* Pediatric laboratory test results must be interpreted in the context of interindividual variation and age- and sex-dependent dynamics. Reference intervals can **only approximate** the age-related dynamics**. Continuous reference intervals** from birth to adulthood are not available for most laboratory results because of the ethical and practical constraint defining reference intervals. In analogy with other development quantities continuous reference intervals specified by age **would seem to be more appropriate**.
* According to the IFCC expert group: ca. **120 samples are needed** for establishing reference intervals for a homogenuous population.
* Reference intervals are especially **important for newborn and infant children** because of pediatric morbidity and pronounced physiological development with consecutive changes in laboratory analytes. But they are **also most affected by the restrictions** establishing reference intervals.
* Efforts to address these issues: CALIPER provides sex-specific reference intervals for >80 analytes

**Asthma:** A new childhood asthma phenotype: obese with early menarche

* Relationship between incidence of asthma, obesity and early Menarche (2015):
  + Association of asthma incidence with BMI and weight gain only reported for women, not for men🡪 obesity may be influenced by female sexual hormones
  + The increase in the peripheral availability of oestrogen and the production of **leptin** by the adipose tissue may be implicated in the association between sexual maturation and obesity (Shimizu et al. 1997)
  + Therefore, it is possible that an interaction exists between age of puberty, obesity and asthma

🡪conclusions of the study: obesity 🡪inflammatory mediators🡪asthma

And a relation of the timing of menarche with increased BMI, but both conditions together with asthma are not described yed, further studies need to be done for this new phenotype of asthma

* **Menarcheal age is modified by** weight gain **in childhood.** **(Cooper et al. 1996)**
* During adolescence, early-maturing girls may be disadvantaged by the discordance of their physical appearance and chronological age ([Waylen and Wolke, 2004](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-51)); younger age at menarche is also a **risk factor for breast** ([Hsieh et al., 1990](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-28); [Rosner et al., 1994](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-43); [Rosner and Colditz, 1996](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-42); [Berkey et al., 1999](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-2)) and **endometrial cancer** ([Karageorgi et al., 2010](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-32)). The occurrence of **later menarche** in girls who have experienced **severe caloric restriction** ([Frisch and McArthur, 1974](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-24)) and earlier menarche in girls with a high **body mass index** (BMI) ([Biro et al., 2006](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-4); [Dunger et al., 2005](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-17)) (i.e. positive energy balance) supports the **importance of nutritional factors in menarcheal timing**. (Carwile et al. 2015)
* Sugar-sweetened beverages (SSB): link between consumption of SBB and earlier menarche (Carwile et al. 2015), pathway independent of weight gain are possible (via increased insulin that up-regulates hormones) ([Janssens et al., 1999](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-31); [Ludwig, 2002](http://humrep.oxfordjournals.org/content/early/2015/01/16/humrep.deu349.full?papetoc#ref-35)).
* Link between certain nutrients (including animal and vegetable protein) with earlier Menarche (Cheng et al. 2012)
* Obese children: alterations in adipose tissue can lead to adipose tissue dysfunction: leptin and CRP-hs serum levels are higher, and correalation to higher HOMA-IR (=marker of insulin restistance). 🡪obesity🡪inflammation:🡪 AT dysfunction🡪 realated to insulin resistance
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