

MODULE 3, CHAPTER 2

00:00:27

We'll move on now to male infertility evaluation, starting with medical history.

00:07

The essential components of male history in relation to fertility or age, surgical history, medications, previous success of conception, for example, if there are live birth, previous partners, any indication of medical or genetic conditions.

00:29

Endocrine abnormalities, including diabetes or hypothyroidism, lifestyle factors are important, and if we think about spermatogenesis here in terms of alcohol use, prolonged cycling, family history is important. Other factors, including surgery, hernia repairs, vasectomy reversals, sleep disturbances, disruption in sleep, for example, can interfere with normal spermatogenesis. Environmental exposure and most recently, exposure to or experience of COVID-19. Currently we refer to your own clinic practices to deal with COVID-19 and your other health care agencies, such as the Center for Disease Control and Health Canada.

01:29

Carrying on with history, use of medications or and or recreational drugs may be associated with erectile dysfunction or cause direct toxicity to sperm. Cancer treatment definitely will interfere with spermatogenesis. Other medications such as antihypertensives, antidepressants, and antipsychotics and antibiotics. Also recreational drugs and alcohol. Chronic alcoholism, cannabis use or illicit use of opiates, cocaine or amphetamines may interfere with sperm production and quality.

02:16

We will now look at physical exam and work up for the male infertility evaluation.

02:24

Physical examination which is most commonly performed by a urologist, will include body proportion and BMI to determine if there is a congenital absence of vas deferens which would interfere with sperm transport. Looking at the testes and scrotum, looking at the size and consistency of the testes to identify if there are any tumors or undescended testicle, if there's any testicular cancer, which would be determined by palpation, if there was any lumps or bumps on the testes. Scrotal examination to determine if there's varicocele and if there is a vas deferens or absence of vas deferens or any epididymal abnormalities such as cysts or tumors. Also to determine if there's any penile factors, such as hypospadias, which is an irregular opening on the underside of the penis, any genital mutilation, which is sometimes called circumcision, also to examine the prostate and seminal vesicles, which is done through a digital rectal exam.

03:45

The routine infertility workup for male, the gold standard and first line diagnostic tool, the semen analysis. If it's abnormal, then there may be a need for addition of FSH and testosterone, genetic screening referral to a urologist. Often the same analysis is done while the male is under the care of a general practitioner and then would be referred on to a urologist. Scrotal ultrasound or other tests such as the sperm DNA fragmentation test.

Other things will include possibly a blood type and screen and virology and serology as per Health Canada guidelines, particularly if a male presents as a possible sperm donor. And these include the sexually transmitted infections and other infectious diseases such as HIV or syphilis, hepatitis, etc. FSH and LH are not routine, but would be done if there was an abnormal semen analysis. Testosterone is a common test and genetic screening if indicated, such as karyotyping.

05:13

So endocrine evaluation of the male. Hormonal abnormalities of the hypothalamic-pituitary-gonadal axis are uncommon causes of male infertility. However, they can occur which is why we do more in-depth testing when indicated. And if there are normal semen parameters, then definitely we would not suspect a hormonal abnormality. However, we would evaluate endocrine function if there with an abnormal semen analysis, if there's a concentration of less than 10 million impaired sexual function or clinical findings, suggestive of an endocrinopathy. Hormonal evaluation would include serum FSH and serum testosterone. If there's a finding of low testosterone, a repeat measurement of total and free testosterone would be indicated, as would serum LH, estradiol, TSH and prolactin.

06:15

So just looking at this diagram, we could see that if we have abnormal semen analysis and we start testing would start with FSH, if the FSH was high, we would suspect testicular failure or called hyper-hypo, meaning that more FSH is required to stimulate the testes and testosterone. If testosterone is high we would suspect the same thing. If FSH is low, then the next level of testing would be to test the function of the pituitary and look at MRI, for example, to rule out any pituitary tumors and do prolactin.

Also we would look at a possibility of hypogonadotropic hypogonadism, which is we know we've already learned is can be unexplained or caused by a tumor. If testosterone is low, we test the LH. If the LH is low similar to if FSH is low, we would carry on with the subsequent testing.

07:31

Looking at this table, if we see that normal spermatogenesis or there is normal spermatogenesis, we would expect all the typical hormones to be normal. In the case of Hypo-Hypo, we would expect FSH, LH and testosterone to be low. Abnormal spermatogenesis we can still can get all normal hormones and not have an answer from an endocrine point of view.

For testicular failure or a hyper-hypo, we would expect FSH and LH to be high and testosterone to be normal or low and prolactin would not be affected. If there was a prolactin secreting pituitary tumor, then FSH would be normal to low, as would LH, testosterone low but prolactin high, which would be a very telltale sign.

08:38

Semen evaluation.

08:42

So this is important for particularly for someone who is preparing a male to give a semen sample. He needs to know that abstinence should be no longer than 2 or 3 days. Sometimes males think that the longer, the better. That's not true is they'll be more dead sperm in the sample. It should be if it's not

produced at the lab, it should be delivered to the lab within an hour of collection, kept at 37 degrees as extreme temperatures will create oxidization of the sperm and DNA fragmentation.

A masturbated sample is preferred. However, sometimes for cultural or religious reasons, this is not acceptable to the male and the sample would need to be collected through intercourse only. So the need to know that a special condom, which is available from the lab, which contains no lubricants or spermicides, needs to be used and not the over-the-counter condoms that you would buy at the pharmacy, for example.

So as we know sperm takes 74 days, spermatogenesis takes 74 days, so if there is an abnormal semen analysis, it's often prudent to repeat in case there was a transient reason, such as a flu or a medication or something that doesn't have a long term effect on the spermatogenesis but may be temporary.

10:29

So we've seen this table before, but these are the normal parameters. We see there is a difference between 1999 and 2010. But what we use now is our reference table is the 2010 and these are the lower limits. So if there's any of these results are lower than seen on this table, there may be a reason for more investigation.

10:55

We also saw before the sperm morphology, looking at what we expect to see in normal sperm is the normally shaped head, the mitochondria and the tail. And on the right-hand side, we see all the variations of abnormal sperm, which would interfere with fertility.

11:17

So, DNA fragmentation can contribute to a low fertilization rate, poor embryo development and reduced implantation rate and may be caused by chemotherapy, advanced age, environmental factors, varicoceles or leukocytes in the semen. And it would be indicated to test in men who have any varicocele issues, unexplained infertility, recurrent pregnancy loss or IUI failures, and it does provide information for couples that have failed IVF or IVF ICSI. If there is a high level of DNA fragmentation, then consideration of testicular sperm extraction would be recommended.

12:10

Other sperm function tests, which are often also done, as with DNA fragmentation after failed treatment, would be acrosomes tests to look at the acrosome reaction and that assesses the ability of the sperm to penetrate the oocyte zona pellucida or the wall of the oocyte. And it is generally reserved for IVF failure. Other tests are fluorescent staining of acrosomal contents, ionophore challenge and CAP- score just used in very specialized circumstances.

12:50

Male infertility evaluation, ultrasound and biopsy.

12:56

We'll look at testicular ultrasound and biopsy, starting with scrotal ultrasound which assesses the testicles and associated structures and the spermatic cord structures. The possible testicular abnormalities which could be identified, would be varicoceles, tumors both benign and malignant, cysts and little crystals called microlithiasis.

Testicular biopsy is indicated if there's obstructed basal sperm, which means there's no sperm in the ejaculate. For testicular sperm extraction used in infertility treatment or to diagnose cancer.

13:45

So in summary male infertility evaluation as similar to female patients, a thorough medical history is a key component of the initial evaluation of a male with infertility. Testicular pathology and medical disorders and endocrine abnormalities are particularly important as are age, sexually transmitted infections, proven fertility, paternal history of assisted conception, fertility altering surgery such as vasectomy, drug or performance enhancing substance use, occupational related impacts, suspected chromosomal abnormality, occupational and environmental toxin exposures.

A semen analysis is the key component of the male workup and we've learned that sperm DNA fragmentation can contribute to infertility. A number of medications may be associated with erectile dysfunction, retrograde ejaculation or direct toxicity to sperm. An endocrine evaluation may have limited be of limited value except in cases where a specific pathology is suspected.

15:02

We will now discuss genetic evaluation.

15:08

Genetic evaluation may be used as possible detection of a genetic cause of infertility. It also determines the risk of transmitting a severe genetic abnormality to offspring. For carrier screening, it identifies risk of parents transmitting an autosomal recessive or sex-linked genetic disorder to their offspring. Also, a genetic evaluation is useful in advanced maternal age to determine the increased risk of chromosomal abnormalities, most commonly the trisomies which trisomy 18 and 13. 21 is associated or is otherwise known as Down's syndrome. 47 double XY, also known as Klinefelter's syndrome, or 47 and three X.

For advanced paternal age, I will say there are no identified increase in trisomy risk, but there is an increased risk for autosomal dominant diseases such as Marfan syndrome.

16:24

So genetic factors of female infertility include 45 X, which is Turner Syndrome, and in this population, only 5 to 10 percent of patients undergo puberty and menstruation and is best treated with IVF using donor eggs. Fragile X syndrome is X linked or sometimes called sex linked dominant disorder and there is an increased risk of premature ovarian failure in this population.

Another genetic factor is congenital adrenal hyperplasia, which is autosomic recessive and can result in hyperandrogenism such as seen in PCOS.

17:13

The 3 most common genetic factors related to male infertility are cystic fibrosis, gene mutations and congenital absence of the vas deferens is a classic finding in this population. Chromosomal abnormalities, sex chromosome aneuploidy, Klinefelter's syndrome, which we see on the right with the X, X, Y chromosomes and impaired testicular function. Also Y chromosome deletions, which on the Y chromosome are isolated, or do cause isolated spermatogenic impairment.

17:59

Module 3 summary.

18:03

Evaluation of the infertile individual or couple involves a detailed review of the numerous factors that affect fertility. Determination of the underlying causes of infertility will guide the choice of treatment. Advances in laboratory and imaging techniques continue to improve the ability to assist patients to build a family. Elective egg freezing is gaining popularity and is an option to help overcome age related infertility.

18:35

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