at 11–14 weeks of gestation. *Obstet Gynecol* 2006; **107**: 678–683.

17. Souka AP, Von Kaisenberg CS, Hyett JA, Sonek JD, Nicolaides KH. Increased nuchal translucency with normal karyotype. *Am J Obstet Gynecol* 2005; **192**: 1005–1021.

18. Hyett J, Perdu M, Sharland G, Snijders R, Nicolaides KH. Using fetal nuchal translucency to screen for major congenital cardiac defects at 10–14 weeks of gestation: population based cohort study. *BMJ* 1999; **318**: 81–85.

19. von Kaisenberg CS, Nicolaides KH, Brand-Saberi B. Lymphatic vessel hypoplasia in fetuses with Turner syndrome. *Hum Reprod* 1999; **14**: 823–826.

20. von Kaisenberg CS, Krenn V, Ludwig M, Nicolaides KH, Brand-Saberi B. Morphological classification of nuchal skin in fetuses with trisomy 21, 18 and 13 at 12–18 weeks and in a trisomy 16 mouse. *Anat Embryol* 1998; **197**: 105–124.

21. von Kaisenberg CS, Brand-Saberi B, Christ B, Vallian S, Farzaneh F, Nicolaides KH. Collagen type VI gene expression in the skin of trisomy 21 fetuses. *Obstet Gynecol* 1998; **91**: 319–323.

APPENDIX

Illustration of calculations

This paper describes a two-component mixture model for the distribution of log(NT) in chromosomally normal pregnancies and in pregnancies with trisomies 21, 18 and 13. We illustrate the calculations for a pregnancy with fetal CRL of 60 mm and NT of 2.5 mm (see Table 2).

CRL-dependent component (normal pregnancies)

- Estimated mean $= -0.8951 + (0.02940 \times 60) - (0.0001812 \times 60^2) = 0.2166$.
- Estimated standard deviation $= (0.07900^2 + 0.02890^2)^{0.5} = 0.08412$.
- The median NT for the CRL dependent process is $10^{0.2166} = 1.6466$
- The measured NT of 2.5 mm is equivalent to $2.5/1.6466 = 1.518$ MoM.
- The probability density at log(2.5) $= 0.3979$ for the fitted Gaussian distribution is 0.4642.

CRL-independent component (normal pregnancies)

- Estimated mean $= 0.3019$
- Estimated standard deviation $= (0.1945^2 + 0.02890^2)^{0.5} = 0.1966$.
- The probability density at log(2.5) $= 0.3979$ for the fitted Gaussian distribution is 1.8007.

Mixture model (normal pregnancies)

- According to the mixture for unaffected pregnancies, the fitted logit of the proportion arising from the CRL-independent process is given by $-0.3319 - (0.03790 \times 60) = -2.6059$. The fitted proportion is then given by $1/(1 + \exp(-(-2.6059))) = 0.06878$

(approximately 7% of observations of NT arise from the CRL-independent component).

- The probability density for unaffected pregnancies is given by a weighted average of two Gaussian densities: the CRL-independent process (weight $= 0.06878$) and the CRL-dependent process (weight $= 1 - 0.06878 = 0.93122$). This gives the fitted mixture model probability density of $(0.06878 \times 1.8007) + (0.93122 \times 0.4642) = 0.5561$.

CRL-independent component (trisomy 21 pregnancies)

- Estimated mean $= 0.5330$
- Estimated standard deviation $= (0.2093^2 + 0.02890^2)^{0.5} = 0.2113$.
- The probability density at log(2.5) $= 0.3979$ for the fitted Gaussian distribution is 1.5393.

Mixture model (trisomy 21 pregnancies)

- According to the mixture model the estimated proportion of trisomy 21 pregnancies arising from the CRL-independent component is 0.9406. This gives the fitted mixture model density of $(0.9406 \times 1.5393) + (0.0594 \times 0.4642) = 1.4754$.

Likelihood ratio

The likelihood ratio of trisomy 21 to normal pregnancies is given by the probability density of trisomy 21 pregnancies divided by the probability density for normal pregnancies $= 1.4754/0.5561 = 2.653$.

Figure 5 shows the behavior of the likelihood ratio for the pregnancy with CRL $= 60$ mm and illustrates how with the mixture model the likelihood ratio rises steeply and then flattens as NT increases. This reflects the CRL independent component of the mixture model.
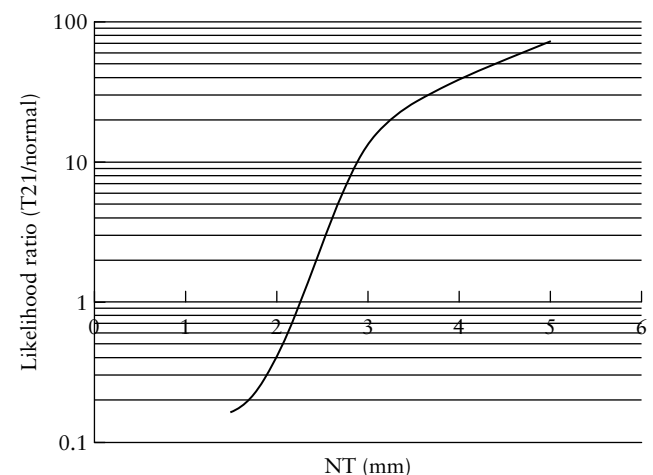
Figure 5 Relationship between likelihood ratio and nuchal translucency (NT) thickness for a crown–rump length of 60 mm.