tion was negative, 5 (22%; 95% CI, 7–44%) were confirmed as crystal arthritis with the repeat examination.

We envision two leading possibilities to explain the increase in sensitivity associated with repeat examination of the same specimen. The increased sensitivity might be attributable to the increased time spent examining the slide. Thus, low concentrations of crystals missed in the first examination may be detected by the second examination. Alternatively, in some patients the number, size, and/or birefringence (visibility) of crystals may increase over time in vitro and in vivo, and this facilitates their identification 24 h after the initial analysis. The latter explanation likely applies to the case we described above because abundant crystals were found on repeat examination and an in vitro maturation of crystals appeared to parallel the in vivo maturation of crystals in the affected joint.

In summary, our study suggests that repeat microscopic examination of the same synovial fluid specimen at 24 h increases the analytic and diagnostic sensitivity for crystal detection and is especially useful in cases with high pretest clinical suspicion for crystal arthropathy. A remaining issue is whether the benefit of this increase in sensitivity exceeds the cost associated with the potential decrease in specificity and the increased resources needed to perform the second examination of the specimen.

We would like to thank Starla Larson, Bryce Miller, Judy Tsoi, and Jean Turgeon for their technical support, and Drs. Daniel D. Bankson and Hossein Sadrazadeh for their collaboration.

References

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Plasma N-Terminal Pro-B-Type Natriuretic Peptide Concentrations in a Control Population of Infants and Children

To the Editor:
Recent studies suggest that the B-type natriuretic peptide (BNP) and its N-terminal fragment (NT-proBNP) may be useful diagnostic tools in children with congenital heart disease or cardiomyopathy (1–3). Reference data, however, are rare, especially for children. The aim of this study was to measure plasma concentrations in a control population of infants and children, using the Eletsys NT-proBNP assay (Roche Diagnostics).

EDTA plasma (centrifuged at 3000g for 5 min and frozen at −20°C) until analysis; stable for 12 months as provided by the manufacturer) was obtained from 13 neonates (<1 month of age) and from 78 children (37 girls and 41 boys; median age, 6.1 years; range, 4 months to 18 years). Patients with cardiac, renal, and hepatic diseases as well as water and electrolyte disturbances were retrospectively excluded from the study according to their diagnoses.

Concentration limits were calculated by regression analysis based on formulas derived from Virtanen et al. (4), which makes it unnecessary to partition the reference data into subgroups. A relatively small sample size is sufficient. This is of great advantage considering the costs and difficulties in collecting samples from large reference groups, especially pediatric samples. Because the variability of NT-proBNP increased with its mean concentration, we used natural log transformations in the regression analyses. After transform- ing the data back to the original scale, we established nomograms using the 2.5th, 50th, and 97.5th percentiles with 95% confidence intervals (Fig. 1).

The NT-proBNP concentration was highest during the first days of life (range, 1121–7740 ng/L) with a rapid decrease (Fig. 1, inset) similar to that described for BNP because of assumed perinatal circulating changes (5, 6). We observed no significant difference between plasma concentrations in male and female children (median, 62.3 ng/L; mean, 83.4 ng/L; range, 11–379 ng/L; Mann–Whitney test, P = 0.74). The lack of significance may be attributable to the small sizes of the groups. A negative correlation between age and concentration was evident for individuals >1 month (r = −0.45; P < 0.001). On the basis of the 97.5th percentile curve, the maximum value of 299 ng/L (age, 1 year) decreased to 48 ng/L (age, 16 years). For adults, increased reference limits according to age are provided by the supplier (97.5th percentiles for age <50 years, 153 ng/L for females and 88 ng/L for males; for adults 50–65 years of age, 334 ng/L for females and 227 ng/L for males).

Very few studies have been pub-
lished on the determination of BNP and NT-proBNP in the blood of neonates and children. Using the Biomedica system, Mir et al. (3) reported considerably higher limits and a slight decrease with age (range, 626–5531 ng/L; mean, 2630 ng/L; n = 109; age range, 11 days to 17 years) in children. Differences in antibody specificity and cross-reactivity with circulating NT-proBNP split products may be responsible (7).

ProBNP is cleaved into the two fragments NT-proBNP and BNP. However, in contrast to the decreasing values of NT-proBNP with increasing age, plasma concentrations of BNP have been reported to be constant in children 1–10 years of age (6). Further investigations are needed to elucidate the determinants for this change in ratio. Differences in the metabolic clearance of both peptides during childhood may cause the different distribution of NT-proBNP/BNP in plasma according to age (1). Nonspecific interference and unknown preanalytical effects cannot be excluded at this time.

In conclusion, in studies involving measurements of blood in pediatric patients, it is important to establish age-matched reference values. Results of BNP studies should be reported with annotation of the assay used.

References

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