BECKWITH-WIEDEMANN SYNDROME (BWS)

AFP SCREENING

What is AFP?

AFP, or alpha-fetoprotein, is a protein that is made by the liver during the neonatal and infant period. At birth, AFP levels are initially high and decrease with age until normal levels are reached. Serum AFP is a marker that is used to detect liver abnormalities and hepatoblastoma.

What can affect AFP values?

AFP is produced at increased rates by rapidly growing liver cells such as hepatoblastoma cells, a rare liver tumor. Benign liver disorders can also cause elevated AFP levels, but levels are typically not as high as seen in hepatoblastoma. In addition, hyperbilirubinemia and hypothyroidism can cause AFP elevations in neonates and infants. More rarely, AFP elevations can also signal the development of a yolk sac tumor. Patients that are premature at birth typically have higher AFP levels than patients that are full-term.

Why should patients with BWS receive AFP screening?

Patients with BWS are at an increased risk to develop hepatoblastomas. More than 95% of patients with hepatoblastoma have elevated AFP levels, and elevated serum AFP has been demonstrated to be the best indicator of hepatoblastoma. Monitoring AFP levels in patients with BWS allows for detection of hepatoblastoma tumors at an earlier stage, which minimizes surgery and treatment required and may improve prognosis for patients.

What is the recommended AFP screening protocol for patients with BWS?

The American Association for Cancer Research (AACR) recommends that all patients with a clinical or molecular diagnosis of BWS receive AFP screening as part of their routine tumor surveillance. The majority of hepatoblastomas occur within the first year of life, with the oldest reported in BWS at 30 months, and AFP screening is recommended every 3 months from birth or the time of BWS diagnosis until age 4 years. AFP screening should be performed along with full abdominal ultrasounds. AFP screening can stop after the 4th birthday; however, patients with BWS should receive renal ultrasounds until the 7th birthday as part of their routine tumor surveillance for kidney tumors.

How should AFP values in patients with BWS be interpreted?

A wide variation in AFP levels exists between patients and an initially elevated AFP value may not indicate a hepatoblastoma. AFP values normally decline over time, and therefore, it is most important to evaluate the trend rather than an individual value when interpreting AFP values. The AFP trend should be followed with the expectation that values will decline over time. Some patients may have a transient spike in AFP value compared to previous values, however persistent AFP spikes and rising AFP values are usually indicative of hepatoblastoma. Any spike in AFP value should be correlated with ultrasound or other imaging techniques.

What are normal ranges of AFP values in patients with BWS?

The following table shows minimum and maximum AFP values observed by age from 147 patients with BWS:

AGE	MINIMUM AFP (NG/ML)	MAXIMUM AFP (NG/ML)
1 day	7,240	476,000
1 month	2,540	396,570
2 months	196	395,420
3 months	36.9	286,000
4 months	12.8	247,451
5 months	18.1	125,000
6 months	2.03	52,411
7 months	6.75	10,669
8 months	5.97	14,543
9 months	4.20	6,668
10 months	3.99	6,168
11 months	4.70	3,504
12 months	1.50	1,498
13 months	2.20	2,245
14 months	2.20	727
15 months	1.10	117.8
16 months	1.56	305.0
17 months	1.20	85.0
18 months	1.50	36.2
19 months	1.70	48
20 months	1.60	39
21 months	1.40	38
22 months	2.01	19.1
23 months	1.30	34.0
24 months	1.50	10.5
27 months	0.80	16.0
30 months	1.15	18.0
33 months	1.20	39.5
36 months	0.70	19.0
39 months	0.60	39.0
42 months	0.60	10.0
45 months	0.80	37.0
48 months	0.60	104.0

As wide variations in AFP values exist between patients, a patient with a value above the maximum value observed from this group may not indicate hepatoblastoma, and the AFP value should be correlated with ultrasound or other imaging techniques.

References

Kalish, J.M., Doros, L., Helman L.J., Hennekam, R.C., Kuiper, R.P., Maas, S.M.,...Druley, T.E. (2017). Surveillance Recommendations for Children with Overgrowth Syndromes and Predisposition to Wilms Tumors and Hepatoblastoma. *Clin Cancer Res*, 23(13), e115-e122.

Duffy, K.A., Cohen, J.L., Elci, O.U., & Kalish, J.M. (2019). Development of the Serum α-Fetoprotein Reference Range in Patients with Beckwith-Wiedemann Spectrum. *J Pediatr*, article in press. https://doi.org/10.1016/j.jpeds.2019.05.051.