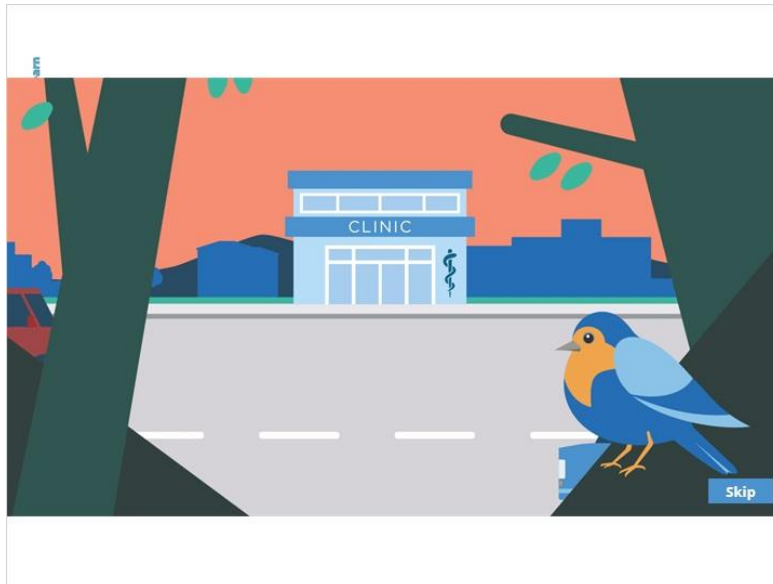


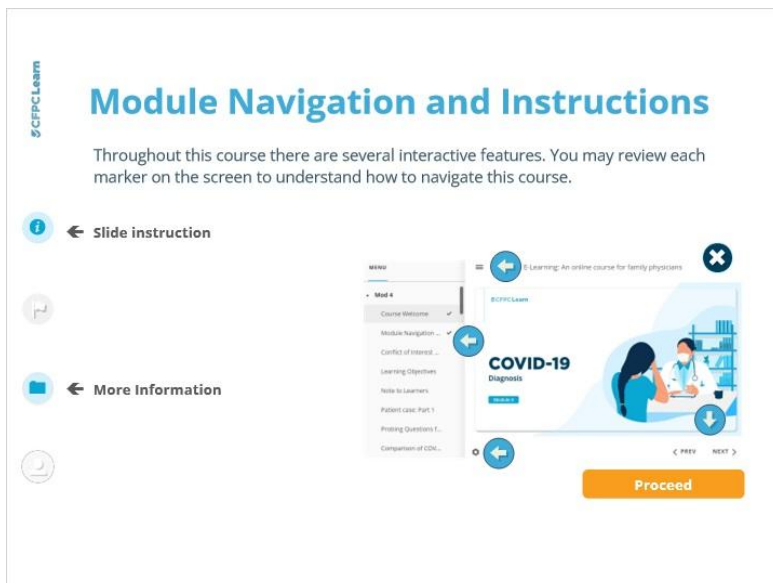
Case 41 Annie Ploidy

1. Conflicts

1.1 Intro Video



1.2 Module Navigation and Instructions



1.3 Learning Objectives

CFPC Learn

1

2

3

4

Learning Objectives

At the end of this module participants should be able to:

1. Identify key factors/findings in family medicine to help establish common clinical diagnoses.
2. Evaluate best evidence/guidance and practice tools to determine preferred treatment options for patients.
3. Synthesize patient preference, evidence and experience to formulate comprehensive plans for patient cases.

Approximately 15 minutes to complete each patient case.

Proceed

2. Annie Ploidy

2.1 Meet Annie Ploidy

CFPC Learn

1

2

3


4

Annie Ploidy, 36

Annie is a new patient to you. She has had a positive home pregnancy test. Her last menstrual period was about seven weeks ago. She is 36 years old, G3P1, with a three-year-old child at home. She is otherwise healthy and has started on prenatal vitamins about 6 months ago.

Conversation I **Conversation II**

Moving Forward



Annie 1 (Slide Layer)

SCFPCLearn

Annie Ploidy, 36

X

There are the routine blood tests and we should talk about additional screening for genetic abnormalities.

Sure - I did the genetic blood test last time, but I figure I will just go for an amniocentesis this time.

Conversation I

Conversation II

Moving Forward



Annie 2 (Slide Layer)

SCFPCLearn

Annie Ploidy, 36

X

Are there any people with chromosomal abnormalities in your family or in your husband's?

No, there are not.

Conversation I

Conversation II

Moving Forward



2.2 Choose all that apply:

2.3 Review

Review

CFPC Learn

First trimester U/S

First trimester U/S, II

Second trimester U/S

First trimester markers

Provincial variability

Screening Test

Age

Click on the buttons to view additional information

Moving Forward

First trimester (Slide Layer)

Review

CFPC Learn

First trimester U/S

First trimester U/S, II

Second trimester U/S

First trimester markers

Provincial variability

Screening Test

Age

First trimester ultrasound between 11-14 weeks is recommended.


- Accurate dating
- Nuchal translucency
- Early identification of major fetal abnormalities and twins

Moving Forward

Ultrasound at 11-14 weeks (Slide Layer)

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Review



First trimester U/S

First trimester U/S, II

Second trimester U/S

First trimester markers

Provincial variability

Screening Test

Age

Ultrasound at 11-14 weeks:


- A nuchal translucency of >3.5 mm is associated with increased risk of structural abnormalities and chromosomal abnormality and patients should be referred for genetic counselling with an offer for invasive prenatal testing.
- Any fetal structural abnormality should be referred for genetic counselling with an offer for invasive prenatal testing.

Moving Forward

Second trimester ultrasound (Slide Layer)

SCFPCLearn

Review



First trimester U/S

First trimester U/S, II

Second trimester U/S

First trimester markers

Provincial variability

Screening Test

Age

Second trimester ultrasound is required to rule out neural tube defects


- Additional fetal anatomy scan

Moving Forward

First trimester serum markers (Slide Layer)

SCFPCLearn

Review



First trimester U/S

First trimester U/S, II

Second trimester U/S

First trimester markers

Provincial variability

Screening Test

Age


- First trimester serum markers: most commonly, free-beta Human Chorionic Gonadotrophin (β hCG) and pregnancy associated plasma protein-A (PAPP-A), alpha fetal protein (AFP) and placental growth factor (PGIF).
- Second trimester serum markers: most commonly, "QUAD" testing of AFP, free β hCG, unconjugated estrogen (UE3), inhibin A.

Moving Forward

Different Provinces (Slide Layer)

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Review



First trimester U/S

First trimester U/S, II

Second trimester U/S

First trimester markers

Provincial variability

Screening Test

Age


- Provinces vary significantly in programs for prenatal screening for aneuploidy including multiple marker serum test, nuchal translucency ultrasound, and cell-free DNA testing.
- Nuchal translucency is provided either routinely in some populations or in response to a positive first trimester multiple marker serum screen.

Moving Forward

Age (Slide Layer)

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Review



First trimester U/S

First trimester U/S, II

Second trimester U/S

First trimester markers

Provincial variability

Screening Test

Age


- Age alone is considered poor minimum standard for referral for invasive fetal diagnostic testing. (SOGC 2017)
- Ultrasound at 11-14 weeks and/or multiple marker serum screening advised depending on province as an initial test, depending on province.

Moving Forward

Screening Test (Slide Layer)

SCFPCLearn

Review



Screening Test	Sensitivity* for Trisomy 21
First trimester serum markers alone	70
Nuchal translucency (NT) alone	71
First trimester serum and NT	87
First and second trimester serum	85-87
First and second trimester serum and NT	92-95
Second trimester serum alone (QUAD)	74-83

*when specificity set at 95% (=false positive rate set at 5%). Specificity can be "set" by moving the threshold for a positive test in a test that has a continuous value.

2.4 Conversation

SCFPCLearn

Annie Ploidy, 36

There are a bunch of blood tests that can be used at different times in pregnancy.

Yes, I had a look at them and couldn't figure it out. I had a friend who just paid for a more accurate one?

Yes, there is a relatively new test that you can pay for but it is sometimes funded by the province.

Moving Forward



2.5 Which statements about cell-free DNA (cfDNA) testing or non-invasive prenatal test (NIPT) are most accurate?

(Multiple Response, 10 points, 1 attempt permitted)


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Which statements about cell-free DNA (cfDNA) testing or non-invasive prenatal test (NIPT) are most accurate?


Choose all that apply:

- ☒ Detects fetal DNA derived from the chorionic villi in maternal blood
- ☒ It is best done after 10 weeks gestational age
- ☒ Leads to fewer invasive procedures for prenatal diagnosis
- ☐ Is too expensive in a publicly funded system
- ☐ It can replace diagnostic testing (amniocentesis or chorionic villous sampling (CVS)).



Submit








2.6 Review



Review





Cell-free DNA

Cost Effectiveness

Cost analysis, I

Cost analysis, II

Sensitivity, specificity


Positive predictive value

False positives



Click on the buttons to view additional information






Moving Forward

cfDNA (Slide Layer)



Review





Cell-free DNA

Cost Effectiveness

Cost analysis, I

Cost analysis, II

Sensitivity, specificity

Positive predictive value

False positives

cfDNA: detects circulating fetal DNA from the trophoblastic layer of the chorionic villi


- Fetal fraction of DNA is variable and increases with gestational age to ~10% at 11 weeks. Failed results (no-call) occur with lower fetal fraction, and are more common at earlier gestational age. Hence it is recommended to do cf-DNA after 10 weeks gestational age.

Moving Forward

cost effective (Slide Layer)

SCFPCLearn

Review



Cell-free DNA

Cost Effectiveness

Cost analysis, I

Cost analysis, II

Sensitivity, specificity

Positive predictive value

False positives

cfDNA testing can be cost effective if certain conditions apply (i.e., "contingent" approach):
For example in Ontario, cfDNA is funded for:


- screen-positive result from multiple marker screening
- maternal age >40 years at estimated due date
- concerning findings on fetal ultrasound
- previous pregnancy with aneuploidy

Moving Forward

Ontario cost analysis (Slide Layer)

SCFPCLearn

Review



Cell-free DNA

Cost Effectiveness

Cost analysis, I

Cost analysis, II

Sensitivity, specificity

Positive predictive value

False positives

Ontario cost analysis (2019) found that total cost of contingent cfDNA was slightly lower than traditional prenatal screening, mainly because of the reduced volume of diagnostic testing.

Cost of blood tests:



- cfDNA test ~\$350-400 (ON)
- Multiple marker screening ~\$125-187 (ON)

Moving Forward

Ontario cost analysis - II (Slide Layer)

SCFPCLearn

Review



Cell-free DNA

Cost Effectiveness

Cost analysis, I

Cost analysis, II

Sensitivity, specificity

Positive predictive value

False positives

From Ontario data of 261,096 pregnancies between September 2016 and March 2019, cfDNA (using contingent approach) resulted in:



- Reduction of prenatal diagnostic testing from 4.4% (from a pre-cfDNA cohort) to 2.4%.
- Women's autonomy protected: Overall uptake of prenatal diagnostic testing (amnio or chorionic villous sampling) after cfDNA screen positive result was 65%. This indicates that 2/3 of women are choosing to go for invasive testing after a positive screen, and 1/3 are not.

Moving Forward

sens,spec (Slide Layer)

SCFPCLearn

Review




	Cell free DNA		Multiple Marker Screening	
	T21	T18	T21	T18
Sensitivity (%)	99.8	94.4	86.3	76.8
Specificity (%)	99.8	99.9	99.8	99.8
Positive Predictive Value (%)	92	90.3	3.9	17.8
Negative Predictive Value (%)	>99.9	99.9	99.8	99.9

Moving Forward

Positive predictive value (Slide Layer)

SCFPCLearn

Review



- cfDNA "is not a substitute for invasive for invasive testing" (SOGC 2017)
- Positive predictive value (PPV) decreases in lower prevalence populations (but same sensitivity and specificity).

	Sensitivity	Specificity	Age 25 PPV	Age 40 PPV
T21	99.3	99.8	33	87
T18	97.4	99.8	13	68
T13	91.6	99.6	9	57


Adapted from SOGC 2017, data from Obstet Gynecol 2014;126:e31-7.

Moving Forward

False Positive (Slide Layer)

SCFPCLearn

Review



Cell-free DNA

Cost Effectiveness

Cost analysis, I

Cost analysis, II

Sensitivity, specificity

Positive predictive value

False positives

False positives are from placental mosaicism where the placenta (the source of the fetal DNA detected in the maternal circulation) may have a chromosomal abnormality but the fetus doesn't.


Moving Forward

2.7 Recommendation

(Multiple Response, 10 points, 1 attempt permitted)

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"Too bad that more accurate test can't just replace the amniocentesis. I was also reading that the miscarriage rate is high!"



i

Miscarriage rate with chorionic villous sampling is 3% and amniocentesis is 1 %.

True


☒ False

Submit

2.8 Review

SCFPCLearn

Review



i

Answer: False


Miscarriage Rates

Early invasive testing



Click on the buttons to view additional information


Moving Forward

Miscarriage Rate (Slide Layer)



Review





Answer: False


Miscarriage Rates

Early invasive testing



- The SOGC reports miscarriage rate as follows:
 - Amniocentesis: 0.5-1%
 - CVS: 0.5-1.0%
- However, a recent meta-analysis found rates to be ~ 0.1% and ~ 0.2%, respectively.


Moving Forward

Amniocentesis (Slide Layer)



Review





Answer: False

Miscarriage Rates

Early invasive testing



- Amniocentesis <15 weeks has been associated with talipes equinus (club foot) so earlier invasive testing is CVS, done either transcervical or transabdominally, depending on expertise of operators.

Moving Forward






2.9 Create a Plan

CFPC Learn

Let's Make a Plan



Using what you have learned write a plan for Annie. It can include any/all of the following: lifestyle intervention(s), prescription intervention(s), lab(s)/test(s) required, follow up appointment time frame, and referral required.





Fill in your plan for the patient here

See how your plan compares






2.10 Plan Answers

CFPC Learn

Annie Ploidy



This is the proposed plan for Annie. How does your plan compare?



Serum Testing

Ultrasound



Select details on the left to see suggested recommendations

What's in a name?

Serum Testing (Slide Layer)

SCFPCLearn

Annie Ploidy



This is the proposed plan for Annie. How does your plan compare?

Serum Testing

Ultrasound

What's in a name?



After answering a few more of her questions, Annie says she will talk to her partner about proceeding with testing.

She is pretty sure she is going to go ahead with serum testing, so you fill out the requisitions for routine prenatal blood work.

Ultrasound (Slide Layer)

SCFPCLearn

Annie Ploidy



This is the proposed plan for Annie. How does your plan compare?

Serum Testing

Ultrasound


What's in a name?

You fill out the ultrasound requisition for nuchal translucency after 11 weeks and for the prenatal screening that applies to your area.



You tell Annie that she needs to arrange the screening blood test for the same day as the ultrasound.

She thanks you and is excited about proceeding with prenatal care under your guidance!



Name (Slide Layer)




Annie Ploidy




This is the proposed plan for Annie. How does your plan compare?




**Meaning Behind the Name:**



Aneuploidy is the condition of having abnormal number of chromosomes in a haploid set. Hence, Annie Ploidy.



2.11 References



References



Thanks for visiting the clinic!

References are available [here](#).

This activity is eligible for up to 0.25 Mainpro+ credits.