TEST

Quadruple screen test

A blood test that estimates the chance of certain chromosome conditions and open birth defects during pregnancy.

WHAT IT MEASURES
Four pregnancy proteins and hormones in the pregnant person's blood

SAMPLE
Blood

FASTING NEEDED?
No

HOW LONG IT TAKES
About 5 to 10 minutes

RESULTS IN
Usually several days; timing varies by laboratory

USED FOR
Screening chromosome conditions and open neural tube defects

MAIN LIMITATION
Incorrect pregnancy dating can substantially distort the calculated risk

Overview

The quadruple screen is a prenatal blood test usually performed during the second trimester. It is called "quadruple" because it measures four substances in your blood:

A laboratory combines these measurements with information such as your age, weight, stage of pregnancy and number of fetuses. It then estimates the chance that the pregnancy is affected by Down syndrome, trisomy 18 or an open neural tube defect.

Down syndrome and trisomy 18 are chromosome conditions. An open neural tube defect occurs when the developing brain, spine or spinal cord does not close fully. Spina bifida is one example.

This is a screening test, not a diagnostic test. It cannot confirm whether the fetus has a condition. A higher-chance result can occur in an unaffected pregnancy, while a lower-chance result cannot rule out every condition.

- Alpha-fetoprotein, or AFP, made mainly by the fetus

- Human chorionic gonadotropin, or hCG, made by the placenta
- Unconjugated estriol, or uE3, made through the fetus and placenta
- Inhibin A, made largely by the placenta

Why the test is ordered

The quadruple screen may be offered when prenatal screening was not completed earlier in pregnancy. It can also be considered when cell-free DNA screening is unavailable, unsuitable or not the option you prefer.

Unlike cell-free DNA screening, the quadruple screen includes AFP, which can help identify pregnancies with an increased chance of an open neural tube defect. AFP may also be raised with an abdominal wall defect or certain pregnancy complications.

The test does not screen for every chromosome condition, genetic disorder or birth difference. It also does not replace the detailed second-trimester ultrasound that examines fetal development.

Who should have the test

All pregnant people should be offered information about prenatal screening and diagnostic testing, regardless of age or previous pregnancy history. Having screening is optional.

The quadruple screen is generally performed between 15 and 22 weeks of pregnancy. The exact accepted window differs among laboratories, and accurate pregnancy dating is important.

It may be particularly relevant if you:

Using several independent chromosome screening tests at the same time can produce confusing or conflicting results. If you have already had first-trimester or cell-free DNA screening, ask how the quadruple screen would add useful information. An AFP-only test may sometimes be considered instead.

Screening is also more difficult to interpret in twin or higher-order multiple pregnancies. The available options should be discussed based on the number of fetuses and the type of pregnancy.

- Did not have first-trimester chromosome screening
- Prefer blood screening over an invasive diagnostic test

- Want second-trimester screening that includes AFP
- Cannot access cell-free DNA screening

How to prepare

You can eat and drink normally before the test. Fasting is not required, and regular amounts of coffee or tea do not usually affect the measurements.

Bring or confirm information about:

Tell the testing service about prescription medicines, non-prescription medicines and supplements. High-dose biotin supplements can interfere with some laboratory methods, although this is assay-specific. Do not stop a prescribed medicine unless the clinician responsible for your care advises you to.

- Your estimated due date and how it was calculated
- Your current weight
- Whether you are carrying more than one fetus
- Diabetes, smoking and fertility treatment
- Any earlier prenatal screening or ultrasound results

What happens during the test

A healthcare professional places a small needle into a vein, usually inside your elbow. A tube of blood is collected and sent to a laboratory.

The blood draw normally takes only a few minutes. There is no contact with the uterus or fetus, so the test itself does not create a risk of miscarriage.

The laboratory measures the four markers and compares them with expected levels at the same stage of pregnancy. It then uses a calculation to produce a screening result.

Understanding your results

Your report may describe the result as screen negative, lower chance, screen positive or higher chance. It may also give a number such as "1 in 500." This means that among pregnancies with a similar result, about one in 500 would be expected to have the condition. It does not mean that your fetus is definitely affected or unaffected.

The marker values may be reported as multiples of the median, or MoM. This compares your result with the middle value expected at the same stage of pregnancy. The laboratory adjusts these values using relevant pregnancy information.

Certain marker patterns are associated with particular conditions. For example, Down syndrome is often associated with higher hCG and inhibin A and lower AFP and uE3. Trisomy 18 is often associated with lower levels of several markers. AFP can be raised with an open neural tube defect.

These patterns are not diagnoses. The individual numbers should not be interpreted separately from pregnancy dating, ultrasound findings and the laboratory's calculation.

There is no single universal normal range. Cutoffs and interpretation vary by laboratory, age, sex-related biology, pregnancy stage and number of fetuses, medicines, and the wider clinical context.

What affects the results

Pregnancy dating is one of the most important influences. Marker levels naturally change from week to week. If the pregnancy is further along or less advanced than recorded, the calculated chance may be misleading even when the laboratory measurement is correct.

Other important influences include:

Some laboratories also include race or ethnicity in their calculations, while others do not. Ask which information was used if it is not clear on the report.

Food, ordinary caffeine intake, exercise and the time of day are not known to cause important changes in routine quadruple screening. A recent blood transfusion is not usually a major issue because this is not a red blood cell test, but it should still be reported if the laboratory requests that information.

- More than one fetus: Twins or higher-order multiples produce different marker levels
- Body weight: Greater blood volume can dilute the measured substances
- Maternal age: Age changes the starting chance used in the calculation
- Diabetes: Pre-existing diabetes can affect some marker levels
- Smoking: Smoking may alter the expected marker pattern
- Fertility treatment: Donor eggs and assisted conception may change the information needed for calculation
- A vanishing twin: A fetus that stopped developing earlier can affect some results

- Fetal or placental conditions: These can change marker levels without a chromosome condition
- High-dose biotin: This supplement may interfere with certain laboratory assays

Accuracy and limitations

The quadruple screen identifies about four out of five pregnancies affected by Down syndrome when a standard screen-positive rate is used. This means it can miss some affected pregnancies. Around one in 20 unaffected pregnancies may receive a screen-positive result, although performance changes with age, pregnancy details and laboratory methods.

Accuracy for trisomy 18 and open neural tube defects also varies. Incorrect dating, multiple pregnancy and incomplete clinical information can make the result less reliable.

Cell-free DNA screening is more accurate than the quadruple screen for common chromosome conditions and produces fewer false-positive results. However, it is still a screening test and does not assess open neural tube defects.

A detailed ultrasound is better for directly examining fetal anatomy. Amniocentesis can provide diagnostic chromosome testing, and testing of the amniotic fluid may help assess an open neural tube defect. These tests answer different questions and carry different considerations.

No lower-chance result can guarantee that the fetus has no chromosome, genetic or structural condition.

Risks and complications

The physical risks are limited to those of a routine blood draw. You may have brief discomfort, a small bruise or light-headedness; infection at the needle site is very uncommon.

An unclear or higher-chance result may cause anxiety and lead to additional appointments or testing. Any risks from later procedures, such as amniocentesis, are separate from the quadruple screen itself.

What happens next

After a lower-chance result, routine prenatal care usually continues. You will generally still be offered a detailed ultrasound because the blood test cannot examine fetal anatomy.

A higher-chance chromosome result is usually followed by a discussion about genetic counseling, a detailed ultrasound and further testing. Cell-free DNA may sometimes provide more accurate screening, but amniocentesis is the test that can usually confirm or exclude a chromosome condition at this stage of pregnancy.

If AFP is raised, the first steps often include checking the due date and number of fetuses with ultrasound. A detailed ultrasound can examine the spine, brain, abdominal wall, placenta and other structures. Depending on the result and local protocol, repeat blood testing or amniocentesis may be discussed.

A screen-positive result needs timely follow-up, but it is not usually an emergency. Seek urgent pregnancy assessment for heavy bleeding, severe or persistent abdominal pain, leaking fluid, fainting, or a clear reduction in your fetus's usual movements once movements are established. These symptoms are not caused by the quadruple screen and should not wait for the result.

Common questions

Can I drink coffee before the quadruple screen?

Yes. Fasting is not required, and an ordinary amount of coffee is not expected to affect the result. Follow any separate instructions given for other tests being performed at the same visit.

Does the time of day matter?

No. The test can usually be taken at any time the collection site is open. The week of pregnancy matters much more than the hour of collection.

Can I exercise beforehand?

Normal activity and exercise are not known to meaningfully alter the result. If exercise makes you dehydrated or light-headed during blood tests, drink water and rest before the sample is taken.

How long will I wait for the result?

Results commonly return within several days, but timing varies by laboratory and location. Ask when and how the result will be shared.

Is a positive result a diagnosis?

No. It means the calculated chance is above the laboratory's cutoff. Many pregnancies with a positive screen are not affected, so ultrasound or diagnostic testing may be offered.

Can the test tell me the baby's sex?

The quadruple screen is not designed to determine fetal sex. An ultrasound, cell-free DNA

screening or diagnostic chromosome test may provide that information in some circumstances.

Sources

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