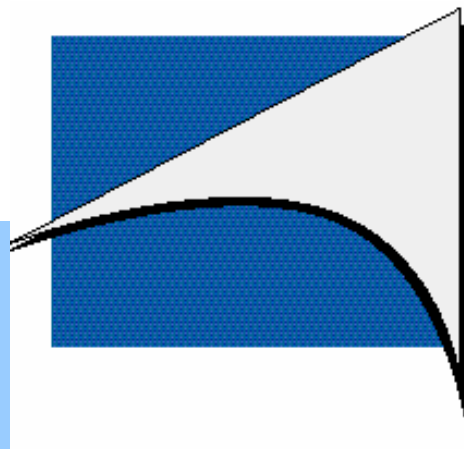


Mathematical Background
*Calculation procedure**

Free testosterone
Bioavailable testosterone

Elecsys® SHBG
Elecsys® Testosterone
Roche-Hitachi Albumin

* according to Vermeulen et. al , 1999



Christoph Berding
Hans Dieter Krämer
Roche Diagnostics Penzberg
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Testosterone Calculator

In this note we describe the mathematical framework for the calculation of the Free and Bioavailable Testosterone according to the work of Vermeulen et al. For the biochemical background and all further details readers are referred to the webpage <http://www.issam.ch/freetesto.htm>.

Notations

c_{TT}	concentration of Total Testosterone
c_{SHBG}	concentration of SHBG
c_{Alb}	concentration of Albumin
$c_{FTcalc.}$	concentration of calculated Free Testosterone
$c_{BATcalc.}$	concentration of calculated Bioavailable Testosterone
c_{Alb-b_Testo}	concentration of Albumine-bound Testosterone
c_{SHBG-b_Testo}	concentration of SHBG-bound Testosterone
c_{F_SHBG}	concentration of Free SHBG

Input parameters

$$c_{TT}, c_{SHBG}, c_{Alb}$$

Output parameters

$$c_{FTcalc.}, c_{FTcalc.} \%, c_{BATcalc.}, c_{BATcalc.} \%$$

Constants are defined for concentrations given in [Mol/l]. The following constants have been used

$$k_1 = 1 + \frac{3.6 \cdot 10^4}{69000} \cdot c_{Alb},$$

where c_{Alb} denotes the concentration of Albumin in [g/l] and $k_2 = 10^9$ denotes the binding constant Testosterone to SHBG.

Equations and Relations

$$(0.1) \quad c_{TT} = c_{FTcalc} + c_{Alb-b_Testo} + c_{SHBG-b_Testo}$$

$$(0.2) \quad c_{BATcalc} = c_{FTcalc} + c_{Alb-b_Testo} = k_1 \cdot c_{FTcalc}.$$

$$(0.3) \quad c_{FTcalc} = \frac{c_{SHBG-b_Testo}}{c_{F_SHBG} \cdot k_2}$$

$$(0.4) \quad c_{Alb-b_Testo} = (k_1 - 1) \cdot c_{FTcalc},$$

$$(0.5) \quad c_{FTcalc} + c_{Alb-b_Testo} = k_1 \cdot c_{FTcalc}.$$

$$(0.6) \quad c_{F_SHBG} = c_{SHBG} - c_{SHBG-b_Testo}$$

Derivation of a quadratic equation in c_{FT} .

From equations (0.1), (0.5) and (0.6)

$$(0.7) \quad c_{SHBG-b_Testo} = c_{TT} - k_1 \cdot c_{FTcalc}.$$

$$(0.8) \quad \begin{aligned} c_{F_SHBG} &= c_{SHBG} - c_{SHBG-b_Testo} = \\ &= (c_{SHBG} - c_{TT}) + k_1 \cdot c_{FTcalc} = d + k_1 \cdot c_{FTcalc}. \end{aligned}$$

where “d” abbreviates $c_{SHBG} - c_{TT}$. Combining equation (0.3) and (0.8)

$$(0.9) \quad c_{FTcalc} = \frac{c_{SHBG-b_Testo}}{c_{F_SHBG} \cdot k_2} = \frac{c_{TT} - k_1 \cdot c_{FTcalc}}{k_2 \cdot d + k_2 \cdot k_1 \cdot c_{FTcalc}}.$$

we obtain a quadratic equation

$$(0.10) \quad k_2 \cdot k_1 \cdot c_{FTcalc}^2 + [k_2 \cdot d + k_1] \cdot c_{FTcalc} - c_{TT} = 0$$

in c_{FTcalc} . The solutions are readily available

$$(0.11) \quad c_{FTcalc} = \frac{-b \pm \sqrt{\Delta}}{2 \cdot a}$$

$$(0.12) \quad a = k_1 \cdot k_2, \quad b = [k_2 \cdot d + k_1], \quad c = c_{TT}, \quad \text{and} \quad \Delta = b^2 - 4 \cdot a \cdot c.$$

For $\Delta \geq 0$ the positive square root is used to estimate c_{FTcalc} .

The equation $c_{FTcalc.}$ (0.11) in a long term description is

$$c_{FTcalc.} = \frac{-\left[k_1 + k_2 * (c_{SHBG} - c_{TT})\right] + \sqrt{\left[k_1 + k_2 * (c_{SHBG} - c_{TT})\right]^2 - 4 * k_1 * k_2 * (-c_{TT})}}{2 * k_1 * k_2},$$

insert of constants

$$c_{FTcalc.} = \frac{-\left[\left(1 + \frac{3.6 * 10^4 * c_{Alb} * 10}{69000}\right) + (c_{SHBG} - c_{TT})\right] + \sqrt{\left[\left(1 + \frac{3.6 * 10^4 * c_{Alb} * 10}{69000}\right) + (c_{SHBG} - c_{TT})\right]^2 - 4 * \left(1 + \frac{3.6 * 10^4 * c_{Alb} * 10}{69000}\right) * (-c_{TT})}}{2 * \left(1 + \frac{3.6 * 10^4 * c_{Alb} * 10}{69000}\right)} \quad \text{and}$$

estimation of each item

$$c_{FTcalc.} = \frac{-\left[\left(1 + 5.21739130434783 * c_{Alb}\right) + (c_{SHBG} - c_{TT})\right] + \sqrt{\left[\left(1 + 5.21739130434783 * c_{Alb}\right) + (c_{SHBG} - c_{TT})\right]^2 - 4 * \left(1 + 5.21739130434783 * c_{Alb}\right) * (-c_{TT})}}{2 * \left(1 + 5.21739130434783 * c_{Alb}\right)}$$

The equation $c_{BATcalc.}$ (0.2) is

$$c_{BATcalc.} = c_{FTcalc.} + c_{Alb-b_Testo} = k_1 * c_{FTcalc.},$$

insert of k_1

$$c_{BATcalc.} = c_{FTcalc.} * \left(1 + \frac{3.6 * 10^4 * c_{Alb} * 10}{69000}\right)$$

and estimation of the one item

$$c_{BATcalc.} = c_{FTcalc.} * \left(1 + 5.21739130434783 * c_{Alb}\right)$$

Worked example

Input $c_{TT} = 10$ [nmol/l], $c_{SHBG} = 40$ [nmol/l], $c_{Alb} = 4.3$ [g/dl] then we have $k_1 = 23.43$,
 $b = 53.43$, $\Delta = 3792.67$ and the results $c_{FTcalc.} = 0.1739$ [nmol/l], $c_{FTcalc.} \% = 1.74\%$,
 $c_{BATcalc.} = 4.07$ [nmol/l], $c_{BATcalc.} \% = 40.75\%$.