

Alpha-fetoprotein (AFP)

What is alpha-fetoprotein (AFP)?

Alpha-fetoprotein (AFP) is the major protein of fetal serum but it is usually undetectable after birth. AFP is made by the yolk sac of the fetus, enters the amniotic fluid and crosses the placenta into the maternal circulation. See also the separate [Tumour Markers](#) article.

Conditions which may lead to raised levels of alpha-fetoprotein

- [Hepatocellular carcinoma \(HCC\)](#): AFP levels are abnormal in 40–60% of patients. The American Association for the Study of Liver Diseases recommends diagnosis of HCC in patients with cirrhosis in the presence of a mass in the liver if AFP is >200 ng/mL^[1] .
- Other gastrointestinal cancers:
 - [Gastric cancer](#): AFP-producing gastric cancer (AFP level >7 ng/mL) is rare but is associated with a poorer prognosis than non-AFP-producing gastric cancer^[2] .
 - [Biliary tract cancer](#).
 - [Pancreatic cancer](#).
- Nonseminomatous germ cell tumours: if suspected, AFP measurement is essential^[3] .
- Alpha-fetoprotein may also be raised in patients with metastatic lung cancer and (rarely) primary [lung cancer](#)^[4] .
- [Cirrhosis](#): patients may have abnormal AFP values, although usually less than 500 ng/mL.
- [Viral hepatitis](#).

- [Ataxia with telangiectasia](#)^[5] .
- Pregnancy is associated with elevated AFP levels, particularly if the pregnancy is complicated by a spinal cord defect or other abnormality:
 - Maternal serum AFP test results, interpreted according to the gestational age. See also the articles on [Prenatal Diagnosis](#) and [Neural Tube Defects](#).
 - Raised levels of maternal AFP at 16–18 weeks of gestation are found in fetal neural tube defects^[6] .
 - Amniotic fluid AFP and acetylcholinesterase concentrations can be used to differentiate between open ventral wall defects ([gastroschisis and omphalocele](#)) and open neural tube defects^[7] .
 - Where there are high levels of AFP levels but there is no fetal abnormality, there may be greater risk of obstetric complications^[8] .

Uses of alpha-fetoprotein measurement

Screening for neural tube defects and trisomy

See also the separate [Prenatal Diagnosis](#) and [Prenatal Screening for Down's Syndrome](#) articles.

AFP screening is a simple maternal blood test, performed at around 15 weeks of gestation, that can detect increased risk to the fetus of certain genetic abnormalities such as:

- Open neural tube defects - eg, spina bifida.
- [Down's syndrome](#)^[9] .
- Other chromosomal abnormalities - eg, trisomy 18^[10] .
- Defects in the abdominal wall of the fetus - omphalocele.

A pregnant woman's AFP levels decrease soon after birth.

Diagnostic aid in premature rupture of membranes (PROM)

A study looking at prolactin, AFP and beta human chorionic gonadotrophin (beta-hCG) in vaginal fluid as markers for diagnosing PROM, showed that AFP had the greatest accuracy (94% sensitivity and specificity) [11]. Further studies have confirmed the reliability of cervicovaginal AFP for diagnosing PROM in equivocal cases [12].

Altered AFP levels, either too high or low compared with normal amounts, can also indicate increased risk of obstetric problems such as placenta accreta/increta/percreta when placenta praevia has been diagnosed [13].

Hepatocellular carcinoma (HCC)

Chronic hepatitis B and C infection may cause HCC. In conjunction with abdominal ultrasonography, AFP can be measured at six-monthly intervals in such patients who are at high risk of HCC (especially those with liver cirrhosis related to hepatitis B or C). However, a Cochrane review concluded that there is not enough evidence to know whether screening is worthwhile [14]. A Health Technology Assessment concluded that the most effective surveillance strategy is to screen high-risk patients with both AFP assay and ultrasound imaging on a six-monthly basis. However, the addition of ultrasound is only cost-effective in those with blood AFP level >20 ng/mL [15].

Acute liver failure

Serum concentrations of AFP that are variably elevated during liver injury have been suggested to be of prognostic importance in acute liver failure, with higher values being associated with improved outcome. AFP values change dynamically during acute liver failure. In a large prospective study, higher absolute values of AFP did not predict a favourable outcome; however, a rising level of AFP over the first three hospital days frequently indicated survival [16].

Further reading

- Adigun OO, Yarrarapu SNS, Khetarpal S; Alpha Fetoprotein. StatPearls, August 2021.

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