

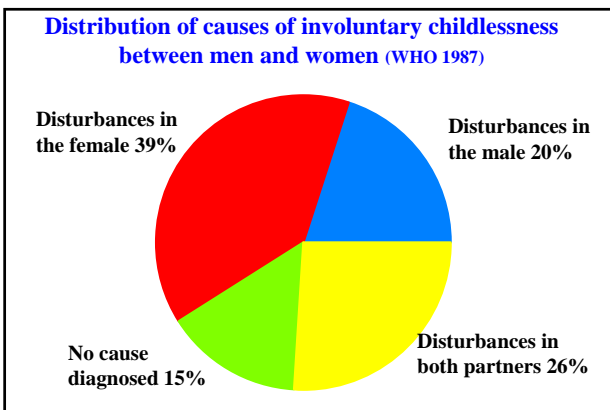
ESHRE Andrology Campus Course
Reproductive Andrology
Brussels 8-10 November 2007

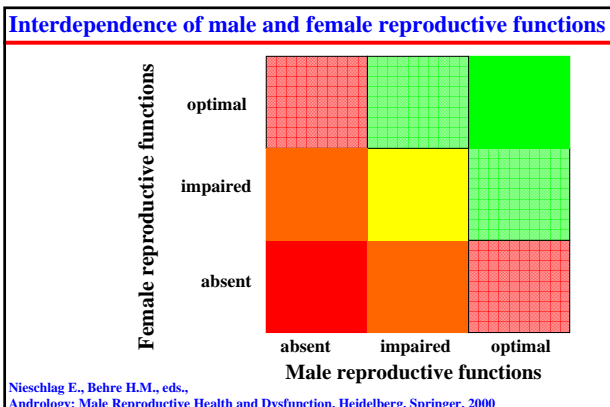


Working-up the infertile men:
 What are the minimal examinations the oligozoospermic man should get and why?

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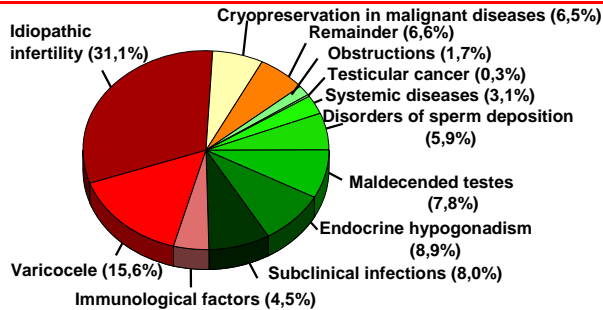






Percentage distribution of diagnoses of 10469 consecutive patients attending the Institute of Reproductive Medicine of the University of Münster

Nieschlag & Behre, Andrology, Male reproductive health and dysfunction, Springer, 2000



When to do an evaluation for male infertility?

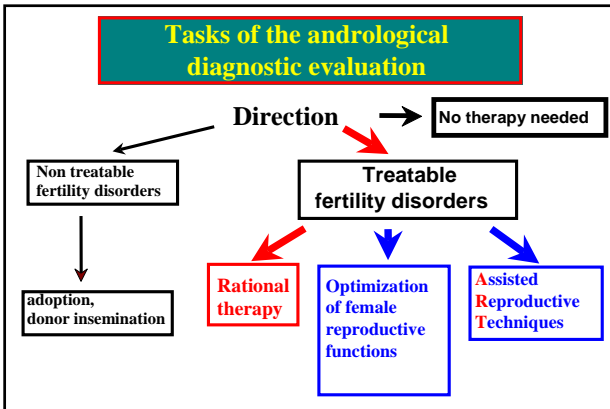
The male infertility best practice policy committee of the American Urological Association (AUA) and the practice committee of the American Society for Reproductive Medicine (ASRM)
Fertil. Steril., 86 Suppl. 4: S202-09, 2006

- No pregnancy within one year of regular unprotected intercourse
before one year if
- Known/suspected male infertility risk factors (e.g. bilateral cryptorchidism)
- Known/suspected female infertility risk factors (e.g. age over 35 years)
- Couple questions the male partner's fertility potential

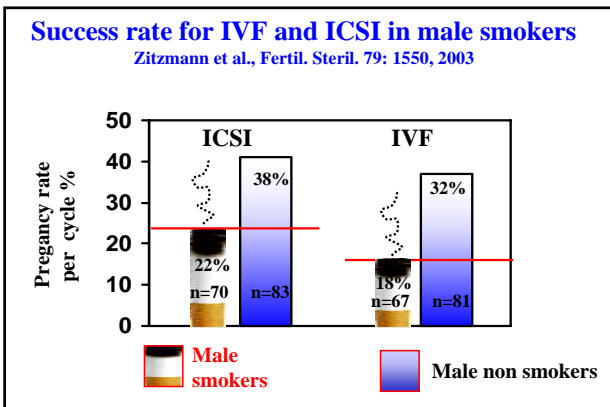
Categories of diagnostic tests for infertility

The ESHRE Capri Workshop, Hum. Reprod. 11: 1779-807, 1996

- Abnormal test results have an established correlation with impaired fertility and in case of unequivocally abnormal test results the fertility is unarguably impaired without therapy
 - Semen analysis
 - Karyotype analysis
- Abnormal test results are not consistently correlated with impaired fertility although abnormal test results are frequently associated with subsequent fertility without therapy
 - Endocrine laboratory analysis
 - Sonography of the testis
 - Molecular genetics
- Abnormal test results do not appear to be correlated with impaired fertility as data either confirm the lack of correlation with pregnancy or follow up studies are missing
 - Evaluation of the plexus pampiniformis



- ### Minimal andrological diagnosis
- The male infertility best practice policy committee of the AUA and ASRM, Fertil. Steril., 86 Suppl. 4: S202-09, 2006
The ESHRE Capri Workshop, Hum. Reprod. 11: 1779-807, 1996
- Semen Analysis (AUA-ASRM / ESHRE)
 - After 2-3 days of sexual abstinence
 - Twice separated by at least one month
 - WHO; 4. edition 1999
 - (Quality control)
 - Medical History/ Couple medical history (AUA-ASRM)
 - Coital frequency and timing
 - Duration of infertility and prior fertility
 - Childhood illnesses and developmental history
 - Systemic medical illnesses
 - Prior surgeries
 - Sexual history including sexually transmitted diseases
 - Gonadal toxin exposure including heat



Complete andrological diagnosis (AUA-ASRM)

The male infertility best practice policy committee of the AUA and ASRM, Fertil. Steril., 86 Suppl. 4: S202-09, 2006

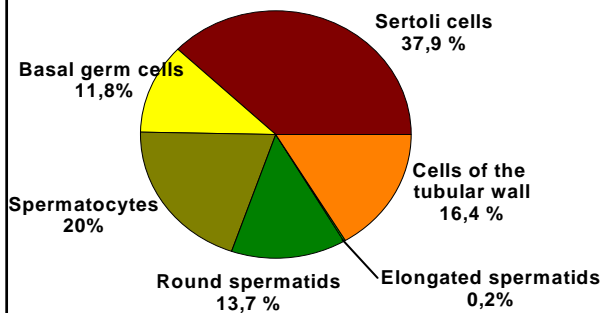
- Semen Analysis
- Medical History/ Couple medical history
- **Physical Examination**
 - **Recommended in cases of :**
 - **Abnormal male medical history**
 - **Abnormal semen analysis**
 - **Couples with unexplained infertility**
 - **Treated female factor and persistent infertility**
- (Ultrasound)

Genital examination (AUA-ASRM)

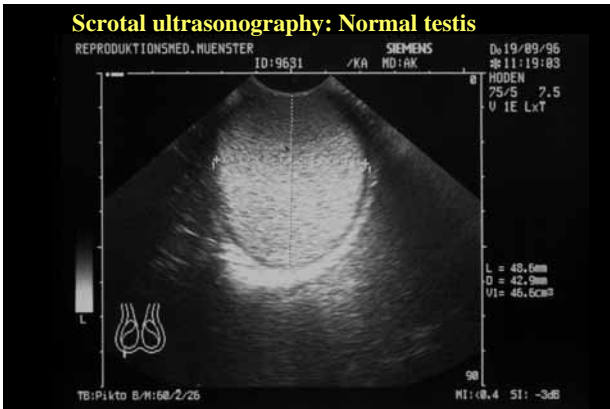
The male infertility best practice policy committee of the AUA and ASRM, Fertil. Steril., 86 Suppl. 4: S202-09, 2006

- Examination of the Penis
- Palpation of the testis and measurement of the size
- Presence and consistency of both vasa and epididymides
- Evaluation of the plexus pampiniformis
- Secondary sex characteristics
- Digital rectal examination

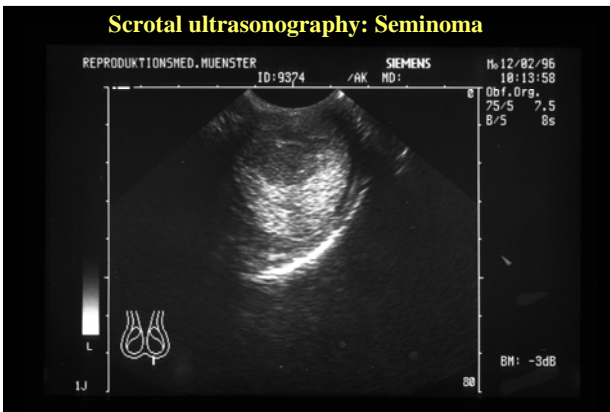
Volumetric composition of human testes (Russell et al. 1990)



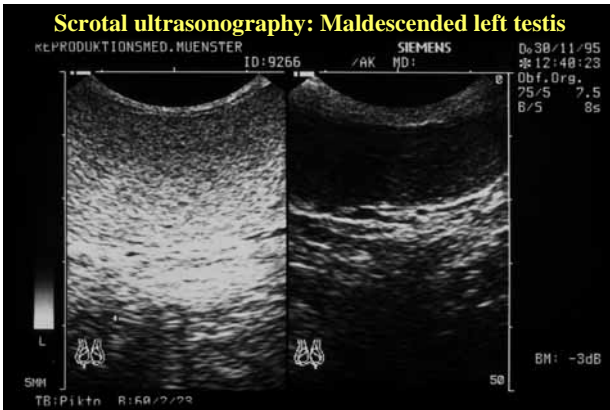
Scrotal ultrasonography: Normal testis



Scrotal ultrasonography: Seminoma



Scrotal ultrasonography: Maldescended left testis



Classification of varicoceles

Dubin L., Amelar RD. Varicocele size and results of varicocelectomy in selected subfertile men with varicocele. Fertil.Steril. 21: 606-9, 1970

Grade I Enlargement of the pampiniform plexus, only palpable during Valsalva maneuver.

Grade II Clearly palpable enlargement of pampiniform plexus.

Grade III Visible enlargement of the pampiniform plexus.

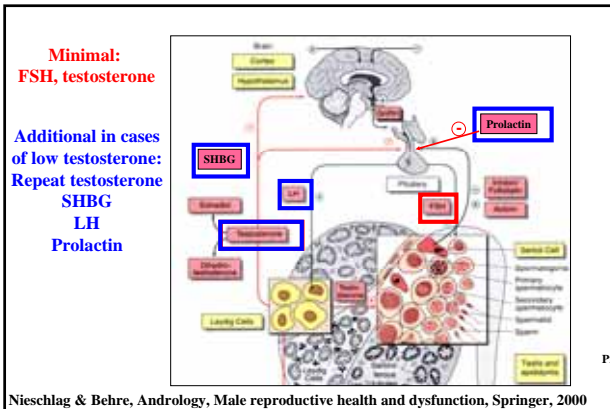
Varicocele: Genital and sonographic diagnosis

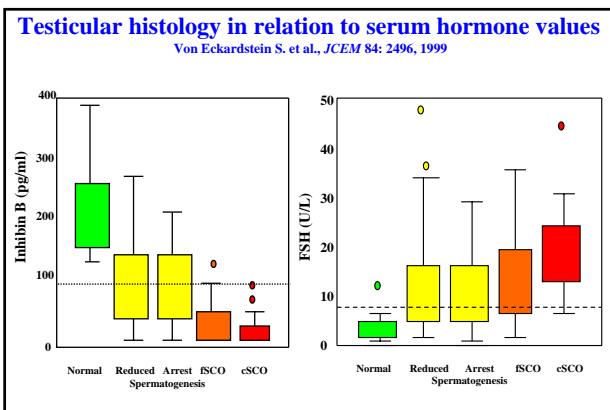


Complete andrological diagnosis (AUA-ASRM)

The male infertility best practice policy committee of the AUA and ASRM, Fertil. Steril., 86 Suppl. 4: S202-09, 2006

- Semen Analysis
- Medical History/ Couple medical history
- Physical Examination
- Endocrine laboratory diagnosis FSH, T (LH,PrI,SHBG)
 - Initial recommended in cases of :
 - Low sperm count especially if less 10 mill/ml
 - Impaired sexual function
 - Clinical findings suggestive of an endocrinopathy





Various diagnoses for male hypogonadism

PRIMARY HYPOGONADISM (LH/FSH↑, T↓)

- Klinefelter syndrome, XX male syndrome
- Testicular damage (tumor, trauma)
- Disturbances of testosterone synthesis
- Inactivation of the LH receptor

LATE ONSET HYPOGONADISM (LH/FSH↑←, T↓)

SECONDARY HYPOGONADISM (LH/FSH ↓, T↓)

- Hypothalamic disorders (e.g. Kallmann syndrome, idiopathic hypogonadotropic hypogonadism)
- Pituitary disorders (inherited, tumor, ischemia/bleeding, chronic diseases, radiation)

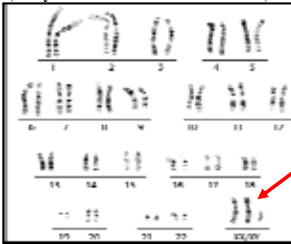
Nieschlag & Behre, *Andrology, Male reproductive health and dysfunction*, Springer, 2000

Additional procedures for andrological diagnosis
Genetic Laboratory Diagnosis

- Karyotyping
 - Suspected Klinefelter Syndrom
 - Recurrent miscarriages
 - Prior to ICSI
- Molecular genetics
 - Y-chromosome microdeletions
 - Prior to ICSI
 - Severe oligospermia or azoospermia
 - Cystic Fibrosis Gene Mutations
 - Congenital bilateral absence of the vas deferens
 - Female partner with known CFTR mutation

Diagnostic work up in case of suspected Klinefelter Syndrom
 (Kamischke et al., J. Androl. 24: 41- 48, 2003)

Indication: Every patient with a hypergonadotropic azoospermia and firm, small testes (usually below < 5 ml bitesticular volume)

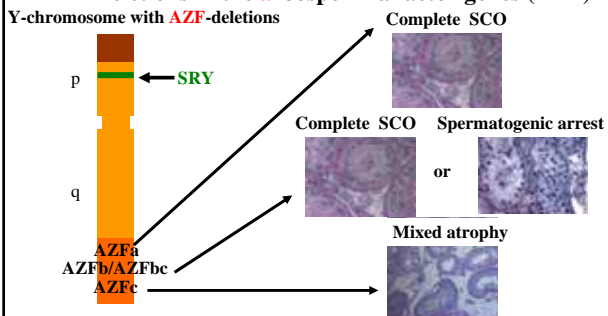


Gold standard: karyotype analysis in GTP banded metaphase lymphocytes



Screening: Barr bodies in buccal smear
 Specificity: 95 % Sensitivity: 82 %

Deletions in the azoospermia factor genes (AZF)



Prevalence AZF deletions: 12 % in 421 patients with azoospermia
 3% in 799 patients with oligozoospermia

Molecular genetic screening for cystic fibrosis transmembrane conductance regulator gene (CFTR gene) mutations

Von Eckardstein et al., Fertil. Steril., 73: 1226-31, 2000

- Positive family history for cystic fibrosis disease
- Known cystic fibrosis carrier state of the female partner
- Suspicion of congenital bilateral absence of the vas deferens (CBAVD)
 - Bilateral absence of the vas deferens / epididymis
 - Missing seminal vesicles in the transrectal ultrasonography
 - Uni- or bilateral congenital kidney defects
 - Seminal plasma volume below 1,4 ml
 - Ejaculate pH below 7,5
 - Seminal plasma fructose below 2 umol/Eja.

Additional procedures for andrological diagnosis
Testicular Biopsy

-Diagnostic / therapeutic testicular biopsy for ultimate differentiation between

-Diagnostic testicular biopsy for diagnosis of malignancy

Obstructive azoospermia Testicular azoospermia Malignancy



Additional procedures for andrological diagnosis
Post-ejaculatory urinalysis

Retrograde ejaculation (Substantial emission of ejaculate into the bladder):

Complete (no antegrade fraction) or incomplete (only minimal antegrade fraction) permanent or intermittent absence of an antegrade ejaculation (< 1 ml) with presence of spermatozoa and/or fructose in postorgasmic urine analysis.

Anejaculation (Failure of seminal emission into the posterior urethra):

Permanent or intermittent complete absence of an antegrade ejaculation combined with a non-viscous, fructose-negative and spermatozoa negative postorgasmic urine analysis.

Murphy and Lipshulz, Anomalies of ejaculation. Urol.Clin.North.Am. 14: 596, 1987
