NIPT – Not invariably perfect test

Dr Boski Shah
Obstetrician and gynaecologist
St V private Hospital

Outline

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- What is NIPT?
- What do we test in NIPT commonly?
- NIPT as primary screening test or after combined screening test
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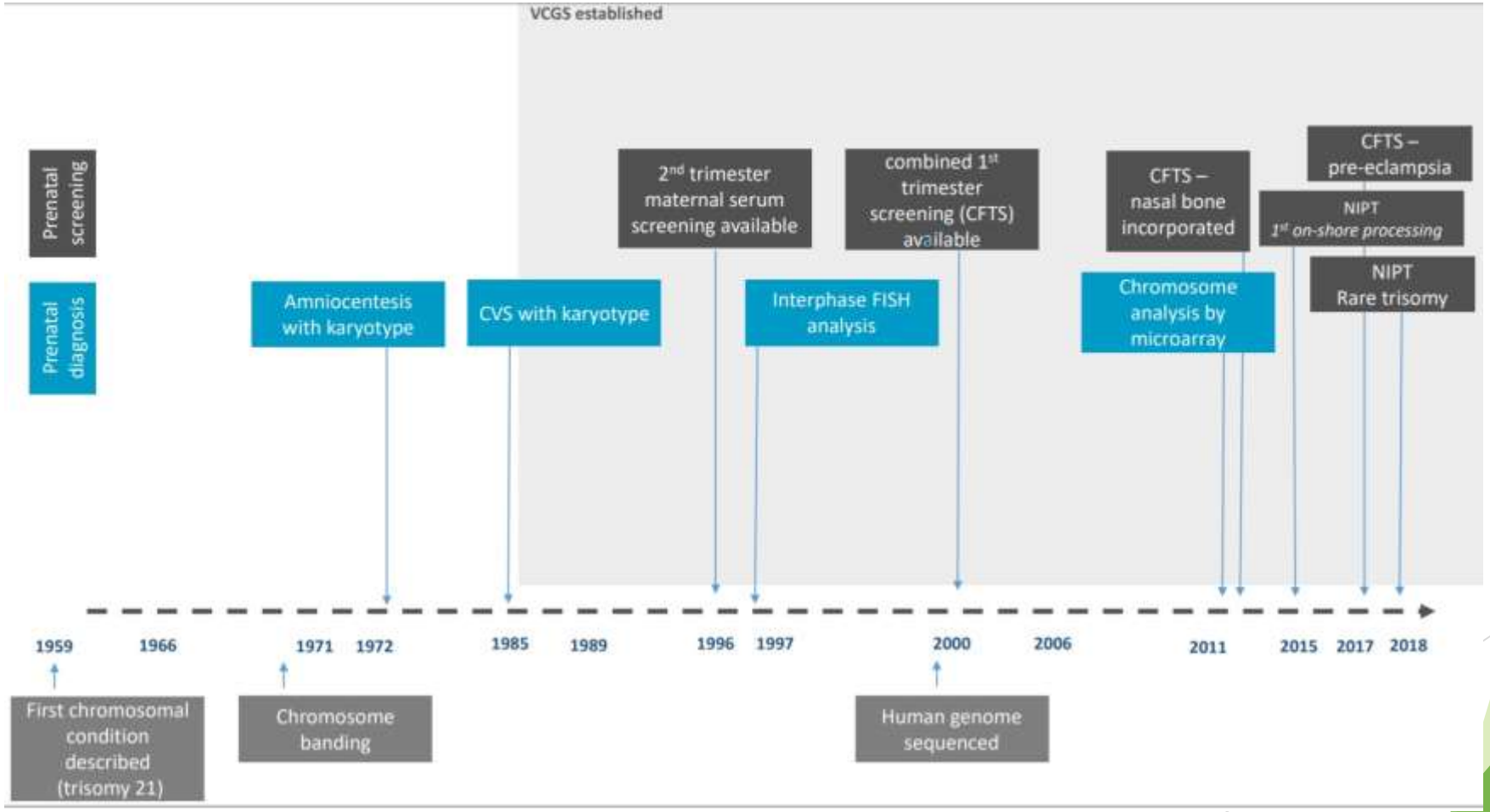
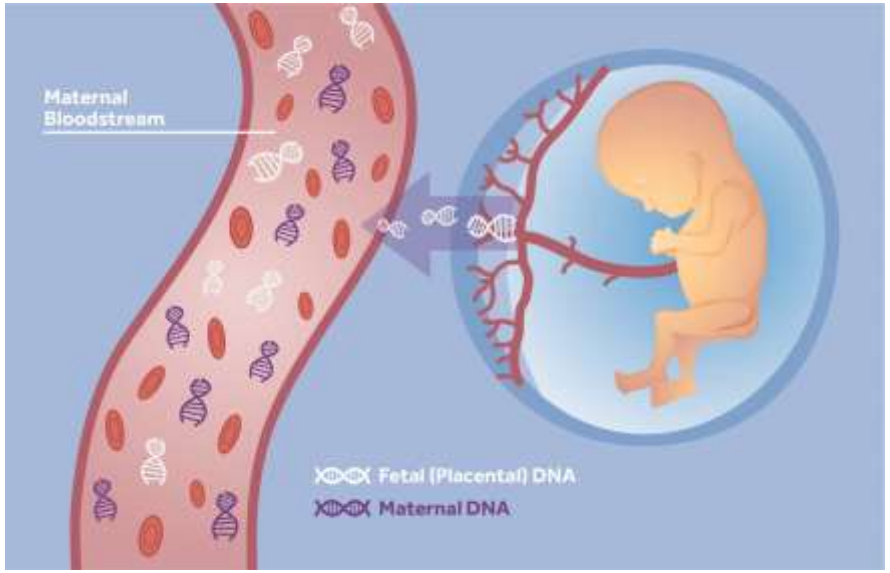
Our journey in prenatal genetic screening



What is NIPT?

- Its a screening test. Maternal blood sample is tested to determine if developing fetus could have certain genetic condition
- During pregnancy, cfDNA (cell free DNA - fragments fetal DNA) get into maternal blood stream. This fetal DNA is analysed.



What do we test in NIPT commonly?

- **Aneuploidies of chromosome 13, 18, 21 and sex chromosomes**
- Percept offered by VCGS now incorporates even **rare aneuploidies**
- Examples of additional findings reported to date include **known chromosome conditions** such as:
  - 2q37 deletion syndrome, 3p deletion syndrome, 4p deletion (Wolf Hirschhorn) syndrome, 5p deletion (Cri du chat) syndrome, 11q deletion (Jacobsen) syndrome, 17p deletion (Miller-Dieker) syndrome, trisomy 9p syndrome, tetrasomy 9p syndrome,tetrasomy 12p (Pallister Killian) syndrome, tetrasomy 18p syndrome
- Percept now offers **translocation analysis for known carriers** – Call genetic counsellor first

NIPT as primary screening test or after combined screening test

- When should you recommend NIPT as primary screening test?
  - Advanced maternal age (>35 years) - low false positive results is a big advantage.
  - When combined screening test has shown high risk result
  - P/H or F/H of genetic condition
  - An u/s showing fetal anomaly that could be linked to genetic condition
  - You can offer NIPT for all cases but might not be worth the cost in low risk patients
- If combined screening test results shows high risk for fetal aneuploidies, NIPT can be done. When the risk is >1:50, careful counselling needed for invasive testing vs NIPT.
- No upper limit to what gestational age you can offer the test but should be done before 16 wks ideally to allow time to follow up the results, do invasive testing and organise termination of pregnancy if needed.

Accuracy

- Highly accurate but not 100%
- More accurate in diagnosing Trisomy 21 (compared to other aneuploidies)
- Sex determination - over 99% accurate
- Less accurate in multiple pregnancy

What is fetal fraction?

- The amount of free fetal DNA as compared to maternal genetic material. Generally it is more than 10%.
- Fetal fraction increases with placental mass (increasing gestational age)
- Fetal fraction is typically low in obese patients (? dilution effect)
- Fetal fraction <4% would result in inconclusive result.
- It has short half life in maternal blood. It is cleared from maternal blood within hours of birth or miscarriage.

Inconclusive results

- Low fetal fraction (<4%) will lead to inconclusive results or test failure
- Early gestational age
- Multiple pregnancy
- Obesity
- Isolated placental mosaicism
- Maternal malignancy

Clinical cases – which test would you choose?

- 42 years old, 9 wks pregnant patient
- 14 wks pregnant, high risk combined screening test (1:160)
- 15 wks pregnant, combined screening test result (1:2)

Clinical cases – NIPT is not perfect

- KD. 39yo G2P1
- Requested NIPT
- BMI 25
- Had blood drawn at 10+2, result = failed due to low fetal fraction
- Bloods done for T1 screen, results T21 reduced from 1:60 to 1:770, but T18 increased from 1:310 to 1:110
- Had repeat NIPT at 13w = failed due to low fetal fraction
- Had scan at 16w with a view to amnio if any abnomalities seen, scan was normal as was next scan at 21w.
- Delivered normal girl at 39w.

Clinical cases – NIPT is not perfect

- RT. 37yo G1P0
- Requested NIPT
- BMI 23
- NIPT at 10w = high risk (1:5) for 45XO
- Wanted CVS if scan of concern, otherwise 15w amnio
- 12w scan = no markers for Turners
- 15w scan = normal, amnio done, normal 46XY
- Placenta = mosaic 45XO/46XY
- 2018 had another baby = chose to do T1 combined screen, 1:17000.

Summary

- Its a screening test done in early pregnancy to detect Down Syndrome and other chromosomal conditions.
- It is non - invasive, safe test
- Currently, there is no medicare rebate
- NIPT is optional test like all other prenatal test
- It is highly accurate test but definite diagnosis of fetal chromosomal condition can only be made after amniocentesis or CVS.