PRENATAL SCREENING FOR DOWN SYNDROME, TRISOMY 18 AND OPEN NEURAL TUBE DEFECTS

Prenatal screening estimates the fetal risk of Down syndrome, trisomy 18, and open neural tube defects. The results will assist in determining the need for further diagnostic testing. The screening tests offered will vary according to the gestational age at the time of presentation, maternal age at the time of delivery, and singleton versus twin gestation.

Table 1: Tests available through the BC Prenatal Genetic Screening Program

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Markers / Measurements</th>
<th>Possible Timeframe</th>
<th>Best Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Integrated Prenatal Screen (SIPS) blood test #1</td>
<td>PAPP-A</td>
<td>9–13 wks</td>
<td>10–11 wks</td>
</tr>
<tr>
<td>SIPS blood test #2</td>
<td>hCG, Inhibin-A</td>
<td>14–20 wks</td>
<td>15–16 wks</td>
</tr>
<tr>
<td>Integrated Prenatal Screen (IPS)</td>
<td>Same as SIPS (blood test #1)</td>
<td>See SIPS for blood tests</td>
<td>See SIPS for blood tests</td>
</tr>
<tr>
<td>Quad blood test</td>
<td>Same as SIPS blood test #2</td>
<td>14–20 wks</td>
<td>15–16 wks</td>
</tr>
<tr>
<td>Non-Invasive Prenatal Testing (NIPT)</td>
<td>Cell-free DNA in maternal blood</td>
<td>10 weeks and onwards</td>
<td>varies by indication</td>
</tr>
</tbody>
</table>

1 If an NT ultrasound is performed, a separate first trimester dating ultrasound is not necessary if LMP is certain.

Resources
- BC Prenatal Genetic Screening Program; guideline and related patient teaching resources; www.bcprenatalscreening.ca
- Perinatal Services BC: T 604-877-2121; E psbc@phsa.ca; www.perinatalservicesbc.ca
- Canadian Down Syndrome Society; T (800) 883-5608; E info@cdss.ca; www.cdss.ca
- Down Syndrome Research Foundation (Canada); T 604-444-3773 or toll-free in Canada at 1-888-464-DSRF; www.dsrf.org
- Lower Mainland Down Syndrome Society (Canada); T 604-591-2722; www.lmdss.com
- Society of Obstetricians and Gynaecologists, Clinical Practice Guidelines (Canada); www.soeg.org/guidelines
- Spina Bifida and Hydrocephalus Association of BC; T 604-877-7000; E info@sbhabc.org; www.sbhabc.org
- Support Organization For Trisomy 18, 13 and Related Disorders (SOFT; US); www.trisomy.org

Genetic counselling services (Medical Genetics)
Victoria: T 250-727-4461 Fax for referrals: 250-727-4295
Vancouver: T 604-875-2157 Fax for referrals: 604-875-3484

Questions about prenatal screening in BC
Prenatal Biochemistry Laboratory: T 604-875-2331

Table 2: Screening options available through the BC Prenatal Genetic Screening Program

<table>
<thead>
<tr>
<th>Characteristics of woman</th>
<th>Gestational Age at the First Prenatal Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 13 wks</td>
</tr>
<tr>
<td>&lt;35 years</td>
<td>SIPS</td>
</tr>
<tr>
<td>35–39 years</td>
<td>IPS; or</td>
</tr>
<tr>
<td></td>
<td>if NT not available, SIPS</td>
</tr>
<tr>
<td>40+ years</td>
<td>IPS; or</td>
</tr>
<tr>
<td></td>
<td>if NT not available, SIPS; or</td>
</tr>
<tr>
<td>Personal/family history that increases risk of fetus with Down syndrome, trisomy 18, or trisomy 13</td>
<td>NIPIT; or</td>
</tr>
<tr>
<td></td>
<td>CVS or Amnio without prior screening</td>
</tr>
<tr>
<td>Personal/family history that increases risk of fetus with chromosomal abnormality other than Down syndrome, trisomy 18, or trisomy 13</td>
<td>CVS or Amnio</td>
</tr>
<tr>
<td></td>
<td>without prior screening</td>
</tr>
<tr>
<td>Twin gestation</td>
<td>IPS; or</td>
</tr>
<tr>
<td></td>
<td>if NT not available, SIPS; or</td>
</tr>
<tr>
<td></td>
<td>CVS or Amnio without prior screening</td>
</tr>
<tr>
<td>Pregnant following In vitro fertilization with intracytoplasmic sperm injection</td>
<td>IPS; or</td>
</tr>
<tr>
<td></td>
<td>if NT not available, SIPS; or</td>
</tr>
<tr>
<td></td>
<td>CVS or Amnio without prior screening</td>
</tr>
</tbody>
</table>

If the prenatal screen result is screen positive for Down syndrome (assuming gestational dating is confirmed) or trisomy 18, women should be counselled by their health care provider and offered further testing. See www.bcprenatalscreening.ca for details.

If the prenatal screen result is screen positive for an open neural tube defect (assuming gestational dating is confirmed), women should be referred to Maternal Fetal Medicine or Medical Genetics for a detailed ultrasound, counselling, and, if indicated, diagnostic testing.
### Table 3: Eligibility, Screen Cut-Offs, and Performance of Screening Tests

<table>
<thead>
<tr>
<th>WHO IS ELIGIBLE</th>
<th>Serum Integrated Prenatal Screen (SIPS)</th>
<th>Integrated Prenatal Screen (IPS)</th>
<th>Quad Screen (QUAD)</th>
<th>Non-Invasive Prenatal Testing (NIPT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women who present for their first visit at ≤ 13 + 6 wks</td>
<td>Women who present for their first prenatal visit at ≤ 13 + 6 wks gestation and who:</td>
<td></td>
<td>All women who present for their first prenatal visit between 14 and 20 + 6 wks gestation</td>
<td>Women with a positive (IPS / SIPS / Quad) screen for Down syndrome or trisomy 18 <strong>OR</strong></td>
</tr>
<tr>
<td><strong>Down Syndrome</strong></td>
<td><strong>Screen cut-off</strong></td>
<td>Detection rate</td>
<td>False positive rate</td>
<td>Chance a screen negative result is a false negative result</td>
</tr>
<tr>
<td>1:900</td>
<td>&lt; 35 yrs:</td>
<td>87%</td>
<td>&lt; 35 yrs:</td>
<td>&lt; 0.1%</td>
</tr>
<tr>
<td>1:200</td>
<td>&lt; 35 yrs:</td>
<td>100%2</td>
<td>&lt; 35 yrs:</td>
<td>&lt; 0.1%</td>
</tr>
<tr>
<td>1:900</td>
<td>&lt; 35 yrs:</td>
<td>87%</td>
<td>&lt; 35 yrs:</td>
<td>&lt; 0.1%</td>
</tr>
<tr>
<td><strong>False positive rate</strong></td>
<td>&lt; 35 yrs:</td>
<td>7%</td>
<td>&lt; 35 yrs:</td>
<td>&lt; 0.1%</td>
</tr>
<tr>
<td></td>
<td>35 – 39 yrs:</td>
<td>20%</td>
<td>35 – 39 yrs:</td>
<td>&lt; 0.1%</td>
</tr>
<tr>
<td></td>
<td>≥ 40 yrs:</td>
<td>39%</td>
<td>≥ 40 yrs:</td>
<td>&lt; 0.1%</td>
</tr>
</tbody>
</table>


2 The detection rates listed are based on the small cohort of Down syndrome pregnancies in BC. SIPS, IPS and Quad are screening tests so may not have 100% detection rate.

3 Higher false positive rate of IPS reflects that this test is done in women who are at a higher a priori risk.

### Table 4: Risk of Down Syndrome and Other Chromosome Abnormalities in Live Births by Maternal Age

<table>
<thead>
<tr>
<th>Maternal Age (At Term)</th>
<th>Down Syndrome</th>
<th>Total Chromosome Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>1 in 1,250</td>
<td>1 in 476</td>
</tr>
<tr>
<td>26</td>
<td>1 in 1,190</td>
<td>1 in 476</td>
</tr>
<tr>
<td>27</td>
<td>1 in 1,111</td>
<td>1 in 455</td>
</tr>
<tr>
<td>28</td>
<td>1 in 1,031</td>
<td>1 in 435</td>
</tr>
<tr>
<td>29</td>
<td>1 in 935</td>
<td>1 in 417</td>
</tr>
<tr>
<td>30</td>
<td>1 in 840</td>
<td>1 in 385</td>
</tr>
<tr>
<td>31</td>
<td>1 in 741</td>
<td>1 in 385</td>
</tr>
</tbody>
</table>

Source: Hecht CA and Hook EB. 1996

April 2019
Algorithm 1

Prenatal Genetic Screening Recommendations
Singleton Pregnancies

Woman with Singleton Pregnancy Presents for 1st Prenatal Visit
(Excluding women with personal/family history that increases risk of fetus with Down syndrome, trisomy 18, or other chromosomal abnormality, who should be referred to Medical Genetics for counselling of their prenatal screening/diagnostic options)

Present at ≤ 13+6 weeks GA

- < 35 years: No risk factors
- 35 – 39 years: No risk factors
- ≥ 40 years: No risk factors

NT available?
- No
  - SIPS
- Yes
  - NT available?
    - No
      - IPS
    - Yes
      - IPS or CVS / Amnio? (patient choice)

CVS / Amnio

Present at 14 – 20+6 weeks GA

- < 40 years: No risk factors
- ≥ 40 years: No risk factors

NT available?
- No
  - SIPS
- Yes
  - NT available?
    - No
      - IPS
    - Yes
      - IPS or CVS / Amnio? (patient choice)

Quad or Amnio? (patient choice)

Present at ≥ 21 weeks GA

- < 35 years: No risk factors
- ≥ 35 years: No risk factors
- ≥ 40 years: No risk factors

Detailed Ultrasound

U/S Abnormal
- Refer to Maternal Fetal Medicine or Medical Genetics
- HCP reassures woman. No further action
- Amnio

U/S Normal
- Amnio

Screen positive for ONTD?
- Yes
  - Risk 1:301 – 1:900
    - Funded NIPT
  - Risk ≥ 1:300
    - Funded NIPT or Amnio (or if < 13 weeks, possibly CVS)
- No
  - No further action

Screen positive for Down Syndrome?
- Yes
  - Funded NIPT
- No
  - No further action

Screen positive for Trisomy 18?
- Yes
  - Funded NIPT
- No
  - No further action

BC Prenatal Genetic Screening Program

See www.bcprenatalscreening.ca for more details on amniocentesis and NIPT options (funded and self-pay)

Legend
- GA = Gestational Age
- NT = Nuchal Translucency
- IPS = Integrated Prenatal Screen
- SIPS = Serum Integrated Prenatal Screen
- NIPT = Non-Invasive Prenatal Testing
- U/S = Ultrasound

April 2019
Prenatal Genetic Screening Recommendations

Woman with Twin Pregnancy Presents for 1st Prenatal Visit
(Excluding women with personal/family history that increases risk of fetus with Down syndrome, trisomy 18, or other chromosomal abnormality, who should be referred to Medical Genetics for counselling of their prenatal screening/diagnostic options)

Presents at ≤ 13+6 weeks GA

- < 35 years No risk factors
  - NT available?
    - Yes
      - IPS
    - No
      - IPS or Amnio? (patient choice)
      - U/S Normal
      - Amnio?
      - Yes
      - Screen positive for ONTD?
        - Yes
          - Funded NIPT
          - Actions based on test results
        - No
          - No further action
      - No
        - Refer to Maternal Fetal Medicine or Medical Genetics

- ≥ 35 years No risk factors
  - IPS or Amnio? (patient choice)
  - U/S Abnormal
  - Amnio?
  - Yes
    - Screen positive for Down Syndrome?
      - Yes
        - Funded NIPT
        - Actions based on test results
      - No
        - No further action
    - No
      - Screen positive for Trisomy 18?
        - Yes
          - Funded NIPT or Amnio
          - Actions based on test results
        - No
          - No further action

Presents at 14 – 20+6 weeks GA

- < 35 years No risk factors
  - IPS or Amnio? (patient choice)
  - U/S Normal
  - Amnio?
  - Yes
    - Screen positive for ONTD?
      - Yes
        - Funded NIPT
        - Actions based on test results
      - No
        - No further action
    - No
      - Refer to Maternal Fetal Medicine or Medical Genetics
  - U/S Abnormal
  - Amnio?
  - Yes
    - Screen positive for Down Syndrome?
      - Yes
        - Funded NIPT
        - Actions based on test results
      - No
        - No further action
    - No
      - Screen positive for Trisomy 18?
        - Yes
          - Funded NIPT or Amnio
          - Actions based on test results
        - No
          - No further action

- ≥ 35 years No risk factors
  - IPS or Amnio? (patient choice)
  - U/S Normal
  - Amnio?
  - Yes
    - Screen positive for Down Syndrome?
      - Yes
        - Funded NIPT
        - Actions based on test results
      - No
        - No further action
    - No
      - Screen positive for Trisomy 18?
        - Yes
          - Funded NIPT or Amnio
          - Actions based on test results
        - No
          - No further action
  - U/S Abnormal
  - Amnio?
  - Yes
    - Screen positive for Down Syndrome?
      - Yes
        - Funded NIPT
        - Actions based on test results
      - No
        - No further action
    - No
      - Screen positive for Trisomy 18?
        - Yes
          - Funded NIPT or Amnio
          - Actions based on test results
        - No
          - No further action
  - No
    - Refer to Maternal Fetal Medicine or Medical Genetics
  - HCP reassures woman.
  - No further action

Presents at ≥ 21 weeks GA

- ≥ 35 years No risk factors
  - IPS or Amnio? (patient choice)
  - U/S Normal
  - Amnio?
  - Yes
    - Screen positive for Down Syndrome?
      - Yes
        - Funded NIPT
        - Actions based on test results
      - No
        - No further action
    - No
      - Screen positive for Trisomy 18?
        - Yes
          - Funded NIPT or Amnio
          - Actions based on test results
        - No
          - No further action
  - U/S Abnormal
  - Amnio?
  - Yes
    - Screen positive for Down Syndrome?
      - Yes
        - Funded NIPT
        - Actions based on test results
      - No
        - No further action
    - No
      - Screen positive for Trisomy 18?
        - Yes
          - Funded NIPT or Amnio
          - Actions based on test results
        - No
          - No further action
  - No
    - Refer to Maternal Fetal Medicine or Medical Genetics
  - HCP reassures woman.
  - No further action

Legend
GA = Gestational Age
IPS = Integrated Prenatal Screen
SIPS = Serum Integrated Prenatal Screen
NIPT = Non-Invasive Prenatal Testing
U/S = Ultrasound
NT = Nuchal Translucency

*Screening in higher multiples will remain based on NT alone.
If NT is not available and the woman is ≥ 35 years old, amniocentesis is an option.

See www.bcprenatalscreening.ca for more details on amniocentesis and NIPT options (funded and self-pay)