them, though this normally takes many years. Those affected go through all manner of emotions, sometimes even questioning whether they are male. Breasts can range in size from small buds to double Ds.

To the individuals involved there can be severe embarrassment and low self esteem, and like KS, many teenagers find it impossible to talk to their parents about it. Often the person will wear loose fitting clothes to try and hide their lumps and will stay covered in public places, such as the beach.

As mentioned, usually gynaecomastia is temporary but in some cases it can persist into adulthood. If this occurs, often doctors will suggest surgery. Prior to the 80s surgery was basic; in some cases brutal and generally disfiguring. However, the latest procedures employ liposuction through a tiny hole to remove the fat deposits. To remove any glandular tissue (the hard lumps), small incisions are made at the lower edge of the areola to minimising the appearance of scarring.

While many individuals will be delighted with the surgery and adjust well to having a flat chest, some males who have lived with

#### Testicular Self-Examination

While it is relatively easy for a typical male to regularly check their testicles, it is far more difficult for those with KS, as often the testes are butter-bean in size. But you should still try.

Testicular self-examination is primarily to help you become familiar with your own anatomy and able to detect changes from a previous exam, such as a hard lump (which could be cancerous).

You are also looking for pain or swelling in the scrotum. (You should seek immediate medical attention if you have **acute** pain or swelling in the scrotum). A missing testicle may mean it hasn't descended properly.

Each testicle should feel firm but not rock hard and can be slightly larger, or higher or lower than the other.

The examination should be done monthly, standing in the shower or bath, while the scrotal sac is warm and relaxed.

1) Gently feel your scrotal sac to locate a testicle.
2) Firmly but gently roll the testicle between the thumb and fingers to examine the entire surface.
3) Repeat for the other testicle.

If you discover anything, or you have questions or doubts, get in touch with your GP (MD).

**Remember, early action can make a difference.**

Based on information from: www.nlm.nih.gov/medlineplus/



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**M1**
Changing from female pattern hair to male can also result in loss of hair. This can be profound and in some men can happen within two years of the commencement of testosterone therapy. But everyone is different and like the general population scalp hair loss is variable.

**M2**
While a large percentage of individuals with KS appear to be happy to be a man/male and to maintain that gender role, other individuals see themselves quite differently.

This is a highly complex subject and one which is explained in full in ***The Sex/Gender Spectrum – Terminology & Usage*** chapter, starting on p63.

So, please don't make casual assumptions about a person based on attributes such as voice, appearance, etc.

**M3**
This sexologist agrees that 'Nurture' plays a role in the formation of our ultimate gender identity.

**M4**
Don't get confused between *Gender Dysphoria* and *Sexual Orientation*; they are quite different. *(See **The Sex/Gender Spectrum** chapter).*

breasts for many years may take some time to come to terms with the change; possibly still wary of uncovering. It is therefore suggested that adults consider either counselling or talk to a support group for advice and help.

And after starting testosterone therapy, even the addition of body hair can be upsetting to some men. Having spent many years with a few hairs spotted here and there, to be confronted with great swathes of long hair on the chest, belly, groin and back within a few years, can create a very negative response, resorting in some cases to covert shaving and waxing.[M1]

## Gender and sex issues

The physical embarrassment is only part of the story as on rare occasions the individual can also start to experience 'feelings' or a sense of being other than their outwardly perceived gender – that is a boy who feels partially or totally feminine.[M2] This can happen from around puberty onwards. Worst of all, it creates anxiety, loneliness and in some cases even thoughts of suicide.

***"Gonads produce hormones that affect the brain and it's our brains that tell us whether we're male or female. In most cases, there's a physical reason why individuals might be unsure about their sex."*** [MD/M3]

Additionally, according to research carried out in the 90s, if you have KS you are no more prone to sexual orientation changes than the general population.[M4]

## Other Karyotypes

While not wishing to detract from the grief you may be going through, like so much in life, there are always others with different concerns. There are other more severe karyotype conditions, with very rare cases reaching three additional X chromosomes (i.e. 49,XXXXY). There are also mosaics (e.g. 46,XY/47,XXY) and the 47,XYY and Triple X Syndromes *(see **Karyotypes** p23)* and of course other genetic and hormone related conditions.





The paramount thing to remember is that ***you are not alone***; there are dedicated people out there right now doing a power of good. People with Klinefelter's Syndrome (and other genetic and hormone related conditions), including parents who have set up support groups to help other families.

These are people who have gone through, and are still going through the same things as yourself, who are ready and waiting to listen and to give valuable support in a caring professional way.

Whatever your age, don't be afraid to contact them – you don't have to suffer in silence. If you feel unable to talk to those close to you, or you're not quite ready to talk to your doctor yet, take a note of one of the groups mentioned in the ***Further Study*** chapter.

From personal experience, it can make a *huge* difference to your state of mind.



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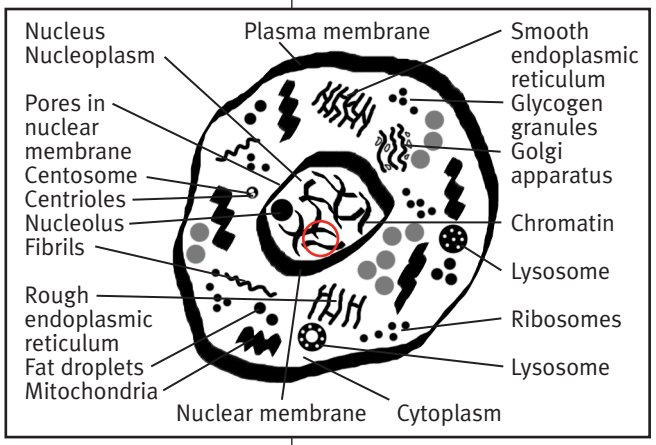
Genetics

# Chromosomes

## What they are and where they are in the body

## The Cell




**Above:**
The various structures within the human cell.

### The Cell

Perhaps the best place to start is within the cell; the basic unit of all living organisms. A human adult has a hundred million million of such cells; making up the bones, tissue and organs of the entire body.

Each cell is contained within a cell membrane of lipids and protein, which controls the passage of substances in and out of the cell. Cells contain cytoplasm, in which are suspended a nucleus and other structures (organelles), specialised to carry out particular activities in the cell.

Laying within the nucleoplasm of the cell nucleus is the chromatin; the material which contains DNA (Deoxyribonucleic Acid) and protein. The substance of which chromosomes are made. *(Diagram above, Red circle).*

### The Chromosome

The chromosome is a thread-like structure in the cell nucleus that carries the genetic information in the form of genes.

It is composed of a long double filament of DNA coiled into a helix, with the genes arranged in a linear manner along its length, together with associated proteins and ATP; for energy.

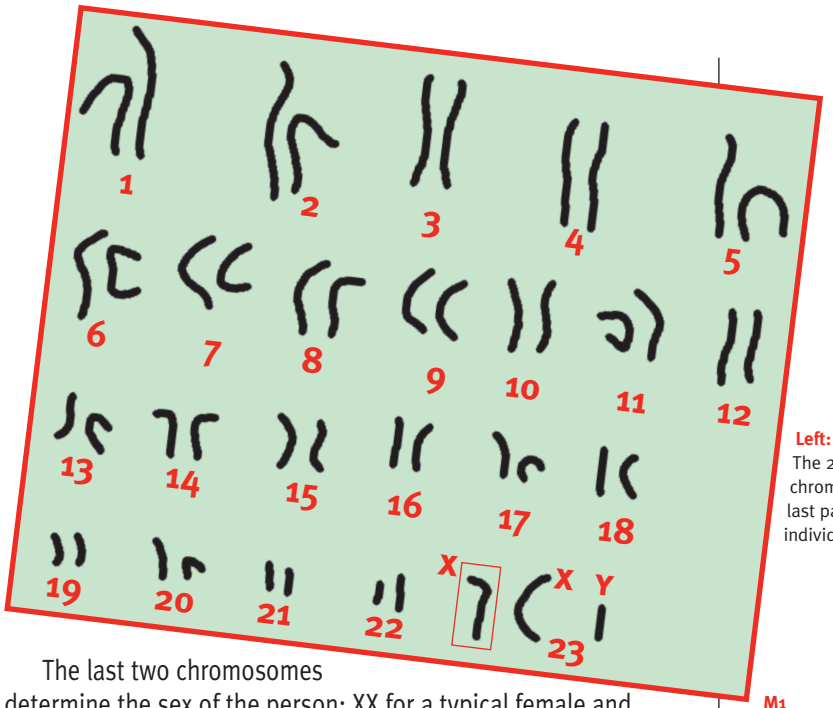
The nucleus of each typical human somatic cell contains 46 chromosomes, 23 of which are of maternal and 23 of paternal origin. The sex cells (sperm & ova = gametes) always contain half the number of chromosomes of all the other cells of the body; at fertilisation a sperm and ovum combine to form a cell with a complete set of chromosomes that will develop into the embryo.

**DID YOU KNOW?**
It was the American cytogeneticist **Nettie Maria Stevens** (1861-1912), who discovered through her fertility experiments with mealworms that there were distinct differences between the sex and the chromosome type of females and males, calling them 'X and Y'.

Her work was published in May 1905.

Based on information from **Net Industries, LLC** and **Advameg Inc** websites.






**Left:**
The 23 pairs of chromosomes, with the last pair determining the individuals sex.

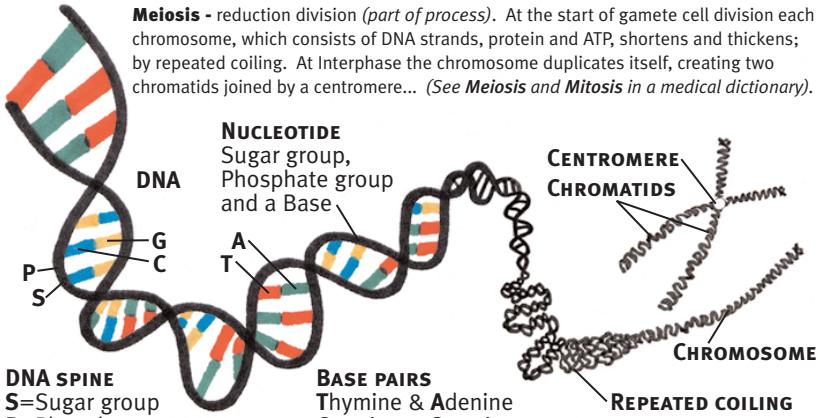
The last two chromosomes determine the sex of the person; XX for a typical female and XY for a typical male.[M1]

Each chromosome is a different part of DNA, or sequence of the four bases. K

**M1**
A boy with Klinefelter's Syndrome has one or more extra X chromosomes; creating, in the above case, a 47,XXY karyotype. *(See also **Karyotypes** on p23).*

## Structure of a Chromosome

**Meiosis -** reduction division *(part of process)*. At the start of gamete cell division each chromosome, which consists of DNA strands, protein and ATP, shortens and thickens; by repeated coiling. At Interphase the chromosome duplicates itself, creating two chromatids joined by a centromere... *(See **Meiosis** and **Mitosis** in a medical dictionary).*



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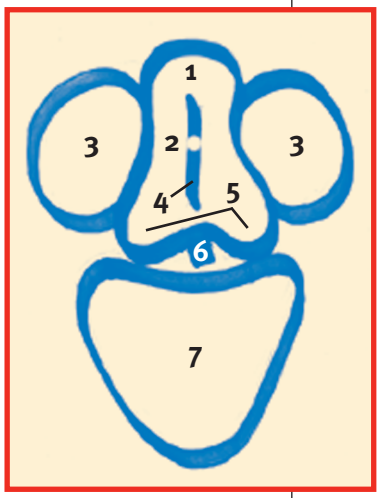
# Human Reproduction

## The Female

### Embryonic external genitalia

1 Glans
2 Urethra
3 Labioscrotum
4 Urethral grove
5 Genital ridge
6 Anal pit
7 Tail




**DID YOU KNOW?**
There is a higher risk of a child developing a genetic condition, e.g. Cystic Fibrosis, Down's Syndrome or Klinefelter's Syndrome, if a woman conceives later in life. Generally, clinicians see this as over 35. Also recent research points generally to a dramatic fall in fertility after 28 years of age.
*(contd. on p46)*

*There are four ways of recognising a baby's sex;*

**Genetic sex** (its karyotype – e.g. 46,XY);
**Biological sex** (according to internal organs);
**Biological sex** (according to external sex organs);
**Brain sex** (structures which are believed to be linked to a particular sex).

At fertilisation, within a Fallopian tube the chromosome type is established (**Genetic sex**) i.e. XX typical female; one X maternal, one X paternal. The cells of the developing zygote begin to divide and within a few days implants itself within the the uterus. The overall term for the products of conception is an 'embryo'. At the 8th week it is known as a fetus. *(See p44-45).*

### From the 3rd to 7th week

Tissue around the developing kidneys and gonads changes into a variety of tubes and ducts; the beginnings of the internal organs of reproduction.

Although all the main organs of the body develop at the embryonic stage, the external sex organs for both males and females start on the same basic path, that is identical **'Biological sex'**, resembling neither female nor male. *(See diagram to left).*

### The 8th to 12th week

At this point the sex organs are formed. If there is an absence of androgen (testosterone), the genitals are pre-programmed to become female, regardless of the genetic sex, (e.g. XX), and alters the developing gonads into ovaries.

An XX foetus will typically have no masculinising hormone (testosterone), and so the male structures called Wolffian ducts begin to die under the influence of Mullerian Inhibiting Hormone (MIH), and the external structures take on the female form of the: clitoris **1** labia majora (outer labia) **3** vagina **4**.

There are also various genes which assist in the process by preventing the development of male hormone producing structures; such as Leydig cells.



After this point the ovaries then produce oestrogens which instructs most of the rest of the development, including assisting the development of the Mullerian ducts into the uterus, fallopian tubes, cervix uteri and upper part of the vagina.

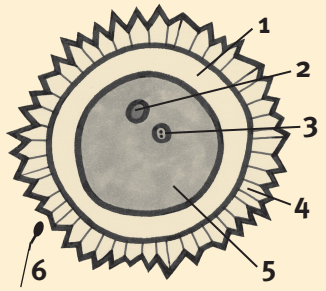
Sexual orientation, sexual identity and gender expression are wired in stages throughout pregnancy. As with the sex organs, differentiation of the female brain takes place due to a lack of testosterone during this period.

In both females and males, currently at birth, social gender is assigned strictly based on external genitalia.

### Not quite the typical

There are many ways in which the aforementioned 46,XX karyotype development can be altered. A change in Meiosis can cause Triple X Syndrome (47,XXX), as well as mosaics. *(See p23).*

### Mature Ovum




**1** Zona Pellucida **2** Nucleus
**3** Centrosome with 2 Centrioles
**4** Corona radiata **5** Ooplasm
**6** Spermatozoon

The absence of anti-male genes can alter the internal anatomy, while the presence of testosterone (secreted from the adrenal glands), can masculinise the external organs (as in the condition Congenital Adrenal Hyperplasia – CAH), and some research suggests even the brain.

### Ongoing research

It is currently believed that for both sexes, the feeling of having a particular gender identity comes predominantly from **Brain sex** (physiological), while, as previously mentioned, **Nurture** plays a part in the formation of our ultimate gender identity.

Recent research in the Netherlands points to a fundamental relationship between physical structures in the brain and gender identity and behaviour. However, ***"we don't know yet whether the sexual dimorphic structures described so far in the brain are the cause, or just a symptom of gender dysphoria and I don't think we will know soon."*** DS/M1/M2

**M1**
**Prof Dick F Swaab,**
Netherlands Institute for Neuroscience, Amsterdam.
*(See **Further Study** chapter for details, p76).*

See also an article on Prof Swaab and other gender related topics, in the **New Scientist,** (12th May 2001, No. 2290, p31), *Gender.*

**Brain Sex related:**
*'IT MAY BE YOUR BRAIN NOT YOUR GENITALS THAT DECIDES WHAT SEX YOU REALLY ARE.'*
Full story, see **New Scientist,** (19th October 2002, No. 2365, p17).

***'Our brains could be hard-wired to be male or female long before we grow testes and ovaries.'***

Contrary to current understanding of early human development (read this chapter), research carried out in the USA on rodents back in the late 90s, showed differences between males and females in the expression (switching on) of a staggering 50 genes, well before the SRY gene gets a look-in.

This of course is sexual differentiation of mice, not humans. So the next step will be to show that these genes truly influence the brain - and not just in mice. It is then hoped that in the future, through a simple blood test, doctors will be able to accurately establish the Brain Sex of new born babies who have ambiguous genitalia, taking the guesswork out of it for clinicians, and the possible emotional turmoil to parents and ultimately the child.

*Continued p44 margin...*

**M2**
*(See **The Sex/Gender Spectrum - Terminology & Usage,** starting on p63).*

*Continued from p43 margin.*

The two papers mentioned in the New Scientist, 19th October '02 article by Andy Coghlan are:
**Vilain, E. et al.**
*Sexually dimorphic gene expression in mouse brain precedes gonadal differentiation.*
Department of Human Genetics, University of California, Los Angeles, USA, and –
**Carruth, L.L.[1] Reisert, I.[2] Arnold, AP.[1]**
*Direct effect of sex chromosome genes on sexual differentiation of the mouse brain in vitro.*
**1)** Department of Physiological Science, and the Laboratory of Neuroendocrinology of the Brain Research Institute, University of California, Los Angeles, USA.
**2)** Unatomie und Zellbiologie, der Universitaet Ulm, Germany.

See also: **Mayer, A. et al.** (1998), *The Y-chromosomal genes SRY and ZFY are transcribed in adult human brain,* Department of Anatomy and Cell Biology, Ulm, Germany and The Netherlands Institute for Neuroscience, and **Reisert, I. et al.** (1995), *Catecholaminergic Systems and the Sexual Differentiation of the Brain.* Anatomy and Cell Biology, Ulm University, Germany.

**DID YOU KNOW?**
Klinefelter's Syndrome is classed as a genetic condition. However, KS is ***not*** an hereditary condition.

It is a change in Meiosis, and is only called a genetic condition because of the additional X chromosome(s).

**DID YOU KNOW?**
***Meiosis*** (reduction division), creates 4 daughter cells with only half the chromosomes of the mother cell (i.e. 23). It occurs before the formation of ova and sperm.

While in body cell reproduction, ***Mitosis*** produces 2 cells, with the full 46 chromosomes.

# The Male

## 3rd to 7th week

Males start off in similar mode to females, however around the 6th week if the embryo is genetically male, genes on the sex chromosome, in this case Y, (SRY gene)[M3] signals the creation of testicular cells, called Sertoli cells. With the assistance of another gene these cause other cells to become testicular cells.

## 8th to 12th week

Leydig cells in the gonadal ridge start to produce the masculinising hormone testosterone, which triggers the development of the male reproductive tract from the Wolffian ducts, and the Sertoli cells make a hormone called anti-mullerian hormone (AMH), which destroys the Mullerian ducts, which would otherwise become the female reproductive tract.

After this point, the chromosomes have only a secondary role in sexual development. The foetus converts testosterone into dihydrotestosterone which masculinises the external genitalia:

the penis (Glans) **1**
the urethra moves to top of Glans from its central position **2**
the scrotum **3** *(see diagram on page 42).*

## 20th week to 3 months postnatal

While sex organs differentiate up to the 12th week of gestation, in males testosterone influence upon the brain will typically occur later; in two peaks, the first at mid gestation (around 20 weeks), and the second around birth — up to a few months postnatally (about 3 months).

***"These are probably the peaks that programme sexual differentiation of the brain. Because of the time lag between sexual differentiation of the sex organs and the brain, they can follow a different course (e.g. in transsexuals)."*** DS

## Puberty

In both males and females, it is at puberty that the secondary sex characteristics are defined by the same hormonal messengers.

## Not quite the typical

As with females, male development doesn't always go to plan. An XY embryo can become female if the SRY gene or testosterone is missing or reduced, or if the foetus doesn't respond to testosterone, as in individuals with Androgen Insensitivity Syndrome (AIS). *(See p23 for the various KS karyotypes).*

## Pre-natal diagnosis

Chorionic villus sampling (CVS) at about 10 weeks or amniocentesis at about 16 weeks is available for older mothers; generally defined as over 35 years of age. However, it should be pointed out that there is a risk of miscarriage associated with the latter tests, currently about 1:100. Your consultant can advise you on this, and any other questions you may have.

*(**Important:** Please also read the **ICSC** chapter p48, which outlines 'Preimplantation Genetic Screening' (PGS) for aneuploidy conditions, which occurs at around 2 days after fertilisation).*

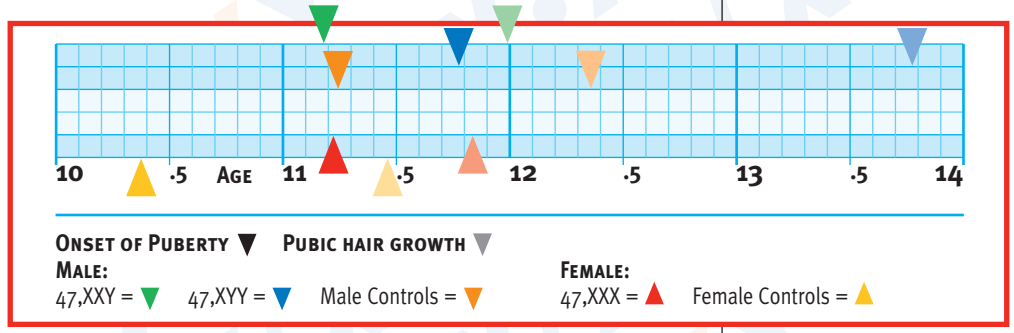
*(Also, see the **Further Study** chapter contacts, p75 for:*
- *Androgen Insensitivity Syndrome*
- *Congenital Adrenal Hyperplasia.*

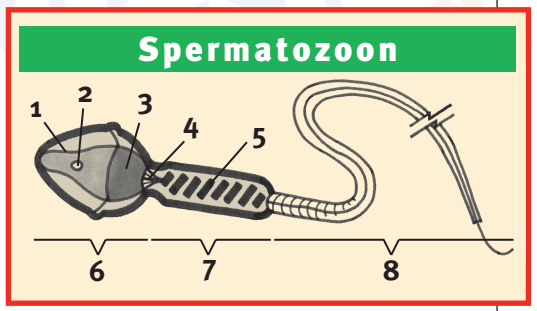
**M3**
SRY:
Sex Determining Region of the Y chromosome.

# Puberty

**Diagram:**
Based on data from:
**Dr Ratcliffe, SG.**
*Children & young adults with sex chromosome aneuploidy: The Edinburgh study of growth and development of children with sex chromosome abnormalities iv.*

This paper also contains valuable additional data on XXY, XYY and Triple X syndromes.




1 Acrosome
2 Vacuole
3 Nucleus
4 Neck
5 Mitochondrial Sheath
6 Head
7 Middle body
8 Tail







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**DID YOU KNOW?**
*(contd. from p42)*
One study on KS, showed that the risk at maternal age 40 is 2-3 times that at age 30.

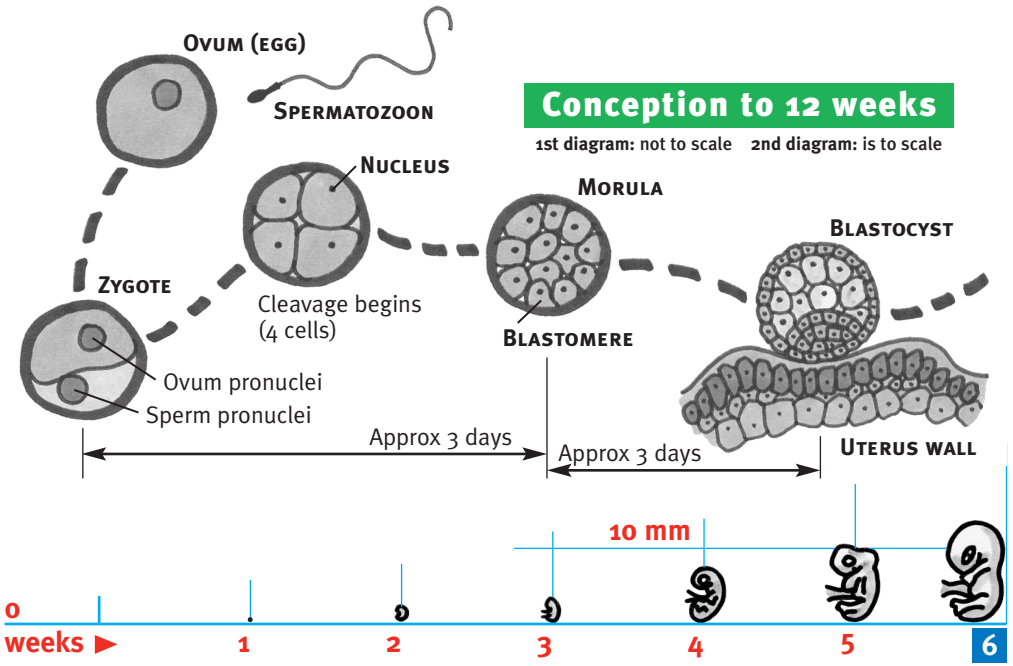
**Carothers, AD. Filippi, G.** (1988) *Klinefelter's Syndrome in Sardinia and Scotland. Comparative studies of parental age and other aetiological factors in 47,XXY.* MRC, Western General Hospital, Edinburgh, UK.

# The early days

I have included the following human reproduction section to outline not only the beauty of design, in all its forms, but to indicate the various stages (*approximate* weeks) at which genetic and hormonal events take place; primarily relating to Klinefelter's Syndrome (in dark blue).

The First Trimester (first 3 months) of development sees the main genetic and hormonal changes. After fertilisation the zygote makes its way along the fallopian tube, dividing as it goes, until after about 3 days it reaches the uterus. By now it is a tiny ball of cells called a morula. The ball of cells floats within the uterus for a further 3 days or so until it forms into a blastocyst (a hollow clump of cells), which is just visible to the eye.

**Week 2** The blastocyst embeds itself into the wall of the uterus. Chorionic villi projections burrow into the wall lining. The outer layer of the blastocyst (trophoblast), begins to develop into the placenta. Blood cells and the first heart cells begin to form.








**Week 4** The heart is already beating and the spine and nervous system are starting to form in the embryo, which is about 7mm long.

***Week 6*** The development of the internal parts of the ears and eyes continues under the external depressions, the latter covered with skin which will form the eyelids. Holes that will become nostrils begin to form, as do the mouth and jaw. The brain and spinal cord are nearly formed. The urinary and digestive tract continues to form and the hand and feet digits are almost recognisable as webbed fingers and toes. Week 6-7 genetic influence takes place; as the embryo's karyotype forges the gonads into testes or ovaries.

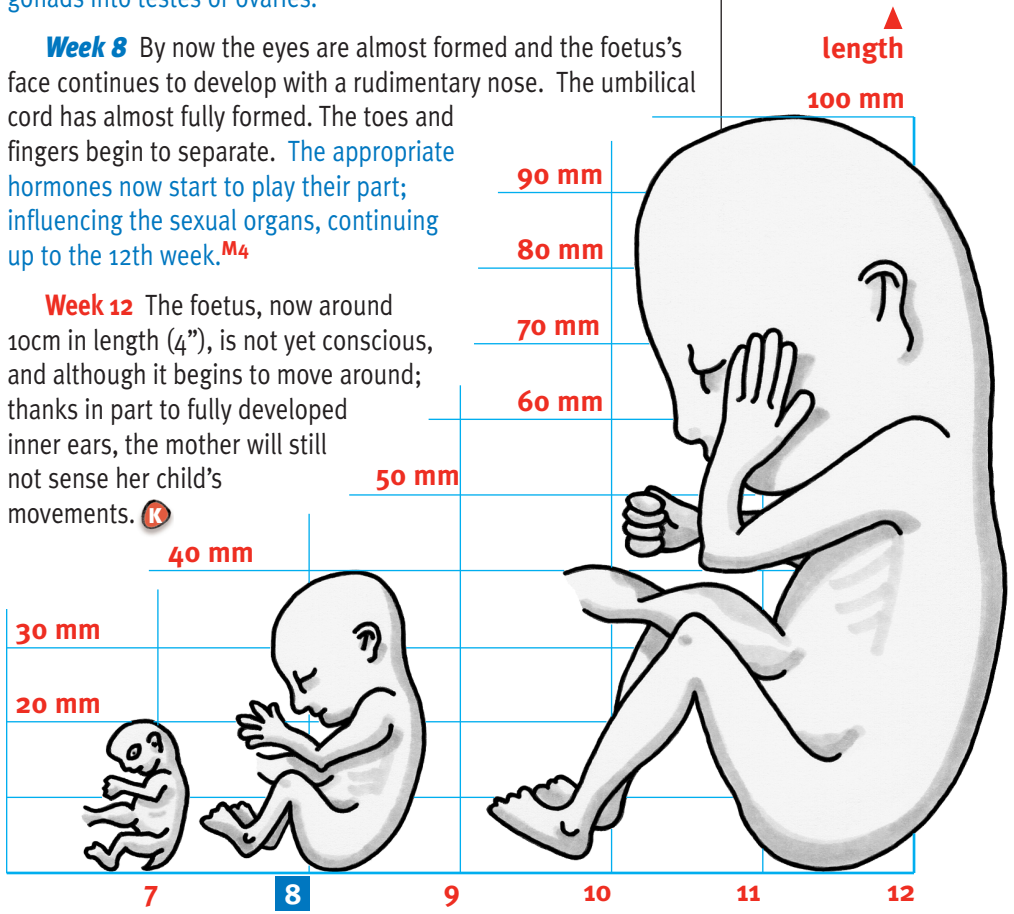
***Week 8*** By now the eyes are almost formed and the foetus's face continues to develop with a rudimentary nose. The umbilical cord has almost fully formed. The toes and fingers begin to separate. The appropriate hormones now start to play their part; influencing the sexual organs, continuing up to the 12th week.[M4]

**Week 12** The foetus, now around 10cm in length (4"), is not yet conscious, and although it begins to move around; thanks in part to fully developed inner ears, the mother will still not sense her child's movements. (K)

**DID YOU KNOW?**
In the last 50 years the typical male sperm count has almost halved; probably due to dietary, lifestyle and environmental factors.

**M4**
**Brain development**
Please see previous chapter ***The Male*** (p44) for details of hormonal *and* gene influence on the brain.

*(Also, please see the **Further Study** chapter, p76).*



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AGTC Genetics

# JCSI

## Intra-cytoplasmic Sperm Injection

For those men in the past with non-mosaic Klinefelter's Syndrome, who wished to have a family, life was bleak. But nowadays there may be the option of ICSI (as in *Pixie*). It basically depends on whether you have live sperm.

ICSI was discovered by Belgian scientists in 1991 and is one of the assisted reproductive technologies (ARTs) that can be particularly useful in cases of male infertility. Here it can literally be true that it takes only a single sperm to bring about fertilisation and hopefully a successful pregnancy.

Sperm retrieval will be by ejaculate or testicular fine needle aspiration (FNA) from the epididymis of the vas deferens (PESA or Per-Epididymal Sperm Aspiration) from the testicles themselves (TESA or Testicular Sperm Aspiration) or extracted from a sample of biopsied testicular tissue (TESE or Testicular Sperm Extraction).

In both ICSI and IVF (In Vitro Fertilisation), embryologists will attempt to fertilise as many eggs as they are able to recover (this could be up to 20). That said, following public consultation, in 2007 the HFEA introduced a policy to reduce the risk of multiple births and attendant problems from patients identified as most likely to conceive twins. Now one embryo (max) should be transferred per cycle.[M1]

The exception to this is for women over 40 using their own eggs who may have up to 3 embryos transferred. During the fertilisation process some eggs may fail to fertilise or fail to develop after fertilisation. While the HFEA guidance on the maximum number of embryos transferred has not changed, because of the complexity of this procedure, the latter policy statement may also be relevant.

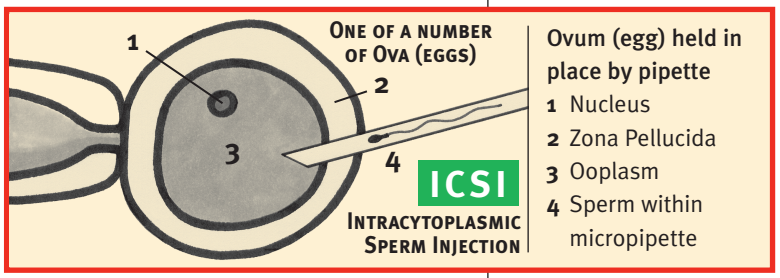
If there are embryos that are surplus to immediate transfer requirements *that are of suitable quality*, these can be frozen and stored for future use. It must however be remembered that not all embryos will survive freezing and subsequent thawing when they come to be used at a later date. Sadly, sometimes none of the stored embryos will survive freezing and thawing.

The difference between the two methods lies with the fertilisation process. With IVF, eggs and sperm are placed in culture medium in vitro ('in glass' – not actually a glass testube but a plastic culture dish) and fertilisation occurs 'naturally'. With ICSI a single sperm in injected into the cytoplasm of each mature egg.

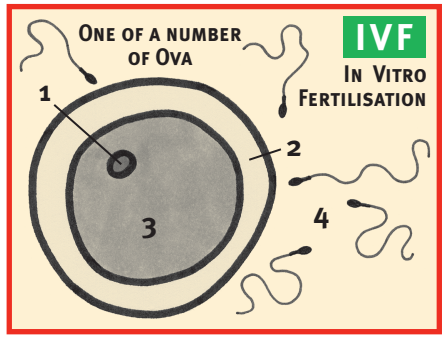
Signs that fertilisation has occurred are usually present 16-20 hours later. 2, 3 or 5 days after eggs retrieval, embryo transfer into the woman's uterus can be carried out. *(See diagrams).*

Although ICSI improves fertilisation rates compared to IVF, once fertilisation has been attained the pregnancy rate is no better than with IVF.[M2]

There have been some follow-up studies on ICSI, the associated risks are outlined on the HFEA website.[M3] When genetic problems have been detected by chromosome analysis (Karyotyping), genetic counselling is essential so that the risk of passing on a genetic problem to a child are completely understood.




**Ovum (egg) held in place by pipette**
1 Nucleus
2 Zona Pellucida
3 Ooplasm
4 Sperm within micropipette




**Ovum within culture medium**
1 Nucleus
2 Zona Pellucida
3 Ooplasm
4 Weak spermatozoon swimming under their own power

### Diagnosis and Screening procedures

In conjunction with ICSI and IVF the most common screening procedures to assess the genetic 'normality' of embryos are ***PGD*** (Preimplantation Genetic Diagnosis) and ***PGS*** (Preimplantation

Chapter updated 10.2010

"Following the publication of the White Paper, Equity and Excellence: Liberating the NHS, the publication of the Department of Health's review of the Arm's Length Bodies (ALBs) in the NHS sets out the Government's intention, *during the course of this Parliament (2010-15)*, to retain the statutory functions of the HFEA and to transfer them to other health bodies, in particular the Care Quality Commission.

These proposals form part of the cross-Government strategy to increase accountability and transparency, and to reduce the number and cost of quangos.

During any transition period the contact details for the HFEA and the HFEA's website address will remain the same. For further details of the Department of Health's review of the Arm's Length Bodies please see the Department of Health's website at: w: http://www.dh.gov.uk."

**M1**
**'One at a time'** is a professionally-led site aimed at reducing the risks of multiple pregnancies from fertility treatment. It also offers a good patient perspective.
w: www.oneatatime.org.uk/

**M2**
The HFEA produces a variety of statistics on the treatment licensed centres provide and have a comparison of birth rates following ICSI and IVF at:
w: www.hfea.gov.uk/2588.html#3038

More information on this and other aspects of ICSI at:
**National Institute of Clinical Excellence (NICE)**
w: www.nice.org.uk/CG11

**NICE** policy covers England, Scotland and Wales. Other guidance for the NHS in Scotland is developed by:
**Quality Improvement Scotland**
w: www.htbs.org.uk
and the **Scottish Intercollegiate Guidelines Network**
w: www.sign.ac.uk

Northern Ireland guidance development from the
**Northern Ireland Executive**
w: www.northernireland.gov.uk/
and the **Department of Health, Social Services and Policy Safety**
w: www.dhsspsni.gov.uk/

**M3**
Description of ICSI:
w: www.hfea.gov.uk/ICSI.html

The HFEA website also has a useful glossary: menu (top right).

The risks:
w: www.hfea.gov.uk/icsirisks.html



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**M4**
The PGD & PGS procedures are based on information kindly supplied by the **Human Fertilisation & Embryology Authority (HFEA).**
**w:** http://guide.hfea.gov.uk/guide/

You can access more information and research papers on everything mentioned, by using the search box at **NCBI:**
**w:** www.ncbi.nlm.nih.gov
(obtains results from PubMed, OMIM and other databases), or search direct from **PubMed** at:
**w:** www.ncbi.nlm.nih.gov/pubmed

**M5**
*HFEA licensed clinic directory:*
**w:** http://guide.hfea.gov.uk/guide/AdvancedSearch.aspx

**Please note**

**M6**
**Pre-implantation Genetic Diagnosis (PGD)**
is a technique that enables people with a specific inherited condition in their family to avoid passing it on to their children.
*For more details visit:*
**w:** www.hfea.gov.uk/preimplantation-genetic-diagnosis.html

**Pre-implantation Genetic Screening (PGS)**
*(also known as aneuploidy screening)* involves checking the chromosomes of embryos conceived by intra-cytoplasmic sperm injection (ICSI) or in vitro fertilisation (IVF), for common anomalies.
*For more details visit:*
**w:** www.hfea.gov.uk/70.html

*Clinics licensed to undertake PGS:*
England **11**; Northern Ireland **0**; Scotland **0**; Wales **1**.
*(For more details see M5 above).*
**There are no clinics (in the UK) licensed to screen for Klinefelter's Syndrome.**
However, centres using PGS will identify KS as a matter of course.

Genetic Screening). PGD is used to test for specific genetic conditions and characteristics. PGS is used to identify the number of chromosomes present in a cell, by analysing them about 2 days *after* fertilisation, when the morula has within it around 8 cells, called 'Blastomeres' *(see diagram on p46)*.

This involves a technique called 'Fluorescence in-situ Hybridisation' (FISH); which uses small pieces (probes) of DNA, which are labelled with different coloured fluorescent dyes, which attach themselves to the various chromosomes of each type in the cell; enabling the geneticist to count them.[M4]

While both these procedures are generally defined as a means to identify 'abnormal' cells and to select 'normal' embryos for transfer, this often refers to inherited genetic conditions within a family history.

However, as I mentioned on page 15 (margin); Klinefelter's Syndrome is a highly complex condition which affects people in different ways. A minority *will* be seriously affected, others will struggle, while the vast majority will overcome earlier difficulties or will be totally unaware of any symptoms. *After all, who wrote and designed this book on Klinefelter's Syndrome?!*

**With regards to Klinefelter's Syndrome, unless there are serious complications, termination should not be the overriding objective in seeking any kind of screening.**

For the number of clinics in the UK licensed for PGD and PGS please see the HFEA website.[M5] There are no centres currently licensed in the UK to carry out PGD specifically for Klinefelter's Syndrome [2010], however, most centres carrying out PGS for chromosomal 'anomalies' will use probes for sex chromosomes and will, as a matter of course, identify embryos with Klinefelter's Syndrome.[M6] In addition to other aneuploidy conditions those clinics licensed for PGS use probes for trisomies: 13, 18, 21 and X & Y.[M7]

***'Polar Body' testing.*** A developing ovum will produce two small cells called 'Polar bodies', which do not develop into functioning egg cells; degenerating after fertilisation.





Examination of these cells provides an indication of the number of chromosomes within the ovum.

After removal of a polar body by micropipette, the ovum is placed in an incubator. This procedure is usually only carried out where there is thought to be a risk of maternal age-related aneuploidy, (e.g. KS), where maternal meiosis stage 1 errors are a factor.

*It is now possible to carry out PGS tests on a Polar body thereby avoiding the need to remove a blastomere from the embryo.*

There is strong opposition to PGS and other procedures of this kind from some groups who see a single cell blastomere as a potential human being. That said, it is not for me to make judgements within this guide, but to leave you to make up your own mind on the ethics.

Your doctor or consultant can give you more up-to-date information on everything mentioned here, including success rates, clinical geneticists and genetic counsellors. There are also information sites on the web on the clinical, ethical and moral aspects of prenatal screening and diagnosis.

**M7**
*"In terms of information the UK National Screening Committee does not provide details about this condition* [KS]*... as there is no programme to screen for this condition."*
**Department of Health**
Richmond House, 79 Whitehall
London SW1A 2NS

That said, if parents have had previous experience of having a child with a genetic condition amniocentesis will be offered by the NHS. With the support of a genetic counsellor, parents can then decide whether to proceed or not.

As mentioned, KS may also be identified *indirectly* during PGS for other genetic conditions. Parents will then be informed and referred to the regional genetics team.

**UK National Screening Committee (NSC):**
**w:** www.nsc.nhs.uk/index.htm

**Department of Health**
**w:** www.dh.gov.uk
For *'Code of Practice & Guidance on Genetic Paternity Testing'* and *'Guiding Principals for Commissioners of NHS services'*.

**Stop Smoking Suggestions**

Breathing through and nourished by the lifeline that is the umbilical cord, the embryo or fetus is a part of the mother. Smoking during pregnancy can increase the chances of producing a child with Klinefelter's Syndrome. Men who smoke reduce their chances of fathering a child by two to three times. The latter study which relates to both IVF and ICSI, also points to a marked reduction in retrievable eggs and fertilisation, if the mother is the smoker.

A study by **Dr Zitzmann, M.** (2002),
*Smoking damages IVF chances.*
Institute of Reproductive Medicine, Münster, Germany.

**For the UK:** Visit the **NHS Choices 'SMOKEFREE'** website. You can also Chat to an adviser online by clicking the link on the Home page, top centre, under the phone number.
**w:** http://smokefree.nhs.uk/
*The website also has numbers for Asian language advisors.*

**NHS Stop Smoking Helpline:** 0800 022 4332
**NHS Pregnancy Smoking Helpline:** 0800 169 9 169
*Lines open Mon to Fri 9am to 8pm, Sat & Sun 11am to 5pm*

**Isle of Man Smoking Helpline:** 01624 642 404
**Northern Ireland Smoking Helpline:** 0800 85 85 85
**Scotland Smoking Helpline:** 0800 84 84 84
**Wales Smoking Helpline:** 0800 1690 169

**If you live outside the UK:** I suggest you either obtain a recommendation from your MD, or do an online search for reputable government based or supported sites. Just type into the search field: 'Stop smoking' followed by your own country's name (obviously in your own language). I tried it, and from the search lists found USA: www.smokefree.gov/ This site also includes a link to: http://women.smokefree.gov/ For Australia: www.quitnow.info.au/ I also tried India, New Zealand and Sweden and got similar results. If you're not sure if the site is government based, look for an official crest or read their About Us link. The aforementioned sites are just suggestions. I strongly recommend that you do your own search.



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## Important personal note

**This chapter was completed in 2005 and does not take into account the *Consensus Statement on Management of Intersex Disorders*, published in 2006.**
***(Please see the end of this chapter (p55) for more details).***

*I have been incredibly fortunate to have had the opportunity to ask questions of so many important scientists, both in the UK and abroad, who's pioneering work spans half a century in the fields of biological and cytogenetic research. Without their support and patience* ***The KS Story*** *would now be so many megabites in a bulging hard drive folder.*

*I appreciate that professional feelings run high regarding this subject, and that I am dealing with lifelong careers and passions. I don't want to rub anyone up the wrong way; particularly those who are trying to help me, but I am no academic, I know only the facts that are supplied by the experts —* ***but I don't know who is right!***

*And so the consequences of asking the above question has troubled me greatly; should I include 'Intersex' within the guide. And having decided, trying to obtain a balanced consensus on the response. Then ultimately afraid of how everyone involved would react to the final chapter...*

*To this day I can't understand how this confused situation hasn't arisen many times before. Relating to Klinefelter's Syndrome, all articles and documents I have found to date, state one explanation or the other and never the twain. Routinely, intersex is never mentioned.*

*Of course, I could simply have avoided the whole issue and moved on to another non-confrontational subject, but I felt that I would be letting the reader down if I didn't at least try to obtain some facts and so I decided to investigate further, and to include* ***ALL*** *viewpoints.*

*Continued in opposite margin...*

# Is KS an Intersex condition?

As mentioned in the chapter ***Human Reproduction***, there are four ways of recognising a baby's sex;

| | |
|---|---|
| **Genetic sex** | its karyotype - e.g. 47,XXY; |
| **Biological sex** | according to internal organs; |
| **Biological sex** | according to external sex organs; and |
| **Brain sex** | structures which are believed to be linked with a particular sex. |

To the outsider, there seems to be a great deal of confusion regarding the classification of Klinefelter's Syndrome as an Intersex condition. So what does Intersex mean?

The **Oxford Concise Medical Dictionary** defines intersex as: ***"an individual who shows the anatomical characteristics of both sexes",*** [M5] while a medical research paper swopped ***'anatomical'*** for ***'biological'***.

However, like everything else associated with KS, it's not that simple. There are basically three schools of thought on the current definition of an Intersex condition. As far as those researchers I have asked, most have declared, in a polite but firm manner that ***"there is no debate."***

From talking to others it would seem there is no right or wrong, since it is a matter of definition. ***"Just well meaning scientists interpreting the same information in different ways."*** [MD] Furthermore, it would seem there is no independent authority who can mediate on these views.

For this chapter a few of the great names in cytogenetics and biology have contributed their expertise, but there is a whole world of opinion out there. In the end, it is for you to decide.

### *Viewpoint A*

***"An individual born with male genitals and a Y chromosome within the karyotype is classified by most medical researchers as male."*** [M1]

***"There is no debate on whether or not Klinefelters are "intersexes." Intersexes are individuals in which both male and female tissue is present in the primary and/or secondary sex organs. Klinefelter's Syndrome individuals have no female characteristics in their primary and/or secondary sex organs, only those of a male. Thus they are not intersexes. It really is as simple as that. There are no rational reasons for considering Klinefelters as anything but male as we know a Y chromosome can overcome the effect of as many as four or five X chromosomes and XXXXXY individuals are indubitably male."*** [M2]

### *Viewpoint B*

***"Absolutely, Klinefelter's Syndrome is an Intersex condition. By definition, an Intersex condition is any one in which individuals have biological characteristics that combine features typically both male and female. Some of these conditions, but not all, are accompanied by ambiguous genitalia.***

***...it is a mistake in thinking that the ambiguous condition is needed or characteristic. For instance, there are even recorded cases of true hermaphrodites having typical appearing genitalia.***

***Along with Klinefelter's Syndrome, there is also Turner's Syndrome that is quite a common intersex condition without ambiguous genitalia. (Turner's have an XO condition, where the 'O' represents a missing chromosome. And this missing chromosome might be an X or Y).*** [M6]

***Considering all those various conditions the intersex conditions without ambiguous genitalia might be as common as 1:100 while those with ambiguous genitalia might occur about 1:1500 - 1:2500."*** [Figures relate at least to US and UK].

Advocates 2 & 3 agree that an XXY individual should be raised as a male, though the latter points out that ***"these individuals also have XX, that is typically a female characteristic. The assignment on the basis of the penis instead of the XX is historic and easy since the XX is not visible.*** Concluding, ***the individual, however, may wish to live as a woman."*** [M3]

It is also pointed out by this advocate that ***Viewpoint A*** ignores the development of breast tissue as a sign of feminization.

*Contd.*





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## Intersex

*Nothing has been left out of this chapter; laying all the facts before you and giving you a broad database in which to investigate further.*

**Last - but definitely not least**
There is a whole world of opinion out there on this subject. For starters, try the following: visit
**w:** www.nlm.nih.gov/pubmed/

**Sax, L.**
*How common is intersex? a response to Anne Fausto-Sterling.*
***(Viewpoint A)***

**Gold, C.** *'The Intersex Spectrum'.*
***(Viewpoint B)***
Adapted from: *Syndromes of Abnormal Sex Differentiation*
The Johns Hopkins Children's Centre, Baltimore, MD, USA
**w:** www.hopkinsmedicine.org/pediatricendocrinology/

*You can also find the latter and other useful information at the following website:*
**w:** www.pbs.org/wgbh/nova/gender/spectrum.html

**M5**
**Martin, E A.**, Editor, (1998), *Oxford Concise Medical Dictionary 5th edition,* Oxford University Press, Oxford, UK.

**M6**
***"Girls and women who have Turner Syndrome, and their families do not see themselves as having an Intersex condition. They are most definitely female."***
**Turner Syndrome Support Society**
**w:** www.tss.org.uk
*(Contact details on p75).*

**Acknowledgement:**
*The majority of contributors wished to be attributed and referenced, and I would like to thank all those involved for their time, politeness and patience.*

**M1** (Viewpoint A)
*Contributor has retired and has not confirmed name inclusion.*

**M2** (Viewpoint A)
**Prof P A Jacobs OBE, DSc, FRS**
Wessex Regional Genetics, Laboratory, Salisbury, UK.
*Stated in a letter to the Compiler. (02.2002).*

**M3** (Viewpoint B)
**Prof M Diamond, PhD**
University of Hawaii, John A Burns School of Medicine, Honolulu, USA.
*Stated in a letter to the Compiler. (10.2001).*

**M4** (Viewpoint C)
**Prof A Fausto-Sterling, PhD**
Professor of Biology and Gender Studies, Brown University, Providence, USA.
*Stated in a letter to the Compiler, (01.2003), with supplied paper:*
**Fausto-Sterling, A. et al.**
*How Sexually Dimorphic are we? Review and Synthesis.*

## *Viewpoint C*

It is clear from the supplied document that Klinefelter's Syndrome is included within this study of intersex. However, this advocate intimated in the covering letter that the 'question' ***"depends on how you define intersex."*** Further, it is pointed out that the study paper ***"is a practical and philosophical question of gender really, and there is no correct answer, only practical, personal and philosophical choices."***

**"'Abstract The belief that Homo sapiens are absolutely dimorphic with the respect to sex chromosome composition, gonadal structure, hormonal levels, and the structure of the internal genital duct system and external genitalia, derives from the platonic ideal that for each sex there is a single, universally correct developmental pathway and outcome. We surveyed the** [International] **medical literature, from 1955 to the present,** [2000], **for studies of the frequency of deviation from the ideal male or female.'**

***"We defined the typical male as someone with an XY chromosomal composition, and testes located within the scrotal sac. The testes produce sperm which, via the vas deferens, may be transported to the urethra and ejaculated outside the body. Penis length at birth ranges from 2.5 to 4.5cm (Flatau et al., 1975); an idealised penis has a completely enclosed urethra which opens at the tip of the glans. During fetal development, the testes produce the Mullerian inhibiting factor, testosterone, and dihydrotestosterone, while juvenile testicular activity ensures a masculinising puberty."***

Within this viewpoint, intersex is defined as the following:

- ***"Sex" chromosome composition. Individuals with XXY, XO, XYY, XXYY, XX males, and XXX females...***
- ***Androgen insensitivity in XY individuals... (Complete and Partial)***
- ***Congenital adrenal hyperplasia... (Classic and Late-onset)***
- ***Vaginal and penile agenesis...***
- ***Hormone-producing tumors and exogenous sex hormones...***
- ***True hermaphrodites and idiopathic mixed genitalia..."*** **M4**



## 'Disorders of Sex Development' (DSD)

In 2006 there was a new medical-based nomenclature for 'hermaphroditism,' 'pseudohermaphroditism,' 'intersex' 'sex reversal' and gender-based diagnostic terms to ***'Disorders of Sex Development'*** (DSD).

According to the authors, this is a term referring to *"congenital conditions in which development of chromosomal, gonadal, or anatomic sex is atypical."* This now includes Klinefelter's Syndrome and its variants *(see Table 2 of 'Consensus Statement on Management of Intersex Disorders')*.

While I would imagine that the vast majority of society are pleased to see the end of the term 'hermaphrodite', it is clear that not everyone is happy with this new terminology.

There are four main areas of opposition: that of minimal consultation with those who are actually 'intersex'; conflict with the word 'Disorder', which implies there is something wrong; the definition of 'Sex Development', which *can* in French-speaking countries mean something entirely different *and* offensive. And finally, it implies the likelihood that this new term will encompass other conditions with different etiologies not previously considered intersex.

Despite the controversial nature of this subject, it has been *politely* suggested that after so long in the making, it was time to stop updating this book and get the first pdf distributed. I will therefore seek comments from all concerned, including the KS community and add an in-depth section in the next pdf update, within the chapter: *Sex/Gender Spectrum - Terminology & Usage*.

Please email any relevant information for the 2012 update to: theksstory@btinternet.com

In the meantime I include some reading material for this new nomenclature. You can also do your own web search for *'Disorders of Sex Development.'*

*' DSD Guidelines and Policies, Consensus Statement on Management of Intersex Disorders,'*
Lee, P.A., MD, PhD, et al., Pediatrics 2006;118;e488-e500. DOI: 10.1542/peds.2006-0738
http://pediatrics.aappublications.org/cgi/reprint/118/2/e488

**Opposition:**
*'Variations of Sex Development Instead of Disorders of Sex Development'*
Beh, Hazel; Diamond, Milton (2006)
www.hawaii.edu/PCSS/biblio/articles/2005to2009/2006-variations.html

*'Changes in Management of Children with Differences of Sex Development,'*
Diamond, M. and Beh, H.G., Nature Clinical Practice: Endocrinology & Metabolism 4(1): 4-5. 2008
www.hawaii.edu/PCSS/biblio/articles/2005to2009/2008-changes-in-management.html

*'What is in a Word?'* Michelle O'Brien, OII, UK
www.intersexualite.org/intersex_not_disorder1.html

*'Why is OII not using the term DSD or Disorders of Sex Development?'*
Organisation Intersex International
www.intersexualite.org/Response_to_Intersex_Initiative.html

## Children and Young People

### ChildLine

**t:** 0800 1111

- *ChildLine is the free 24-hour helpline for children and young people in the UK.*
- *Children and young people can call about any problem, at any time – day or night.*
- *ChildLine is confidential, which means they won't tell anyone about your call unless you want them to talk to somebody for you, or you are in danger.*
- *If lines are busy, please keep trying and you will get through.*

ChildLine is the free helpline and online service for children and young people in the UK. Children and young people can call **0800 1111** or visit **www.childline.org.uk** to talk to a trained counsellor about any problem, or talk to other young people on the message boards.

# Bullying

In general, bullying is a harrowing and relentless experience, with individuals subjected to verbal threats and actual physical abuse.

### *At school...*

Individuals of school age who are bullied often feel alone and unable to tell anyone in authority; particularly teachers; in case of reprisals. Even if the bully responsible is punished or expelled there is still the real risk; in the victim's mind, that the bully will 'get them back' somehow, at some point in the future; perhaps when the person feels safe.

For children and teenagers with Klinefelter's Syndrome there is already an aura of low self-esteem and a sensitive nature. They're generally unwilling to fight and to participate in rough contact sports – all traits the bully can reinforce to their advantage. Kids with KS also make ideal victims since they are easily brought to tears by the merest of threats of gang beatings or extortion.

Often with a reluctance to involve parents, bullied individuals with KS may not get the full support they need and will struggle within the abuse/fear cycle until they either crack under the pressure and seek help, or resort to truancy to avoid any confrontations. In extreme instances, some only see one way out.

I experienced bullying at primary and secondary school, though thankfully it was sporadic. Occasionally I even managed to interact and even receive praise from 'the enemy'; those boys who saw themselves as far superior to myself, which brought forth a kind of pride that I had been accepted. But all too often it was short-lived.

Given enough harassment I occasionally snapped into a kind of damage limitation frenzy, but with blind rage and limited fighting abilities the fracas was usually over relatively quickly, with me nursing my wounds – and usually in tears. So more often than not I gained a reputation for swift strategic withdrawals; preferring flight rather than fight.

Kids can be cruel at the best of times and bullies know all too well that they can always have another go at the 'soft-touches' who seem unable to challenge their authority.



There is nowadays the added fear of Cyber bullying; the use of information & communication technology, particularly mobile phones logged-on to social networking sites (SN), which penetrates even the perceived safety of the victim's home. Cyber bullying can also take place between children and adults; such as a teacher, which can cause great stress and depression.

Apart from accidentally uploading personal details or images which can later cause upset, there are trends on certain SN sites, such as the 'Like' button (2010), generally intended to embarrass a person, possibly with crude comments about their sexuality.

Usually close school friends have each other's mobile phone number, so if pals fall out it can be extremely harrowing to receive text message abuse and threats, particularly as x-pals will probably know some very private and possibly sensitive information about the other person.

Many schools today have set up peer support groups and there are specific helplines available for children and teenagers in this situation, but it is still vital that teachers and parents play their part in listening and supporting all vulnerable individuals of bullying; whether they have Klinefelter's Syndrome or not.

Of course it should be stressed that often there are underlying reasons why a child resorts to bullying, such as conflict elsewhere, resulting in low self worth, and that by informing a teacher about an incident it may also bring to light these problems; allowing counselling and support.

### *...college, university and work*

Bullying doesn't stop when a teenager leaves school. Further education and in the workplace, unchallenged; those who seek power; at whatever level of authority, will seek out and create victims. And it's not just women who are victimised at work.

As a well practiced coward it is easy for me to say that workmates should try to support their colleagues and wheedle out those people who bully, but sadly in the big world it's not that easy. A victimised employee hasn't even the luxury of truancy. And if the bully is a director of the company – what then? Perhaps talking to a trusted family member, close friend or one of the adult support networks, such as those mentioned in the margin or within the ***Further Study*** chapter, may be the answer.

## Children, Young People and Parents

Use one of the popular search engines to access several other valuable sites, including:

**BullyingUK**
*Formally Bullying Online*
**w:** www.bullying.co.uk

**Kidscape**
**w:** www.kidscape.org.uk

## People of all ages

There are many good samaritans out there waiting to listen to you and offer confidential support.

Use a search engine and type: **'Adult bullying in** *[type in your own country]***'**, or **'talk to someone'**, or experiment with text yourself.

It may be that your website browser has a search button specifically for results from your own country (e.g. **'pages from the UK'**). Clicking on it.

Whatever you decide to do, go carefully. Choose a well known and trusted organisation.

### Further details and Legal Support

*Please see the **Further Study** chapter p78 for information on all contacts mentioned in this chapter, including advice on legal support.*



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# Klinefelter's Syndrome

## Links to other conditions

**Avascular necrosis, cancer, diabetes, leg ulcers, osteoporosis...**

All these conditions have been linked to Klinefelter's Syndrome in one medical paper or another. But as mentioned several times before, everyone is different. There are also generally applied criteria for having these conditions, for example; current medical thinking states that it is unlikely KS is involved in leg ulcers if there is venous insufficiency, or other underlying causes.

The following will give you a basic background to these conditions and their association with Klinefelter's Syndrome (KS). By all means study these links, but don't get bogged down in self-analysis and worry — ***everyone is different.***

### *Avascular necrosis*

If you have KS or have been recently diagnosed, then you should be either under the care of an endocrinologist (in the UK referred by your GP), or be receiving hormone replacement therapy. The sex steroid (hormone) testosterone is necessary to maintain healthy bones.

**DID YOU KNOW?**
Approximately 10% of testosterone is converted into oestradiol (an oestrogen) to maintain bone growth.

Avascular necrosis is a disabling condition which, in severe cases, can lead to joint collapse.

The condition can start with few warning signs, perhaps only with a dull ache in an unrelated area. Although it can happen in any bone it most commonly affects the femur. Other common sites include ankle, upper arm, knee and shoulder.

#### What is Avascular necrosis?

It is caused by the death of blood vessels to a particular area, and in the case of the femur, the joint becomes weakened; through lack of oxygen and nutrients; slowly dying, to the point of its collapse.

#### What causes this condition?

There are several general causes; from trauma, and damage to blood vessels, fat blockages and embolisms.

**Associated conditions:**
These include Caisson's disease, Crohn's disease, Cushing's Syndrome, Gaucher disease, Sickle Cell disease, Chronic Pancreatitis, Rheumatoid Arthritis, Steroid usage, Systemic Lupus Erythmatosis, Alcoholism... and Klinefelter's Syndrome (*allegedly*).

*In my own case, there is a dichotomy of opinion on this link. Rheumatology sees it as endocrine based, while endocrinology is not convinced that testosterone deficiency is the culprit. To be fair, both consultants agree that there is considerable medical literature linking Klinefelter's Syndrome to Osteoporosis. However, there seems to be no specific case studies of KS directly linked to Avascular Necrosis (a form of osteoporosis).*

#### What are the symptoms?

In the early stages there may be no symptoms at all, however, as the condition progresses, which can take months, most individuals will experience joint pain, and/or referred pain in areas such as the knee, quadriceps or back. There will be limited motion and stiffness of the joint and weakness within the leg muscles.

The condition can affect just one joint; such as the hip, or both hips, or different joints at different times.



In the later stages the pain and associated weakness can be dramatic. Motion can also be restricted as both bone and cartilage are broken down and the smooth head of the femur becomes jagged and worn within the pelvic socket.

The time between the first symptoms and loss of joint function is different for everyone; ranging from several months to over a year.

#### How is it diagnosed?

Initially, in the case of the femur, the doctor or rheumatologist will rotate and flex the joint to check for pain and stiffness.

Avascular necrosis diagnosis is often made by X-ray. However, by the time film X-ray tests show up substantial damage can already have been inflicted on the bone (up to 30% bone density loss),[M1] therefore this form of X-ray is usually considered for later-stage findings.

To detect early signs, MRI scanning (magnetic resonance imaging) may be used to see the condition of the internal bone structure, and particularly to the neck of the femur. Alternatively, a DEXA scan (Duel Energy X-ray Absorptiometry), also known as DXA, will be used to assess the density of the bone, and the risk of fracture.

#### What treatment is available?

This depends critically on what stage the avascular necrosis has reached. In the early stages (before changes show up on film X-ray), there are some treatments, such as bone grafts. Later stages typically lead to surgery, e.g. a partial or total hip replacement. This involves replacing the femoral head with a titanium prosthesis and a special polyethylene cup fitted into the pelvic socket. *(Try a computer web search for an illustration or photograph of a hip prosthesis).*

#### What about pain management?

To try and maintain a decent quality of life, progressively stronger analgesics can be prescribed, as well as NSAIDs (non-steroid anti-inflammatory drugs). In severe cases, an anti-inflammatory can be injected directly into the joint area; under a local anaesthetic; which gives pain relief for up to 9 months. This usually require a 2-3 day in-patient stay; to monitor the application.

#### Continued bone maintenance?

Including the testosterone replacement therapy you take for Klinefelter's Syndrome; to ensure the bone does not deteriorate, you may be placed on a non-steroid osteoporosis therapy, which entails taking a daily tablet, for at least 3 years —possibly life.

This treatment temporarily stops 'turnover' (the breakdown of bone) for 14 days, followed by a calcium tablet for 76 days (three month pack).

### *Cancer*

#### Male breast cancer

Of the very limited research currently available, it is clear that generally, men have a very low risk of


**M1**
w: www.nos.org.uk
**National Osteoporosis Society (NOS).** See ***Further Study*** p78 for contact details.

**M2**
*What is Klinefelter's Syndrome?*
An introduction paper by the **Klinefelter Organisation.** See p74 for contact details.

**M3**
w: www.medicinenet.com/
Diseases & Conditions/
Klinefelter's Syndrome.
This was in turn based on text from **NICHD** (part of NIH), **Dr A Robinson,** Uni. of Colorado, USA.

**M4**
w: www.cancerhelp.org.uk
Go to the **Cancer Research UK**, website on p76 for details.

**M5**
**Swerdlow, AJ. et al.**
*Mortality and cancer incidence in persons with numerical sex chromosome abnormalities: A cohort study.*
Section of Epidemiology, Institute of Cancer Research, Sutton, Surrey, UK.

**Meguerditchian, AN. et al.**
*Male breast carcinoma.*
Dept. of Surgery, Universite Laval, Quebec City, Quebec, Canada.

**M6**
**Swerdlow, AJ. et al.** (2005)
*Cancer incidence and mortality in men with Klinefelter's Syndrome: A cohort study.*
Section of Epidemiology, Institute of Cancer Research, Sutton, Surrey, UK.

**M7** See **M3**.




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developing 'breast' cancer, with a possible higher risk for individuals with gynaecomastia, though one KS support group suggests that it may be the hormonal imbalance in KS which causes cells to become cancerous rather than actually having the breast tissue.[M2]

A couple of sources and one website puts the risk factor as similar to women, at 50 times that of a typical male.[M3] The same source mentions the need for XXY adolescents and adults to practice regular breast self examination.

The ***Cancer Research UK*** website suggests a 20 fold increase in a person with KS, but concludes that this is still a very low risk factor.[M4]

### Germ cell cancer

Those with KS also have a very small risk of developing germ cell cancer, and the risk factor is greatly reduced after the age of 30, the peak being between 15-30.

Judging by recent research into KS links to cancer, the incidence of these cancers are very low or inconclusive.[M5] *(See **Obesity**)*.

### Other cancers

In 2005 a study of other possible associated cancers, on behalf of the *UK Clinical Cytogenetics Group*, suggested that men with Klinefelter's Syndrome may be at substantially elevated risks for non-Hodgkin's Lymphoma and perhaps lung cancer.[M6]

#### Chest/Breast self-awareness

While it is well known that men should regularly check their testicles for lumps, it is becoming clear that they should also check for lumps within their chest or breasts. This is particularly important for individuals with KS who have a hormone imbalance.

*(Based on guidance for a female, but equally suitable for a male with KS and/or gynaecomastia).*

1) Using a mirror, look for any differences between the two sides, in-drawing of the nipple and changes in the skin.

2) *(Raise your arms above your head)*. Check for changes in the contour of your chest/breasts, as tumours can cause in-drawing or puckering of the skin.

3) *(Lower your arms)*. With your opposite hand feel one side at a time, starting at the armpits and upper area of chest wall (tissue extends this far). Press gently but firmly in a circular motion with the pads of your fingers. Feel for any thickening of the tissue or a new lump.

4) Don't miss anything. Make sure you check the whole area, working inward towards the nipple. Pay particular attention to the area beneath the areola, (brown or pinkish area around the nipple). Don't forget about the nipple, look for dry flakiness. Squeeze it gently to detect any discharge, (red, brownish, milky or yellowy).

Look also under arms and above clavicals (base of neck) for swollen lymph nodes (glands).

If you discover anything, get it checked out by your GP. It could just be fat tissue — on the other hand it may not.

You should do the above once or twice per month, around the same time of day. It's easier to do this in the shower or bath with a soapy hand.

**It is important to become familiar with your chest/breasts and to know what is normal for you. Remember, early action can make a difference.**

In general, males take 8-9 months before contacting their GP about sexual matters, compared with 3 months for females.

## Diabetes

***"Compared with other males individuals with KS have a slightly higher risk of autoimmune disorders."***[M7]

The most common of these conditions is type 1 diabetes. In a British study, ***"the increased frequency of diabetes in Klinefelter's Syndrome, Turner's Syndrome, and possibly Down's Syndrome lead to the hypothesis that non-disjunction may, in some way be associated with a predisposition to diabetes."*** While a Taiwan study states that patients with Klinefelter's Syndrome ***"have a higher incidence of diabetes mellitus."***[M8]

## Leg ulcers

One study from France reported that an individual with chronic leg ulcers, (six years), was diagnosed with Klinefelter's Syndrome. It also stated that there was a higher frequency of venous insufficiency in patients with KS.[M9] While a study from The Netherlands stated that leg ulcers, especially in combination with hyper-pigmentation or atrophie blanche of the surrounding skin can be a symptom of Klinefelter's Syndrome and are not necessarily to be attributed to venous insufficiency.[M10]

Both these papers contradict a verbal medical statement that leg ulcers are only likely to be linked to KS if there is ***no*** underlying venous insufficiency.





## Obesity

There is no doubt that Klinefelter's Syndrome is linked to obesity, but KS is not the direct cause. Eating the wrong diet is the culprit.

Obesity is a very serious condition – one in which I know all too well, having spent most of my adolescent and adult life trying to correct and is linked to cancer, strokes and heart disease.

Those with KS will find it easier to gain weight and harder to lose it, and many with KS will be over-weight or obese.

For a child, sweet things are a favourite and all to easily they are on the slippery slope to weight problems. For this reason, parents of a diagnosed KS child, or teenager, will be advised by their GP or dietician, as to the most appropriate diet for their child – ***and this should be for life!***

### Cancer link

One of the causes of breast cancer in males is from high oestrogen levels. All males produce some oestrogen, which helps to maintain our bones, but high oestrogen levels have been linked in the past to breast cancer. Besides chronic liver conditions and genetic conditions obesity is a causal element; in that oestrogen is partly made in fat tissues of the body.

## Osteoporosis

There are many people with KS who have an aversion to medical establishments and particularly to injections, dropping vital therapy and perhaps never commencing hormone replacement in the first place. **This *can* lead to extreme osteoporosis.**

***Yes — you're right, I am trying to scare you.*** For it's the only way to get the message across. Remember what I said on page 15? ***'If you take only one piece of advice from this guide.'*** Will this is it! No excuses now... ***GET YOUR TESTOSTERONE TREATMENT!***

Osteoporosis worsens silently, and when breaks occur they can be caused by a small amount of force and are painful and debilitating, leading to months of pain and stress.

If you have been without hormone replacement for decades then you should talk to your GP. The procedures will be much like those mentioned in the ***Endocrinology*** chapter.

### What is Osteoporosis?

It is the loss of bone density, which in advanced stages can leave individuals vulnerable to frequent bone fractures, particularly of the spine, hip and wrist, destroying quality of life.

Generally, osteoporosis is worse in the elderly, and in women following the menopause. While more women are affected by osteoporosis (1 in 3, compared with 1 in 12 men),[M11] generally, more men suffer from 'Avascular necrosis.'


**M8**
**Robinson, S. et al.**
*Diabetes secondary to genetic disorders.*
Unit of Metabolic Medicine, St Mary's Hospital Medical School, London, UK.

**Pei, D. et al.**
*Insulin resistance in patients with Klinefelter's Syndrome and idiopathic gonadotrophin deficiency.*
Division of Endocrinology and Metabolism, Tri-Service General Hospital, Taipei, Taiwan.

**M9**
**Villemur, B. et al.**
*Leg ulcer and Klinefelter Syndrome.*
Service de Chirurgie Vasculair (Pr. Guidicelli), CHU, Grenoble.

**M10**
**Varaart, JC. et al.**
*Leg ulcers with hyperpigmented maculae and white atrophy as manifestation of Klinefelter's Syndrome.*
Academisch Ziekenhuis, afd, Dermatologie, Maastricht, The Netherlands.

**M11**
For more details contact the **National Osteoporosis Society (NOS).** See ***Further Study*** p78.
**w:** www.nos.org.uk

**M12**
**Breuil, V. et al.**
*Gonadal dysgenesis and bone metabolism.*
Rheumatology Dept, CHU de Nice, Hospital l'Archet 1, France.

**M13**
**Delmas, P. et al.**
*Osteoporosis in Klinefelter's Syndrome Quantitive bone histological data in 5 cases and relationship with hormonal deficiency.* (French paper, no establishment details available).

**M14 & M15**
Try the ***'Search'*** facility at:
**w:** www.nlm.nih.gov/pubmed/
(**National Institute of Health** website, USA).




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### What causes this condition?

For those with Klinefelter's Syndrome, as well as males in general, one of the risk factors is from low levels of testosterone and dihydrotestosterone (called hypogonadism).[M12] Because these sex steroids (hormones) play an essential role in the maintenance of bone mass, some studies have been done to investigate males with gonadal dysgenesis, particularly those with Klinefelter's Syndrome.

Studies have shown a reduced osteoblast function and reduced 5 alpha-reductase activity; which is responsible for partial resistance to androgens, with increased bone turnover, particularly at the femoral neck.[M12] In another case it was suggested that bone rarefication in KS is associated with a reduction in hormones, not directly with the chromosome condition.[M13]

**DID YOU KNOW?**

Like any subject, take care what you read. Even if viewed from reputable newspapers or websites, back-up with proof from other sources, i.e. medical papers or specific support groups.

For example: ***January 2004*** – saw press coverage for a new drug with strong claims that it would give hope to thousands of women crippled by osteoporosis, after it was found that the risk of spinal fractures was reduced by 90% after taking it.

One source said that *"[it] is the first drug to not only halt the disease, but to begin to cure it."* Another source said that the drug was also available for males.

At that time the drug was actually only being prescribed to a limited number of patients with very severe osteoporosis, who had to fulfil certain criteria. It was *not* a cure for osteoporosis, nor was it licensed for men.

However, that's not to say situations like this are static. Guidelines can change, and some men may be able to join trials of certain drugs.

For more detailed information on this treatment, or osteoporosis in general, contact the **National Osteoporosis Society.** M11

**Associated conditions:**

These include chronic use of corticosteroid drugs, Crohn's disease, chronic immobility, gastric surgery, heavy drinking, a history of fractures, low body weight, smoking and specifically to KS; those with low levels of testosterone (hypogonadism). There is also a recognised and well documented link between KS and Systemic lupus erythematosis, and the latter to osteoporosis.[M14]

### What are the symptoms?

Warning signs are usually a broken bone resulting from a minor fall, curvature of the spine and height loss.

In itself, osteoporosis causes no pain; it is purely the thinning of bone tissue. However, in advanced cases, if that breakdown is part of the femoral head for example, pain is very much in evidence when exposed ragged bone interacts with the muscle and cartilage of the surrounding pelvic socket and tissue.

### How is it diagnosed?

As with avascular necrosis, normal X-rays do not highlight osteoporosis soon enough, and again, DEXA (DXA) scans are employed to measure the bone density. ***"It is currently the most accurate and reliable means of assessing the density of bones. It is a 10-15 minute painless procedure, that uses very low doses of radiation."*** M11

### Treatment, Pain Management and Ongoing bone maintenance

Basically as Avascular necrosis.

As with the latter condition, there is one thing that anyone with KS can do right now, and that is to discuss possible hormone replacement therapy with their doctor or an endocrinologist.

***Don't jeopardise your future health for the sake of a few seconds (possible) discomfort each month.***

Of course if you're suited to the testosterone gels *(see p24)* there should be no excuse!

### *Other conditions*

There are also (possible) KS links to conditions such as Taurodonism and Radial Ulnar Synostosis, and because of the slightly increased risk of autoimmune conditions, there are links to Asthma and Chronic Thyroiditis.[M15]



# The Sex/Gender Spectrum

## Terminology & Usage

Chapter updated 07.2010

**In-depth information**
Please see end of chapter for details to more information on the following definitions.

### Understanding and Compassion

As yet there are no controls over how our body's blueprint creates us. *We are born how we are born.*

It is strange that the older humanity gets the more confused it becomes. Aren't we supposed to learn from our experiences? Why can't humanity abandon outdated Victorian attitudes, put aside sensationalistic notions, flip negative to positive —***and celebrate the diverse spectrum of its offspring?!***

**VERY IMPORTANT**

- Use 'Transsexual' as an adjective, never as a noun, e.g. ***"He is a transsexual person."*** Not, ***"He is a transsexual."***
- Use pronouns preferred by intersex and trans people. Don't ever call them 'he/she' or 'it.'
- Do not make assumptions that someone is gay, intersexed or a transsexual person based on voice or appearance.

Why does it have to be difficult; why can't it be easy? Unacceptance often comes from ignorance of the facts and unfamiliarity. With just a little more understanding *and* compassion, think how much less grief there would be in the world.

That said, today, more than at any other time, there *are* those who are willing to cast aside outdated prejudices towards minority physiological and social groups, and to try and understand. But accepting other sex or gender groups is one thing, but what terms do you use without causing offense?

### Terminology and Usage

As far as Sexology is concerned, around the globe language is in flux; altering the meaning of well established terminology and definitions. This is compounded by various social communities who periodically interact, incorporating themselves into other groups' politics, which can cause serious inter-group disputes and confusing terms and definitions. The situation also changes from country to country. And if that wasn't confusing enough, it also seems that even to those working in sexology on a daily basis sex/gender terminology and usage is confusing!

So opening your mind is one thing, but when you don't understand the answer, then you're going to wonder why you bothered; i.e. what is and what isn't PC. And to cap everything else, terminology is fluid, so what you are about to read will undoubtedly change.

I would be lying if I said the following wasn't complicated; it took over a year to get this chapter right, but I hope like me, you will be astonished at what you are about to read. And please persevere, for the more we understand and use these terminologies the more we help everyone – *and* made a difference.

**Key words:**
***Sex, Gender, Sexual Identity, Gender Identity, Gender Role, Gender Dysphoria, Gender Identity Disorder, Transsexualism Transgendered, Androgyne, Sexual Orientation, Intersex, Transvestism.***



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## Sex and Gender

While these two terms are generally used interchangeably by society without any difficulty, it is when medical, research, political, legal and religious aspects arise that this generalisation can lead to confusion and misunderstanding.

'Sex' describes the perceived external or anatomical or biological image; 'phenotype', while **'Gender'** is the psychological identification of the individual, it is how individuals experience themselves. Gender is also the social/cultural expression of that identity. Typically, of course, these elements of sex and gender are consistent, ***"Sex typically, but not always, represents what is between one's legs, whereas Gender represents what is between one's ears."*** [MD]

## *Identity* – Sexual Identity

As mentioned, terminology and its definitions vary enormously around the world and the above term is no exception. Originally this book was targeted at the UK reader, but now covers other parts of the world. Because of this, the above term varies from country to country. Trying to explain this has caused much confusion, stress and gnashing of teeth.

For my sanity and as there is limited space here to explain it all, the following are the terms and definitions originally supplied to me by ***Prof M Diamond, University of Hawaii, John A Burns School of Medicine, Hawaii, USA,*** which relates to a sizable part of the world.

However, the **name** 'Sexual Identity' is an issue in the UK, Australia, New Zealand and *some* parts of the USA, where it refers to 'Sexual Orientation'. For this reason I strongly advise you to contact the ***Gender Identity Research & Education Society (GIRES)*** [M1] or another gender information group for the current terms. *(Please see p76 for contact details).*

## *Sexual Identity & Gender Identity*

'Sexual Identity' is the way someone sees his or herself as **male** or **female**, based on the person's outward physical appearance (phenotype). 'Gender Identity' is the perceived social image of being a ***boy/man,*** or ***girl/woman.***

For example, a KS person may see their 'Sexual Identity' as **male** but see their 'Gender Identity' (their psychological self) as feminine and prefer to live as a ***woman*** e.g. *"I am a woman trapped in a male body."*

In the typical individual sexual identity and gender identity are in agreement. It is only when the individual is possibly a Transsexual person or Transgendered that it becomes an issue – and only in certain societies.

It is believed that like Sexual Identity, Gender Identity is hard-wired into our brains, but there is insufficient evidence to be certain. There is likely to be some 'modification', which does not show itself until after birth when behaviour patterns are observed.

**M1**
Paper by the **Gender Identity Research & Education Society,** UK.
*'Atypical Gender Development – A Review.'* Available on their website. **w:** www.gires.org.uk/

**M2**
**Prof Dick F Swaab,** *Director,* Netherlands Institute for Neuroscience, Amsterdam, and **Prof LJG Gooren,** Free University Hospital, Amsterdam, respectively, have produced papers, recognising clear physical structures within the brain relating to gender dysphoria. *(Please see **Further Study** p76 for more details).*

**M3**
**Prof Gooren, LJG.** (1993), *It is expected that the diagnosis of Transsexuality may be modified with increasing scientific and medical knowledge to Neurological Intersex.* Free University Hospital, Amsterdam, The Netherlands.





Gender identity may or may not be in accord with the sex characteristics of the rest of the body. Where there is profound and persistent discord the individual may be said to be a transsexual person.

Nothing stands still in research and some studies have shown a fundamental relationship between Gender Identity and ***"hormonal changes at puberty, which alter previously set neuronal systems within the hypothalamus of the brain."*** [DS/M2]

In fact, ***"Transsexuals clearly show evidence of mixed structures."*** [LG/M3] Although it has not yet been determined if this is causal or symptomatic. (These areas are called SDNs, or Sexually Dimorphic Nuclei).

## *Gender Role*

'Gender Roles' refer to our idea of how boys and girls and men and women should act and be treated in society.

For example, it used to be that men's 'Gender Roles' were typically associated with strength, aggression and dangerous occupations, while women's 'Gender Roles' related to a gentle nature, childrearing and nurturing. Nowadays, to a certain extent, these roles are more blurred, with women becoming the sole bread-winners while the man becomes the house-husband. Of course these descriptions change around the world, for example, in African societies roles will be very different to those in the UK.

'Gender Roles' on the other hand, could be said to be openly or discretely dictated by society, for example, in the way girls learn to keep their knees together, properly adjust their clothing and apply make-up, while boys tend to sit with their legs spread wide open, memorising the rules of sport.

Throughout life, gender role will be influenced by interactions with family and the rest of society.

Not all transsexual people will decide to change their gender role so that it conforms to their gender identity.

## *Gender Dysphoria or Gender Identity Disorder (GID)*

This relates to the conflict between a person's gender identity and the sex characteristics of the rest of the body.

***"Despite considerable gradations most [people] are close enough to one end or the other of the gender/sex spectrum that they never have to question whether their gender identity is consistent with their sex. Since this is true for most, it is assumed to be true for all babies - that what you see is what you get. But this is not always so."*** [M4]

Some people are born **male** but their brain, as they develop, tells them that they are a ***girl*** or ***woman***, or born **female** and feel that they are a ***boy*** or ***man***. It is as natural to them as it is to others who are, for example, born **male** and know they are a ***boy*** or ***man***.

There are cases of gender conflict in children as young as 4.[M5]

Whatever the reason, and there are many, it is a powerful and compelling force. *We are, what our brains tell us we are.*

**M4**
**Gender Identity Research & Education Society (GIRES)**
*(See **Further Study** page 76).*

**M5**
**Zucker, KJ. et al.** (1992), *Gender Identity Disorder in children.*



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## Transsexualism

Transsexualism arises from a conflict between the brain and the rest of the body. Transsexual people are those who exhibit the criteria for Gender Dysphoria or Gender Identity Disorder (GID).[M6]

Sometimes distinctions are made as to whether the person is a preoperative or postoperative transsexual person.

To partly remove the distinctions of Gender Identity Disorder and Gender Dysphoria which are clinically associated with the term 'Transsexual', the terms 'Transman' & 'Transwoman' were adopted – later modified to 'Trans Man' and 'Trans Woman.'

These recent terms are used, at least in the UK; rarely in the US, in the context of, for example, ***"That person was born female, but is now living as a trans man,"*** and vice versa.

There are other transsexual people who extend the MtF/M2F (**male** to **female**) or FtM/F2M (**female** to **male**) acronyms, to WBM (***woman*** born **male**), or MBF (***man*** born **female**), or MBT and WBT (***man*** or ***woman*** born transsexual). ***"These designations are used to indicate that they believe their condition is natural and that they were born in*** **'the wrong skin'.***"*[MD]

**M6**
It should be noted that GID is not used for children; who have separate criteria. A child or adolescent with gender dysphoria is generally not considered a transsexual person until he or she is an adult.

**M7 & M8**
Take a look at the research papers by **Prof Diamond** mentioned at the end of this chapter, for more information on these complex subjects.

## Transgendered

This term is currently open to several definitions.

In the past the term was ***"adopted by individuals who might otherwise be identified as intersexed, transsexual or even homosexual or bisexual"***,[MD] exhibiting traits of both men and women and who preferred to slip in and out of these gender roles or maintain the combination. Lately however, it has taken on the reverse meaning, including ***"transsexuals, transvestites, drag queens [and kings] and others who bend society's usual gender boundaries. Some welcome the term owing to its inclusiveness and others abhor it for the same reason."***[MD]

From recent studies it is clear that individuals who exhibit transgender behaviour want to change aspects of their gender, but don't necessarily want to permanently change their sex. That said, in 2010 the UK media still use the same definition for transgendered and transsexualism.

As with different social groups so there are global changes to the definitions. In some states of Australia for instance, they use 'transgender' exclusively for 'transsexualism', (generally shortened to 'Tranny').[M7]

It seems like the Australians, that some other communities around the world, such as homosexual and bisexual people and also other groups such as intersex, are adopting the term transgender.

About five years ago, in the UK the term '3rd G' (Third Gender) and in the States the term 'TGV' (TransGender Variant) were adopted, though it is not clear if these terminologies took hold and became commonplace.





## Androgyne

There are two definitions for this term. One refers to the androgynous (sexual) aspect of **males** and **females** *(see **Intersex** p68)*, the second to the androgynous aspect of ***masculinity*** and ***femininity*** (gender).

The latter definition is explained here, as it is often used, particularly in the UK and parts of the USA, where this community of people are called 'Androgynes'. *Other terms include: agendered, between genders, bigendered, gender fluid, gender-neutral, intergendered, non-gendered and pangendered.*

Society has grown up within a sex and gender binary system. As we welcome the dawn of life we are assigned a gender governed by what genitalia we have. But there are those who see a whole spectrum of genders; individuals on the fringe of both the transsexual and transgender communities.

It relates to a person who's gender transition isn't 100%, e.g. a **male** who feels that they are both genders, a ***man*** and a ***woman*** at the *same* time, in comparison to a transsexual person who knows that they are totally the opposite gender, example: a **male** who feels she is a ***woman.***

This divided gender mix can sit anywhere along the ***man/woman*** spectrum e.g. 70% ***man***/30% ***woman*** or 30% ***man***/70% ***woman***.

Like any gender related issue, these feelings can be an extremely sensitive and emotional aspect of a person's life and may not be divulged even to a partner, spouse or close family members.

While I have heard of three individuals with KS with this gender mix, because of my limited study so far, it is not clear how they view their situation (Androgyne, Transsexual or Transgendered person).

Two individuals have a female partner and while one is happy to be a ***man***, the other lives and works as both a ***man*** and a ***woman***. So, I can only really comment on the third case history... myself.

I had a slow gender shift, resulting in *around* an 85% ***masculine***/15% ***feminine*** shift. I am unsure if the gender shift was caused by a chromosomal or hormonal influence on my brain during gestation caused by the Klinefelter's Syndrome or some other physical or psychologically unconnected factor.

While this diagnosis was not made by a healthcare professional, it does not detract from how I feel. And although I don't openly discuss my dysphoria, I can say that I have – and will continue to be, happy to maintain my ***man***/**male** persona and to embrace my ***feminine*** side. My only regret was in not telling those closest to me until recently. I am heterosexual and previously married. *(See **A Personal Message** p30).*

Maybe others with Klinefelter's Syndrome hide their mixed gender feelings too. It would be intriguing to discover just how widespread this trait is within the KS community and what the mean percentage shift is, but sadly my efforts to find out have, understandably, yielded silence.

## Sexual Orientation

This term relates to whether you are attracted to the opposite sex, your own sex, or both. In other words Heterosexual (Straight), Homosexual (Gay male or Lesbian) or Bisexual (Bi). Also, Pansexual and Asexual.

Currently the above terms are used to describe a person (e.g. ***"He is Bisexual."***).



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However, it has been suggested that for clarity the terms should be used to describe behaviour, rather than people and to use non sex/gender terms which avoid the stigma that goes with terms such as 'homosexual' etc.

These relate to the erotic/love preference of an individual, that is:
Androphillic = male loving (attracted to people with male sex organs); Gynoecophillic = female loving (attracted to people with female sex organs); Ambiphillic = both loving.[M8]

**DID YOU KNOW?**
It has been suggested that:
*"It will be familiarity rather than knowledge that finally takes away [Intersexuals] supposed strangeness."*[AF-S]

**DID YOU KNOW?**
Regarding Intersex and Transsexualism, *"Socially the groups are quite distinct. Whether or not biological factors exist that cross the definitions is debatable."*[MD]

**DID YOU KNOW?**
*"Intersex is genetic, except in very rare cases of environmentally induced intersex from drugs, chemicals and hormones that have entered the mother prior to, or during pregnancy, or damage to the father's sperm."*[MC]

## Intersex

**Please note:** See p52-55 for 'Intersex' definitions, or contact the AHN, AIS and CAH support groups for an extensive description of Intersex, relative to their own conditions. *(Contact details p77-78).*

The majority of this chapter was completed in 2005 and does not take into account the *Consensus Statement on Management of Intersex Disorders*, published in 2006. Please see p55 for more details.

***"Intersex (IS) groups are against shame, secrecy and non-disclosure. IS groups, adults and teens in particular, are also against surgery without informed consent, unless life-threatening circumstances due to both the psychological and physical damage to sensate and sexual function.***

***Parents and clinicians though still often opt for early surgery, as society is so unaccepting of IS because it's not understood."***[MC]

***"Sometimes even specialist clinicians use the term 'Intersex' to mean 'Ambiguous genitalia' forgetting that they are excluding a large proportion of intersexed patients who have a complete female phenotype (and usually no sexual or gender identity problems). This causes us a lot of problems as the media pick up on this... conveying to the general public that gender identity is, of necessity, an issue in intersex which it is absolutely not."***[MS]

You may come across the terms 'Hermaphrodite' and 'Pseudo-hermaphrodite.' Medicine took on these terms in the 1800s. The name originates from a Greek mythical character which had a complete set of female and male internal and external reproductive organs, ***"which in reality is totally impossible."***[MS]

However, it is possible to be born with one ovary and one testis, or one organ with both ovarian and testicular cells (ovotestis). This is an extremely rare condition and can affect those with KS.

That said, some people (including those with KS) consider themselves – *and* are considered by others, to be 'Androgynous' and call themselves 'Androgynes.' This term applies primarily in Australia and parts of the USA.

The term 'Hermaphrodite' is very occasionally used in the USA and UK, but 'Intersex' is now the preferred term. ***"Most of our members detest these hermaphrodite terms." "...we feel these terms should be banned from the medical literature."***[MS]

## Transvestism (or Crossdressing)

Like many of the other terms this one can mean more that one thing.



The original term made by Magnus Hirschfeld (1910) identifies all orientations participating (i.e. straight, gay and bi). However, to most sexologists today the term refers to heterosexuals only.

Up to now the term has meant a person, usually male, who acquires erotic pleasure by wearing clothes of the opposite sex. While this will be true for some, in recent years many heterosexuals have disagreed with the latter definition, stating that autoerotic pleasure is not the motive, but a part of their personality which cannot be expressed in any other way.

That said, for some individuals there can be a sexual element to it; for example, feeling the texture of the clothes, or observing the reaction of other people.

Around the world there are societies in existence specifically for heterosexuals and their wives, with the Society of the Second Self (SSS) being the largest organisation of its kind in the US. The latter shows that the way people dress doesn't always identify our preferred partner.

To postoperative transsexual people crossdressing is not generally sexually arousing as it is their typical everyday attire.

Females also cross-dress, however, the term transvestite is rarely applied, since females are able to wear male clothing far more easily. For instance, in business circles it is common to see female fashion depict grey pin-stripped trouser suits & ties.

There are also those who cross-dress for theatrical purposes and they will be of any orientation.

**In-depth information**
***This chapter has been compiled with the invaluable assistance of the following people:***

**MC Miss M Cull,** Adrenal Hyperplasia Network (AHN), UK.
**w:** www.ahn.org.uk

**MD Prof M Diamond,** University of Hawaii, John A Burns School of Medicine, USA.
Some definitions used from: *'Sex and Gender are Different: Sexual Identity and Gender Identity are Different,'* and *What's in a name? – Some terms used in the discussion of Sex and Gender.'*
**w:** www.hawaii.edu/PCSS

**BR Mr B Reed,** Gender Identity Research & Education Society (GIRES), UK.
**w:** www.gires.org.uk/

**MS Ms M Simmonds,** Androgen Insensitivity Syndrome Support Group (AISSG), UK.
**w:** www.aissg.org/

## Common confusions

**Transsexualism and Intersex:**
***"'Transsexualism' may be understood as a conflict between the psychological identification as male or female on the one hand, and on the other, the phenotype (external sex appearance), and the gender role which is associated with that phenotype."***[BR]

'Intersex' is a person who shows anatomical characteristics of both sexes and embraces a wide range of different conditions. ***"Intersex is genetic, except in rare cases where drugs, chemical and hormone factors are involved."***[MC]

**Transsexualism and Sexual Orientation:**
Transsexual people aren't automatically attracted to the same sex. For example, a male to female (MTF/M2F) transsexual person believes she is female, but may seek a male partner (which should be regarded as a heterosexual relationship), or a female partner (which should be regarded as a lesbian relationship).

According to current studies, ***"it is more common for FTM/F2M transsexual persons to be attracted to females predominantly."***[MD] *(See also the Sexual Orientation section).*

*Hopefully one day, (undoubtedly when I'm fertilising the ground), humankind will celebrate the diversity of its offspring.*

*No longer will it be viewed as a dichotomy, but will look back at these dark ages and wonder why we had such difficulty recognising and accepting our illuminated sex/gender spectrum.*



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# Further Study

## Addresses and Websites to Support Groups Medical Specialists and Research Units

I hope that the following contacts help you to find what you are looking for; be it a few explanatory leaflets, someone to talk to on the phone or through correspondence, or understanding and help from another family going through the same things as yourselves.

I wish you every success with your studies, but like so much in life, be sensible about it. Just because there might be a Klinefelter's Syndrome link to another medical condition, don't automatically assume you've got it too. Even with the same karyotype everyone is different and will have vastly differing symptoms and traits.

If you feel really strongly about a subject, then talk to your GP. But ***please,*** remember that doctors have a very heavy workload, so be sure no one else can help you first.

When you do visit your GP take a written note of all your symptoms, explain how you feel, try not to leave anything out; you may regret it later, and if you want to talk about emotional things consider asking to see a counsellor.

Like your doctor, things you say to a counsellor are strictly confidential. Don't expect quick results though, as it can sometimes take a number of weeks.

You may prefer to initially contact one of the support groups. They are usually run by people with the same condition and offer support and information. Support groups also have a louder voice than just one person, if you want to be heard.

### Libraries

Take full advantage of your local library's resources and the expert knowledge of the staff, who can also acquire published research for you to borrow. There may be a small charge for loans outside your region.

Most libraries offer Internet access. There is usually a maximum time limit (e.g. 1 hour) and there may be a charge for this service.

There is a small list of books and published research papers at the end of the contacts, which may be of interest to you. Support groups will be happy to advise you on publications for your particular condition.

### Need to make an international phone call?

If phoning outside your own country, please remember to include the ***International Access Code*** of your own country; the ***Country Code*** for the place you are calling; the ***Area Code*** (if it has one) and the ***Local phone number***.

For instance, to phone the UK, dial ***00 44*** before the Area Code. Examples: to phone *Contact a Family*, dial ***00 44 020 7608 8700.*** You will have to drop the first zero of the Area Code (tinted). To phone Canada dial ***00 1*** first.



### Cautions, Suggestions & Useful tips

Every effort has been made to check out the following contacts. However, occasionally inter-group politics and other situations can arise and you can get the odd bogus organisation that slips through the net – so get into the habit of thoroughly checking out any group or individual; whether it is included here or elsewhere. Try obtaining information from two or three groups, for comparison. A good place to start is the ***FAQ*** and ***About us*** links on a group's website.

Names and addresses can also change, as well as websites. I have included some contact names, which are preferable to 'Madam/Sir', but please remember people move on. Websites can also be in the process of being upgraded. Don't give up though, go back to the site another day.

It is possible that like me, you will settle on your own favourite and trusted contacts; giving the best information for your particular condition. I have tried to include as many as possible to aid in your search. And hopefully once the book is circulated, more organisations will wish to add their contact details, which I can include at the next pdf update in 2012.

There are also some contacts which are included as a 'thank you' for their invaluable assistance with specific chapter facts and figures, and aren't necessarily linked to Klinefelter's Syndrome.

In most countries, particularly the USA, the word *Klinefelter* is used, rather than *Klinefelter's*.

Please remember when enquiring about information from support groups; even if you're not asked, to enclose a SAE or stamps; as the majority are run as charities, by people who rely on donations for their funding.

If the person you are dealing with is in another country, consider asking what a suitable donation would be (particularly if you plan to access information on a regular basis). But nobody will expect you to do this if you are getting pocket money!

### Do you live outside the UK?

If you are not from the UK please adapt the information within the ***Further Study*** chapter to suit your own country; particularly when making international phone calls. *(Please see foot of previous page).*




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## Website search tips

***Unused to using the Internet? Here are some tips to get you started on your studies.***

When you first access a particular website, quite often you can gain a good deal of valuable information from the *FAQ* page (Frequently Asked Questions).

If you are unable to access the information you require from a particular site, go to the *Home page* and if a **'Search'** facility is available, type in key words within the field: e.g.*'Klinefelter's Syndrome and Osteoporosis'*, or variations. An **'Advanced Search'** facility will give better results, with less chance of non-related material. Also look out for similar linked information (e.g. *'Related articles'*).

Specific paper titles or the author can be typed into a search field in a general search engine, though you would be better going to a reputable medical or support site. There are also specialised websites for finding specific organisations or people. Have a word with your local library staff for books on the Internet.

If a dialogue box states that the web address you asked for cannot be found, try experimenting e.g:

**.co .com** (company) **.org** (organisation)
**.gov** (government) **.ac** (academic)
**.ed .edu** (education) **.net** (network).

You may also have typed a dot instead of a dash.

There are going to be times when a particular site will link you to a related article site, and that to yet another site (ad infinitum). If you wish to return to your original site then add it to your **'Favourite'** or **'Bookmark'** folder.

If you have difficulty getting back to your original site, go into **'History'** and click on the appropriate site.

### USING GENERAL SEARCH ENGINES

Here are a more Internet tips for you to try.

#### 'Plain-English' searches

The simplest search for beginners. For instance, to find other international Klinefelter's Syndrome support groups, type a question into the field, e.g. *where can I find swedish klinefelter syndrome support groups?* Or non-specific: *...klinefelter syndrome support groups?*

Note: Plain-English searches don't work on all search engines.

#### Key words

To reduce the quantity of non-relevant information, in the search field try to use the most unique key words. Also try swopping around your key words, as some search engines take more notice of the first word.

#### Multi-step searching

If looking for a specific subject linked to KS, e.g. Diabetes, try a multi-step process. First, give it your best shot, then review the results of the first couple of pages picking out key words linked to diabetes, then use these words within your next search. Narrow the results by using 'set searching'. To do this, most leading engines offer a 'search within these results' field.





#### Title words

Try using words that might be in the title of the document you seek, for example (starting with the search term): *title:"klinefelter syndrome"* (note, no space between colon and first quotes, and no apostrophe 's' for US sites). For Google use the search terms **allintitle:** or **intitle:** The former term will look for *all* words in the title, while the latter *any* words. For Yahoo use **t:**

#### Case-sensitive searches

Always use lower-case unless searching for a person, location, book/paper, etc; then use initial capitals.

#### Spelling

Often a *'no results'* outcome will be caused by poor spelling. 'nough said!

### FURTHER STUDY pdf LINKS TO WEBSITES

#### Addresses in two lines

Due to technical aspects beyond my comprehension (grrr), website links on the following pages which are in two or more lines, will not function. For these links, take a note of the address or adjust your web browser window so you can read the address link in the book, then manually add the additional lines of text to your browser's search field.

Facebook and Twitter also don't link.

#### No hash key?

Please note that some addresses use the hash symbol (#). For those people who use UK keyboards, you will not have this symbol, instead, type: Alt + 3.

## The end of the KS story?

As long as there are people out there trying to understand Klinefelter's Syndrome; whether for research, support, treatment, or just you and I trying to understand how our mind and bodies function, then the KS story will continue.

Whatever you decide to do. However you decide to do it. I wish you peace of mind — *and body*.

***And as you look through the following pages, remember...***

You are never alone



REFERENCES p11

# Klinefelter's Syndrome

## UNITED KINGDOM:

**BBC Health** (UK)

***Klinefelter's Syndrome***

**w:** www.bbc.co.uk/health/physical_health/conditions/klinefelter1.shtml

*General information on KS, as well as Diabetes, Osteoporosis, Thyroids and other medical conditions.*

**Contact a Family** (UK)

209-211 City Road London EC1V 1JN

**t:** 020 7608 8700 **f:** 020 7608 8701

**textphone:** 0808 808 3556

**helpline:** 0808 808 3555

**e:** helpline@cafamily.org.uk

**w:** www.cafamily.org.uk

***Please note:*** *both Textphone and Helpline are Freephone numbers, and Helpline is for parents, families and carers only (10am-4pm).*

***Contact a Family*** *is a UK based charity offering information and advice to parents on many different conditions.* ***Use the search facility to access Klinefelter's Syndrome.***

**Klinefelter Organisation** (UK)

PO Box 9969 Colchester CO1 9FQ

**e:** ask@klinefelter.org.uk

*Or use the Contact Us link on the website.*

**w:** www.klinefelter.org.uk

*Valuable information and an opportunity to contact other KS people, including wives, partners and parents. Membership is available to all KS individuals from the UK and Ireland.*

**Klinefelter's Syndrome Association** (UK)

Contact: Mrs Sue Cook

*Founder and National Co-ordinator*

56 Little Yeldham Road Little Yeldham

Halstead Essex CO9 4QT

***All telephone enquiries:***

**t:** 0845 230 0047 (Local rate UK number)

***Family, child & young people enquiries:***

**e:** coordinator@ksa-uk.co.uk

***Adult enquiries:***

**e:** adults@ksa-uk.co.uk

*Information can be posted; please send an SAE (C5 or DL). Membership details on website.*

**w:** www.ksa-uk.co.uk

*Information and membership are available to those with Klinefelter's Syndrome or its variants, their families, spouses/partners, friends and carers.*

*The KSA accepts that it is the individual's right to self-determine if they consider themselves to be intersex or not. This charity supports and respects, regardless of that individual choice, those with KS.*

***Forum:***

**w:** www.xxytalk.com

**DID YOU KNOW?**

Although the underlying cause of the additional X chromosome is unknown, the following is generally agreed.

Paper by: **Jacobs PA, et al.**
Dept. of Pediatrics, Cornell University Medical College, NY, USA, that nondisjunction is attributed to:

53% paternal meiosis stage 1
34% maternal meiosis stage 1
9% maternal meiosis stage 2 3% post-zygotic mitosis

[1% short]

**Age Linked:**

**Maternal derived XXY** *Age causes a marked difference in maternal meiosis stage 1, but not in stage 2 errors.*

**Paternal derived XXY** *There is no affect caused by age.*

Some papers waver either side of the above. Example: paper by: **Smyth, CM. et al.** University of Seattle, USA, shows:

53.2% paternal meiosis stage 1
34.4% maternal meiosis stage 1
9.3% maternal meiosis stage 2 3.2% post-zygotic mitosis

[1% over].





## INTERNATIONAL:

**47xxy.com** (CA)

**e:** 47xxyorg@gmail.com

**w:** www.47xxy.com

**klinefeltersyndrome.org** (USA)

Contact: Stefan D Schwarz

**e:** stefan13@cox.net

**w:** www.klinefeltersyndrome.org

*This website was created for boys, men and their families to have a resourceful place to get information. The website also acts as information for those learning about the condition for potential diagnosis or for research projects.*

**Klinefelter's Support Group of Western Australia** (AU)

14 Shetland Drive Morgan Fields Estate

Henley Brook Western Australia 6055

**t:** (61) 08 9296 8661

**e:** kerrygavey@iinet.net.au

**w:** www.klinefelterswa.websyte.com.au/

*An important aspect of the Klinefelter's Support Group is to provide support, information and resource materials about Klinefelter's syndrome to affected individuals and families in Western Australia.*

*It also endeavours to provide health professionals and the community with information about our Support Group and Klinefelter's syndrome.*

**Klinefelter Syndrome Support Group (KSSG)** (AU)

**t:** (61) 02 98362970

**m:** (61) 0425 240 773

**e:** klinefeltersaus@hotmail.com

*We have phone support, email support, discussing issues around Klinefelters, we give referrals to GPs & Specialists. We offer 1 on 1 chats. We seek out information for clients on other matters to do with their condition.*

# Other Sex Chromosome Conditions

## UNITED KINGDOM:

**Unique** (UK)

**Rare Chromosome Disorder Support Group**

Contact: Beverly Searle

*Chief Executive Officer*

PO BOX 2189 Caterham Surrey CR3 5GN

**t & f:** +44 (0)1883 330766

**e:** info@rarechromo.org

**w:** www.rarechromo.org

*An international group providing support and information to anyone affected by a rare chromosome disorder. Support & information for individuals or families. Rarer karyotypes,* ***not 47,XXY.***

**Triple-X Family Network Support Group** (UK)

32 Francemary Road London SE4 1JS

**t:** 020 8690 9445

**e:** helenclements@hotmail.com

*This is a support network started in 1997, offering support to families of children with karyotype 47,XXX. It publishes a biannual newsletter and has information available on request. There are over 360 families in the UK and abroad in touch with the network.*

**Turner Syndrome Support Society (UK)** (UK)

13 Simpson Court 11 South Avenue Clydebank Business Park Clydebank G81 2NR

**t:** 0141 952 8006 **f:** 0141 952 8025

**helpline:** 0845 230 7520

**e:** Turner.Syndrome@tss.org.uk

**w:** www.tss.org.uk

*The Society offers support and information to girls and women who have Turner Syndrome (TS), their family and friends.*

*Aims of the Society; membership details and support; information on links with research units, health professionals and other support groups, please contact the TSSS, or check out the website.*

For XYY Syndrome support and rarer KS karyotypes, some of which are now considered separate conditions, please contact **Unique** or try a web search.



REFERENCES p11

# Other Issues

## BRAIN RESEARCH:

**Netherlands Institute for Neuroscience** (NL)

Contact: Prof Dick F Swaab MD PhD *Professor of Neurobiology, University of Amsterdam and Leader Research Team* Neuropsychiatric Disorders
Meibergdreef 47 1105 AZ Amsterdam ZO NL
**t:** +31 20 5665500 **f:** +31 20 5666121
**e:** d.f.swaab@nih.knaw.nl **w:** www.nih.knaw.nl
*Go to NCBI for various research papers by Prof Swaab et al., related to sex differences in the human brain linked to transsexualism, and to developmental, adolescent, and adult gonadal steroid levels.*

## CANCER:

**Cancer Information Nurses Cancer Research UK** (UK)

PO Box 123 Lincoln's Inn Fields London WC2A 3PX
**t:** 020 7061 8355
**e:** cancer.info@cancer.org.uk
**w:** www.cancerhelp.org.uk
*For information on male breast cancer go to:*
**w:** www.cancerhelp.org.uk/type/breast-cancer/about/types/breast-cancer-in-men

## DIABETES:

**Diabetes UK** (UK)

10 Parkway London NW1 7AA
**t:** 020 7424 1000 **f:** 020 7424 1001
**e:** info@diabetes.org.uk **w:** www.diabetes.org.uk
*Diabetes UK is the charity for people with diabetes. We fund medical research, provide information and support to people with diabetes and campaign on their behalf. There are currently 2.6 million people diagnosed with diabetes in the UK. It is believed that there are also 500,000 people who have the condition but are unaware of it.*

## ENDOCRINOLOGY:

**Division of Pediatric Endocrinology & Metabolism** (USA)

Johns Hopkins University School of Medicine
**w:** www.hopkinsmedicine.org/
***Endocrinology:***
**w:** www.hopkinsmedicine.org/endocrinology/index.html
*Contact and appointment information is available at each of these sites. Additional information on KS at:*
***Pediatric Endocrinology:***
**w:** www.hopkinschildrens.org/tpl_rlinks_nav1up.aspx?id=2574

**Society for Endocrinology** (UK)

22 Apex Court Woodlands Bradley Stoke
Bristol BS32 4JT UK
Healthcare professionals only
*General enquiries:* **t:** +44 (0)1454 642200
*Publications:* **t:** +44 (0)1454 642220
*Conferences & Events:* **t:** +44 (0)1454 642210
*Fax:* **t:** +44 (0)1454 642222
**e:** public@endocrinology.org
**w:** www.endocrinology.org
*The role of the Society is to represent the needs of doctors, nurses and scientists who work in endocrinology.*
*'You & Your Hormones' is a new website being launched in January 2011, which aims to give patients and the general public reliable information on all aspects of hormone science, including hormone-related conditions (examples: Klinefelter's Syndrome, Osteoporosis, Obesity).*
Patient & General public enquiries
**w:** www.yourhormones.info/

**Please note.** In the UK referral to an endocrine clinic is through a General Practitioner.

## GENDER:

**The Beaumont Trust** (UK)

BM Charity London WC1N 3XX UK
**t:** 07000 287878
**e:** bmonttrust@aol.com
**w:** www.beaumont-trust.org.uk/
*Registered UK charity which aims to relieve the mental and emotional distress of people who cross-dress or who are transsexual, their partners, families etc and to educate the public.*

**The Gender Identity Research & Education Society (GIRES)** (UK)

Melverley The Warren Ashstead Surrey KT21 2SP
**t:** 01372 801 554 **f:** 01372 272 297
**e:** admin@gires.org.uk **w:** www.gires.org.uk/
*Promotes and communicates research and provides education.*

**The Gender Trust** (UK)

Community Base 113 Queens Rd Brighton BN1 3XG
**helpline:** 0845 231 0505 (UK only)
**e:** info@gendertrust.org.uk
**w:** www.gendertrust.org.uk
**facebook:** Gender Trust **twitter:** gendertrust
*The only UK registered charity specifically helping adults who are Transsexual, Gender Dysphoric or Transgender and seek to live their lives as men or women despite their genetic background.*





## GENETICS:

**Genetic Alliance UK** (UK)

Unit 4D Leroy House 436 Essex Road
London N1 3QP
**t:** +44 (0)20 7704 3141 **f:** +44 (0)20 7359 1447
**e:** mail@geneticalliance.org.uk
**w:** www.geneticalliance.org.uk/

## GENERAL MEDICAL:

**Department of Health** (UK)

Customer Service Centre Richmond House
79 Whitehall London SW1A 2NS
**t:** 020 7210 4850 **textphone:** 020 7210 5025
*Opening hours: Monday to Friday 8.30am-5pm*
**w:** www.dh.gov.uk

**National Institute for Health and Clinical Excellence (NICE)** (UK)

Level 1A City Tower Piccadilly Plaza Manchester
M1 4BD United Kingdom
**t:** 44 (0)161 870 3133 **f:** 44 (0)845 003 7785
**e:** nice@nice.org.uk **w:** www.nice.org.uk/
*The National Institute for Health and Clinical Excellence (NICE) provides guidance, sets quality standards and manages a national database to improve people's health and prevent and treat ill health - regardless of where they live in England and Wales.* [See p48 for Northern Ireland and Scotland].

**Prof Milton Diamond PhD** (USA)

University of Hawaii John A Burns School of Medicine
Department of Anatomy and Reproductive Biology
Pacific Center for Sex and Society 1960 East-West Road Honolulu Hawaii 96822
**t:** (808) 956-7400 **f:** (808) 956-9722
**e:** diamond@hawaii.edu **w:** www.hawaii.edu/PCSS
*Professor Diamond has published a prolific amount of material on sex and gender issues and lectures widely. More details on website.*

**MedicineNet** (USA)

**w:** www.medicinenet.com
*Comprehensive articles on health and medical topics produced by US Board Certified Physicians. Go to:*
**w:** www.medicinenet.com/9610
*to read the main article on Klinefelter Syndrome.*

**National Center for Biotechnology Information** (USA)

**w:** www.ncbi.nlm.nih.gov
*A highly recommended site for information on KS and other associated conditions. For research papers use the **Search** field to find specific authors or titles (will access PubMed and other databases). For **MedlinePlus** **('Health Topics'** (KS definitions and general health issues), **'Medical Encyclopedia'** and **'Medical Dictionary')**. Go to **National Library of Medicine** at:* **w:** www.nlm.nih.gov

## INFERTILITY:

**Human Fertilisation & Embryology Authority** (UK)

21 Bloomsbury Street London WC1B 3HF
**t:** +44 (0)20 7291 8200 **f:** +44 (0)20 7291 8201
**w:** www.hfea.gov.uk
*The HFEA is a non-departmental government body that regulates and inspects all UK clinics providing IVF, donor insemination or the storage of eggs, sperm or embryos. The HFEA also licenses and monitors all human embryo research being conducted in the UK.*

**Infertility Network UK** (UK)

***Infertility practical & emotional support***
Charter House 43 St Leonards Road Bexhill-on-Sea
East Sussex TN40 1JA
**t:** 0800 008 7464 **f:** 01424 731858
**e:** admin@infertilitynetworkuk.com
**w:** www.infertilitynetworkuk.com
*Factsheets; publications; quarterly magazine; local and regional support groups; videos and information days held regularly.*
*We are also part of the Fertility Show; a dedicated and discreet environment where you can learn about your fertility issues with experienced and sympathetic professionals. For more information please visit:*
**w:** www.fertilityshow.co.uk/

## INTERSEX:

**Adrenal Hyperplasia Network (AHN)** (UK)

**e:** webmaster@ahn.org.uk
**w:** www.ahn.org.uk
*Provides support, information, meetings to people with CAH. Also provides support for research, researchers and clinicians. Works closely with the medical profession to improve treatment and raise awareness of CAH within society.*

**Androgen Insensitivity Syndrome Support Group (AISSG)** (UK)

*Please see website for current contact details.*
**w:** www.aissg.org/
*Worldwide support group originating in the UK, providing information/support to adults and families affected by Androgen Insensitivity Syndrome (AIS) – and similar XY-female conditions. For more information on cAIS (Complete) and pAIS (Partial), please check the website.*

*INTERSEX contd.*



REFERENCES p11

## INTERSEX contd:

**Chris Somers xxy** (AU)
M.Ed. by Research (UWA); B.Ed. (Melb); Hons. Diploma of Creative Photography (Trent Poly, now Nottingham Trent University, UK)
e: Sark47@westnet.com.au
A Board member of the *Organisation Internationale des Intersexués:*
w: www.intersexualite.org/ & www.oiiaustralia.com/
*Please see p79 for a research thesis and one paper by Chris Somers xxy.*

**Congenital Adrenal Hyperplasia Group** (UK)
Contact: Mrs Sue Elford *CAHG Chairperson*
2 Windrush Close Flitwick Bedfordshire MK45 1PX
t: 01525 717 536
e: webmaster@livingwithcah.com
w: www.cah.org.uk
*Provides support, newsletters, information and meetings for families and people with CAH. They also aim to raise awareness of the condition with the general public and the medical profession.*

## LEGAL SUPPORT:

**UK and International**
I suggest that for *England & Wales, Northern Ireland* and *Scotland*, that you pop into your local Citizen's Advice Bureau for information on contacting a law society or a lawyer/solicitor. If you are in another country, try your equivalent public advice service.

## OSTEOPOROSIS:

**National Osteoporosis Society** (UK)
Camerton Bath BA2 0PJ
t: 01761 471771 helpline: 0845 450230
e: info@nos.org.uk w: www.nos.org.uk
*The National Osteoporosis Society is the only UK-wide charity dedicated to improving the diagnosis, prevention and treatment of osteoporosis.*

## PLANNING A FAMILY:

Please discuss options with your GP.

## SOMEONE TO TALK TO:

**ChildLine** (UK)
*ChildLine is the free helpline and online service for children and young people in the UK. Children and young people can call or visit:*
t: 0800 1111
w: www.childline.org.uk
*to talk to a trained counsellor about any problem, or talk to other young people on the message boards. (See p56 for more details).*

## SOMEONE TO TALK TO:
### Specifically about Bullying

**BullyingUK** (UK)
*Formally Bullying Online*
10C Mornington Terrace Harrogate North Yorkshire HG1 5DH
e: help@bullying.co.uk w: www.bullying.co.uk

**Kidscape** (UK)
***Helping to keep children safe from bullying and abuse***
2 Grosvenor Gardens London SW1W 0DH
t: 020 7730 3300 f: 020 7730 7081
helpline: 08451 205 204
*Operates Monday to Friday between 10am and 4pm for parents of bullied children.*
e: info@kidscape.org.uk
w: www.kidscape.org.uk
*Send an A4 SAE with 6 First Class stamps for free booklets and leaflets on bullying and personal safety. Runs one-day ZAP courses for children who have been severely bullied.*

**EVERYONE!**

For this first edition of the book, I have tried to include as many of the main information, advise and support groups as possible, but there are many more out there in countries around the world; specifically for Klinefelter's Syndrome and its variant karyotypes, and for associated conditions.

Many of the contacts in this chapter include on their websites, useful links to organisations around the world.

They also have resource links to genetic groups, conference details, support group campaigns, current research, activities to get you out the house and meeting other...

*If you are a support group committee and would like your group's contact details included in the next pdf update in 2012, please get in touch:*
e: theksstory@btinternet.com





## BOOKS & RESEARCH PAPERS:

***A case of Human Intersexuality having a possible XXY sex-determining mechanism*** Paper
by: Patricia A Jacobs and Dr J A Strong
(Reprinted from Nature, Vol 183, pp 302-303, Jan 31, 1959).

***Androgen Insensitivity Syndrome and Klinefelter's Syndrome: sex and gender considerations*** Chapter within book
by: Milton Diamond, PhD and Linda Ann Watson, MEd
(© Elsevier Inc. 2004. Child and Adolescent Psychiatric Clinics of North America, 13, (2004), pp 623-640).

***As Nature Made Him - The boy who was raised as a girl*** Book by: John Calapinto
(Perennial, 2001)

***Edinburgh study of growth and development of children with sex chromosome abnormalities iv*** Paper by: Dr Shirley G Ratcliffe
(John Wiley and Sons, 1991) *Contained within a paperback of research papers, titled:* ***Children & Young Adults with Sex Chromosome Aneuploidy.***

***Atypical Gender Development – A Review*** Article
(International Journal of Transgenderism, to be published by the Hayworth Press Inc). Can be viewed on the GIRES website: w: www.gires.org.uk

***Gynecomastia – A Medical Dictionary, Bibliography & Annotated Research Guide to Internet References***
(Icon Health Publications, March 2004) Book
*"For doctors, medical students, researchers & patients..."*

***The Human Hypothalamus: Basic & Clinical Aspects***
***Part II: Neuropathology of the Human Hypothalamus and Adjacent Brain Structures. Handbook of Clinical Neurology***
(Elsevier, Amsterdam. 596pp, 2004)
Volume by: Dick F Swaab
*Chapter* ***24.4*** *deals with 'Klinefelter's Syndrome or testicular dysgenesis.' Additionally, chapter* ***24.5*** *covers 'Sexual differentiation of the brain and sexual behaviour.' (Please see p74 for contact information).*

***Intersex in the Age of Ethics*** Book
(Weidenfeld & Nicolson, 1999) by: Alice Domurat Dreger

***Klinefelter's Syndrome*** Paper
by: Dr Shirley G Ratcliffe
*An Introduction to Klinefelter's Syndrome, for parents, adolescents and adults. Available from the* Klinefelter's Syndrome Association (UK) *(See p74).*

***Klinefelter's Syndrome*** Paper by: Dr C M Smyth et al.
(Arch Intern Med. 1998; 158: pp 1309-1314).

***Klinefelter's Syndrome in adolescence*** Paper by: Dr Shirley G Ratcliffe et al.
(Archives of Diseases in Childhood, Vol 57, pp 6-12 © 1982 by Archives of Disease in Childhood).

***Long term outcome in children of sex chromosome abnormalities*** Paper by: Dr Shirley G Ratcliffe
(BMJ, 1999). *Paper reprinted from Archives of Disease in Childhood, February 1999, Vol 80, No 2, p 192.*

***Reflecting The Androgynous Perspective through Art*** Masters by research thesis
by: Kai Chris Somers xxy
*Held at the Scholars Library, within the Reid Library, Main Campus, The University of Western Australia.*
*Copies can be ordered for a small administration, copying and packing fee through Dr Toby Burrows at*
e: tburrows@library.uwa.edu.au

***Retroperitoneal teratoma as first sign of Klinefelter's Syndrome*** Paper
by: S Hachimi-Idrissi et al.
(Archives of Disease in Childhood, Vol 72, pp 163-164, © 1995 by Archives of Diseases in Childhood).

***Sex In the Brain*** Book (PhD thesis)
© 2004 by: Frank PM Kruijver
'Gender differences in the human hypothalamus and adjacent areas; Relationship to transsexualism, sexual orientation, sex hormone receptors and endocrine status.'
*Conducted at the Netherlands Institute for Brain Research.*
*Available on loan from GIRES.*
*Contact:* e: admin@gires.org.uk

***Sexing the body - Gender politics and the construction of sexuality***
(Basic Books, 2001). Book by: Dr Anne Fausto-Sterling

***Sexing the Brain*** Book
(Basic Books, 1999). by: Lesley Rogers

***Sexing the Difference in Gender and the Anomalies of Interpretation*** Paper by: Kai Chris Somers
*Requested and written for the* ***14th annual Australian and New Zealand Society of Criminology Conference.***
*Available free of charge by email from Chris Somers xxy or may be seen on the www sites of OII, (p73 for addresses).*
e: Sark47@westnet.com.au

## MEDICAL JOURNALS AND SCIENCE MAGAZINES:

**British Medical Journal** (UK)
Contact: Ms Geetha Balasubramaniam
*Product Manager*
BMJ Publishing Group BMA House Tavistock Square London WC1H 9JR
t: +44 (0)20 7383 6396 f: +44 (0)20 7383 6661
e: Geetha@bmjgroup.com
w: www.bmj.com
*All research articles are free, but all other full text articles, after 2006, are subject to a subscription charge. For more details go to:*
w: http://resources.bmj.com/bmj/about-bmj

**The Lancet** (UK)
e: editorial@lancet.com
w: www.lancet.com
*The Lancet is a weekly general medical journal that publishes peer-reviewed research papers and review articles on all aspects of medicine.*

**New Scientist** (UK)
e: enquiries@newscientist.com
w: www.newscientist.com
*Excellent science and technology magazine. Also published in Australia and USA.*



REFERENCES p11

# An important message

2010

The KS Diaries

LIVING WITH KLINEFELTER'S SYNDROME

*It's one thing to spout facts & figures, but another matter to actually live every moment with Klinefelter's Syndrome. And you can help. No matter what your association with Klinefelter's Syndrome, you can make a huge difference to someone's life – by telling your story. You will be communicating directly with those in a similar situation, who can take strength from how you cope living each day with Klinefelter's Syndrome.*

## Welcome to 'The KS Diaries'

This second book (pdf) will contain histories supplied by people who have Klinefelter's Syndrome or in some way are involved with this condition. It is their story; their account of life; or a moment in time.

Wherever you live on this blue planet, if you feel your Klinefelter's Syndrome story can make a difference to others, then please think seriously about contributing. And I'm not just talking about those that have Klinefelter's Syndrome. You can be a parent, parents-to-be, spouse, partner, brother or sister, grand-parents, friend, healthcare professional or work with children and young adults, and you too can make a huge difference to ease the mind of those in similar circumstances.

'*The KS Diaries*' will be dedicated to those courteous people who, through strength of spirit, tell their story in the hope of helping others with Klinefelter's Syndrome.

## Guidelines for safely creating & sending your manuscript

Whether you experience Klinefelter's Syndrome personally or see KS from a professional viewpoint, if you wish to submit your KS story, it is **vital** that you please contact me first to receive guidelines (pdf) in safely creating and sending your manuscript. **If you do not do this I cannot include your story.**

## Total anonymity

Authors' stories will NOT include personal names or contact details. Due to this anonymity, and the frank and sensitive nature of some stories, proofs will not be sent to authors for final checking. **I will do my utmost to ensure accuracy, but will not be held responsible for errors.**

## Author's written permission

While all stories within the book will be anonymous, I will still need you to include written permission with your manuscript, stating that you are happy to have your story included in the book (pdf), and that includes those authors who have already sent me their manuscripts.



*For Guidelines in safely creating & sending your manuscript (pdf):*
theksstory@btinternet.com

Authors' manuscript, written permissions and any personal details will be filed in a secure location. **Please note, I will not include your story on the pdf without your written permission.**

## No automatic inclusion

I cannot guarantee that your story will be accepted for the book (pdf). There will be various reasons for this. For example, extreme language or descriptions which are far too graphic, will be rejected, as individuals as young as 11 could be reading it. I appreciate that you want to get your story across as you experienced and felt it, but please keep the latter example in mind. The guidelines will give you more details on this.

## Non-profit venture

Like *The KS Story*, there is no money involved in this second book (pdf); I and story authors will not receive royalties or other rewards, nor is there a fee for inclusion in the book. Also, like the first book, any donations must be sent directly to specific KS support groups and allied organisations to assist in their educational projects. **Do NOT send monies to me.**

*Please remember, this book will not happen without people like you! If I don't receive enough interest the book will be shelved – and that's not a joke.*

## Got 5 minutes?...

I have already received 10 stories and begun to create '*The KS Diaries*'. Please take a moment to read the following pages. I hope they will galvanise you into action, to open your heart and tell your own KS Story.

Thank you so much.

**Iain W McKinlay** xxy



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# Introduction to The KS Diaries

## A book is born

Four years on from my diagnosis, signed off work and gathering dust, at the tender age of 45, I had the bright idea of utilising the data I had collected from my KS studies to create a small pamphlet for my GP's practice. It was a way to exercise my brain, keep my graphic design skills honed and give something back for all the medical help I was receiving.

As contacts in the UK and around the world began expressing an interest in my wee venture, the pamphlet took on a life of its own; taking on more subjects *and* more pages. Then it suddenly dawned on me that **'he who can't spell'** was now writing and compiling an *actually* book!

I then thought it would be good to break up the masses of data with snippits of my own KS tale, hence the title: ***'The KS Story'***, but one of my advisors strongly advised against mixing facts & figures with personal events. I had also read accounts from other people and it was brutally clear that my story would have bored the reader senseless. So in the end I decided that once *The KS Story* was finished I would contact KS support groups to see if I could access members' stories. And so ***'The KS Diaries'*** was conceived.

## Here we are again!

In 2005, in the midst of finding a publisher for *The KS Story* a major contributor and supporter of the book suggested that adding personal histories would immeasurably improve it, and so I tentatively asked for stories from UK KS support group members and received ten initial manuscripts. I then developed another health issue and *The KS Diaries* was placed on hold.

## The next Booker Prize?

During my studies into KS I was shocked to read that a substantial percentage of couples around the globe choose termination when given prenatal test results that their child has Klinefelter's Syndrome.

And that dear reader, for all of us with Klinefelter's Syndrome, and for couples on the verge of parenthood, for consultants and for those that see us as a waste of space, to take heed. If only one thing is learnt from creating *The KS Story*, it is that we are all different – even those with the same karyotype and that given the opportunity, the vast majority of us are capable of such amazing feats. Indeed some of the stories I read from other people with KS were eloquent, poignant and powerful pieces, which touched me greatly.

Despite academic shortfalls many people with KS go on to become managers, executives, teachers; gain higher education and degrees; start their own businesses.

Barring acute physical or psychological traits and symptoms that could seriously affect quality of life, we have as much right as any typical person to exist and to contribute to the world around us.

## Selfless courage

As the following stories are about Klinefelter's Syndrome, most contributors are focusing on specific events within a lifetime.



Like myself, I would imagine that a large proportion of these people have had joyous times in their life, with loving parents, siblings, spouse/partner, friends, and have achieved remarkable things to be proud of.

While sadly not for everyone, it *is* truly inspiring how many people who have been bathed in Klinefelter's presence; who have run the gauntlet of symptoms, bullying, fear, self-loathing, surgery and more, emerge (perhaps not a stronger person in their own eyes), more forgiving and able to not only talk about their experiences but to help others in need.

It is never easy to bare your soul, even if trying to help; letting closely guarded emotions into the open. Some brave souls are still in pain, yet manage to support and advise others. *A selfless act of courage in anyone's book.*

## Nearest and dearest

But dealing with a diagnosis of Klinefelter's Syndrome isn't just the preserve of the patient. Parents, family members, partner, spouse, also have to cope with this revelation and the associated aftermath.

Whether diagnosis is made prenatally, during childhood, adolescence or in adulthood, parents feel responsible for their offspring (I'm 58 and 16 stone yet I'm still my mother's wee boy). Even when told the facts of Klinefelter's Syndrome parents may still blame themselves.

After an amount of time a spouse or partner almost become one entity; you know each other inside out, you finish each other's sentences, you become comfortable together. Then with diagnosis enters hormone replacement therapy and all hell breaks out! It's a kind of puberty all over again; a maelstrom of emotions, with social and sexual experimentation; increased body and facial hair; personal expectations...

We often forget that it is the parents and/or spouse/partner who have to be strong and supportive for their loved one despite a whirlpool of emotions swirling around in their own head. Physical and emotional changes in the person with KS can put a great strain on a family, marriage or partnership, particularly for older couples who may find it difficult to talk about innermost feelings and sexual issues.

As a responsible adult I thought I could cope with male hormone replacement therapy. **WRONG!** No matter your age, life experience, sensibilities, responsibilities, go sailing out the window when hormones are involved – and those closest to you are generally the first to get the flack.

There is also the prickly question of fertility and how couples cope. Tests; anger; counselling; self-doubt; hopelessness; it can tear couples apart. But thankfully with love, support and a degree of give and take, it can also bring them closer. *And remember*, KS and sterility aren't carved in stone.

## Peace of mind

Sometimes just knowing that you're not the only one in the world going through something is often a comfort in itself. And when you can read other people's accounts of how they reacted and how they dealt with a particular situation I think you'll agree, it truly brings home just what living with Klinefelter's Syndrome is all about.



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## Closing thoughts

*It seems ironic that someone who has such difficulty with academia should end up working with text. However, as a graphic designer I see the beauty and form of letters, words, phrases, from a different angle; a technical perspective, as individual entities – compare and balance the spaces between them. In some cases, components of a story I will never know. I understand and see the true meaning hidden in the characters – someone's education, someone's life, in shapes.*

*Eyes darting back and forth from manuscript to monitor, the contributor's story in abstract form. Afraid to miss punctuation, afraid to misspell; to, too, bare, bear, never picked out by the spell checker. And ever the perfectionist, torn whether to change the contributor's single to double quotes – but stopping short, realising in time that it's their content; their learning, their story.*

*A pitifully slow reader all my life, packets of words are inwardly repeated, filling my head until the computer keys are struck.*

*Back and forth from manuscript to monitor; light between the dark, fear and joy behind the words.*

*OK, perhaps not a poet, but I am a graphic designer to my bones. I trust and revel in my skills as an artist. 43 years of graphics experience, yet I have no confidence selling that work... and I have Klinefelter's Syndrome.*

Having read the stories sent to me for this second book, many of whom have the same karyotype as myself, my story does not compare. In a world of pain and suffering, both past and present, to individuals and social communities, my own KS story is nothing. It is the pinnacle of the tip of the iceberg in terms of physical and psychological complexity and severity.

But these pages aren't about who is worse than the other, but about making known the many facets of Klinefelter's Syndrome, no matter what the karyotype, or whether you are the person with KS, a parent, parents-to-be, partner, spouse, sibling, grandparent, friend...

It's about lifting a child from the darkness of loneliness and fear. It's about shedding light on prejudice and misinformation.

It's also how *everyone* associated with Klinefelter's Syndrome copes with the diagnosis: guilt, anger, fear, doubt, even a sense of bereavement as treatment begins and physical and emotional changes occur which, to varying degrees, can affect an individual's character, perhaps by growing a beard or by sexual experimentation.

But equally it's about understanding, love, support, caring. It's about sharing *all* those experiences in the hope that others who mirror that life can benefit in some way.

Many with Klinefelter's Syndrome never tell their own story or discover the stories of others, suffering their lot relative to their own lives; how family, friends and work colleagues interact and treat them. Locked in their own experiences of life.

But often by telling your story it is somehow comforting, often lifting something out into the open is spiritual, a kind of therapy. And that's not my words, the latter comes from people who have already contributed their KS story.

Whether you look back on 3 score years and ten or look to the future of adolescence and adulthood with trepidation, I hope these personal accounts have helped to ease your worries; to show that you are infinitely more than your atypical parts, to motivate and encourage you to go out there and make your own unique mark on the world.

Throughout the past 12 years of ill-health, when I felt burdened by pain, self-pity, doubt and fear for my future, several lines of text reinforced my will to persevere and gave me courage to overcome those glitches in my life. In a way the words are also relevant to us folk associated with Klinefelter's Syndrome, as individuals and as a social community...

*Tho' much is taken, much abides; and tho'*
*We are not now that strength*
*which in old days*
*Moved earth and heaven;*
*that which we are, we are;*
*One equal temper of heroic hearts,*
*Made weak by time and fate,*
*but strong in will*
*To strive, to seek, to find, and not to yield.*

**Tennyson, A L.** (1908),
*Poems of Tennyson: Ulysses* (part of),
Oxford Edition, Oxford University Press, London.





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# Disclaimer

The person who created this guide is *The Compiler.*
Any person obtaining this guide is *The Reader.*
Any individuals or organisations who are involved in medicine, research or studies, support & information or caring etc., are *The Specialists.*

## To the Reader

### *General information:*

***The Compiler*** is not an expert regarding this condition and does not offer medical advice. He will also not debate the rights and wrongs of any particular medical procedure. ***Unless in quotes, the content of this book is The Compiler's opinion or assumptions drawn from other sources during his own studies.*** Having absorbed and discussed the ethics, risks, advantages etc with your consultant and/or GP, genetic counsellor and ideally a support group, it is for ***The Reader*** to choose the most appropriate course of action. **The information contained within *The KS Story* is not a substitute for professional health care and is supplied for guidance only.**

If ***The Reader*** suspects they may have Klinefelter's Syndrome, or they know of someone who may have it, they should contact their GP, an endocrine consultant, or one of the appropriate ***Specialists*** in the ***Further Study*** chapter, for more information relating to their own specific needs.

***The Compiler*** has endeavoured to make this guide as accurate as possible and every effort has been made to verify information supplied. However it should be noted that research is ongoing and facts do change, also subtle differences in research data can occur from various sources, and depending on which country the information is sought.

Besides seeking the editorial advice from various research individuals and groups, ***The Compiler*** has generally taken the most widely held view or beliefs on current research. But not everything within these pages is so clear cut.

### *Further Study chapter:*

Please remember, Klinefelter's Syndrome is a highly variable and complex condition (even within the same karyotype), and this guide is but an overview. It is up to ***The Reader*** to seek their own viewpoint and up-to-date facts, through further study of their own particular condition.

Every effort has been made to check out the contacts and supplied details within this book and to obtain only reputable sources. However, from time to time inter-group politics and other situations can arise, and very occasionally a bogus organisation can slip through the net creating confusing or conflicting facts. It is therefore strongly suggested that ***The Reader*** get into the habit of verifying the qualifications and experience of individuals and support groups. An idea of this can be gained from their websites, from the *FAQ* or *About us* links. Try obtaining information from two or three groups and seek recommendations whenever possible and appropriate.



### *Important:*

*Please note, all **Further Study** contacts have kindly given their approval for inclusion within that chapter; in writing.*

*The inclusion of these contacts are for the convenience of **The Reader**. **The Compiler** does not endorse any particular service or product, nor any particular group or individual. He is however, a full member of two British KS support groups. Also, there are some contacts within these pages who do not endorse **The KS Story** guide.*

*The Compiler does not take the creation of this guide lightly; in that he appreciates that he is dealing with other people's lives.*

*The Compiler has made every effort to offer the facts truthfully and to the best of his knowledge, and he offers it to The Reader in good faith.*

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### *Further Study chapter:*

This guide has been specifically created to act as a conduit to ***The Specialist.*** All these extracts and contacts are here to assist and encourage ***The Reader*** to seek out such experts, in order to understand their own situation relating to Klinefelter's Syndrome.

### *Important:*

***In light of the aforementioned efforts; The Compiler has produced this book in good faith and he shall have no liability to any person, group or entity, in respect of anything arising from the information contained within this guide; which is for information only.***