An exploration of James lean body mass (LBM) formulae: time to consider others!

Richard Muirhead, Rotherham General Hospital, Moorgate Road, Rotherham S60 2UD UK.
rmuirhead@compuserve.com

Introduction

Lean body mass estimates have been used in the propofol model by Dr Schnider[1] and remifentanil model by Dr Minto[2]. The equations used were those attributed to James in the publication 'Research into Obesity'[3]. However these equations are known to have a major shortcoming in that they appear to underestimate lean body mass in the obese[4,5]. As such commercial target controlled infusion (TCI) pumps are often patient weight limited.

As such I investigated the origin of the 'James' equation and compared this the other lean body mass equations, namely Hume(1966)[11], Hume & Weyers(1971)[6] and Janmahasation(2005)[10].

The 'James' formulae

The lean body mass formulae used by Drs Schnider[1] and Minto[2] for their TCI data sets were derived from equations attributed to T P Eddy in 'Research into Obesity'[3] as a means of estimating the total body fat from the Body Mass Index (BMI) and are used therein to illustrate tables. There was no other discussion within the publication of lean body mass. Firstly for men:

Table 2.2 *Mean values for the weight-height index (W/H²) and calculated body fat* of men in different surveys undertaken in the UK during the last 50 years*

Year of survey	Group	Age (years) 20–25 W/H²	20–25 Fat %	35–40 W/H²	35–40 Fat %	55–60 W/H²	55–60 Fat %	Reference
1930	National	21·3	17·1	22·8	19·0	23·3	19·7	40
1943	National	21·8	17·7	22·7	19·0	24·6	21·3	40
1960	Birmingham	22·8	19·1	24·9	21·7	24·9	21·7	40
1965	Port Talbot	24·3	21·0	26·2	23·4	26·2	23·4	40
1969	Directors	—	—	25·6†	22·7	26·0	23·1	41
1971	BP Employees	22·5	18·7	24·3‡	20·9	25·4§	22·3	42
1974	Richmond	22·6	18·8	24·9	21·8	24·7	21·5	21‖

Weight in kg; height in metres

* Calculated as: Fat % = 1·281 (W/H²) — 10·13
Equation derived by T. P. Eddy from data of Hume and Weyers[38], Boddy *et al.*[39] and Womersley *et al.*[34]

A similar table also appeared for women:-

Table 2.3 *Mean values for the weight-height index (W/H²) and calculated body fat* of women in three surveys undertaken in the UK*

Year of survey	Group	Young adult† W/H²	Young adult† Fat %	Early middle age‡ W/H²	Early middle age‡ Fat %	Late middle age§ W/H²	Late middle age§ Fat %	Reference
1943	National	20·7	23·4	22·5	26·3	23·6	27·9	40
1971	BP Employees	21·6	25·0	22·9	26·9	25·9	30·6	42
1974	Richmond	21·6	25·0	23·7	28·1	25·1	30·1	21

Weight in kg; height in metres

* Calculated as: Fat % = 1·48 (W/H²) — 7·0
Equation derived by T. P. Eddy from data of Hume and Weyers[38], Boddy *et al.*[39], and Womersley *et al.*[34]

Both of the equations appear to have been derived from data in other publications, namely Hume & Weyers[6] 1971 paper which measured the total body water via tritium dilution and thence the lean body mass could be calculated from an earlier animal study[7] which found lean body mass to be 73% water. Of the other papers quoted, Boddy[8] used the Hume and Weyers equation to estimate total body water. Wormesley[9] also used the Hume and Weyers equation to compare with anthropometric methods (e.g. skinfold thickness).

Neither equation as such directly derives lean body mass but as

$$LBM = weight - (weight\ of\ fat)$$

$$Then\ LBM = w - w*(fat\%)/100$$

Substituting, we have the 'James' equations (weight as kg, height as cm):

$$LBM_m = 1.1*w - 128*w^2/h^2$$

$$LBM_f = 1.07*w - 148*w^t/h^2$$

To test the assumption that the lean body mass rises to a certain BMI and then falls with increasing weight requires some very simple calculus. As both equations are of the form:

$$l = a*w - b*w^2/h^2$$

then the first differential will give the gradient, setting this to zero will give us the maximum:

$$dl/dw = a - 2*b*w/h^2 = 0$$

Hence

$$a = 2*b*w/h^2$$

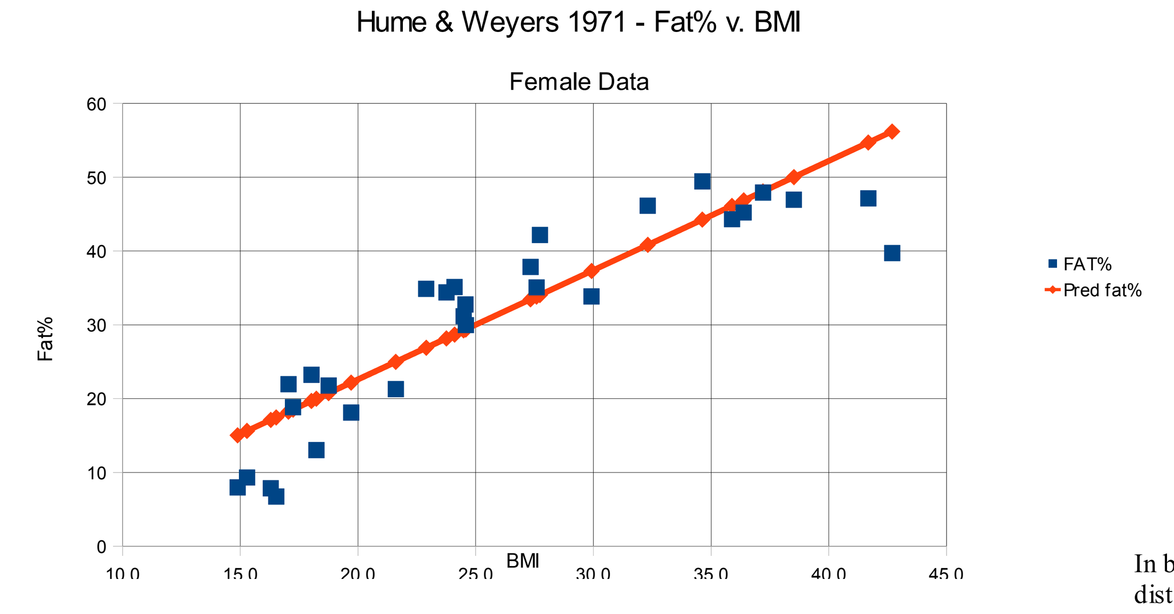
$$w/h^2 = a/(2*b) = BMI$$

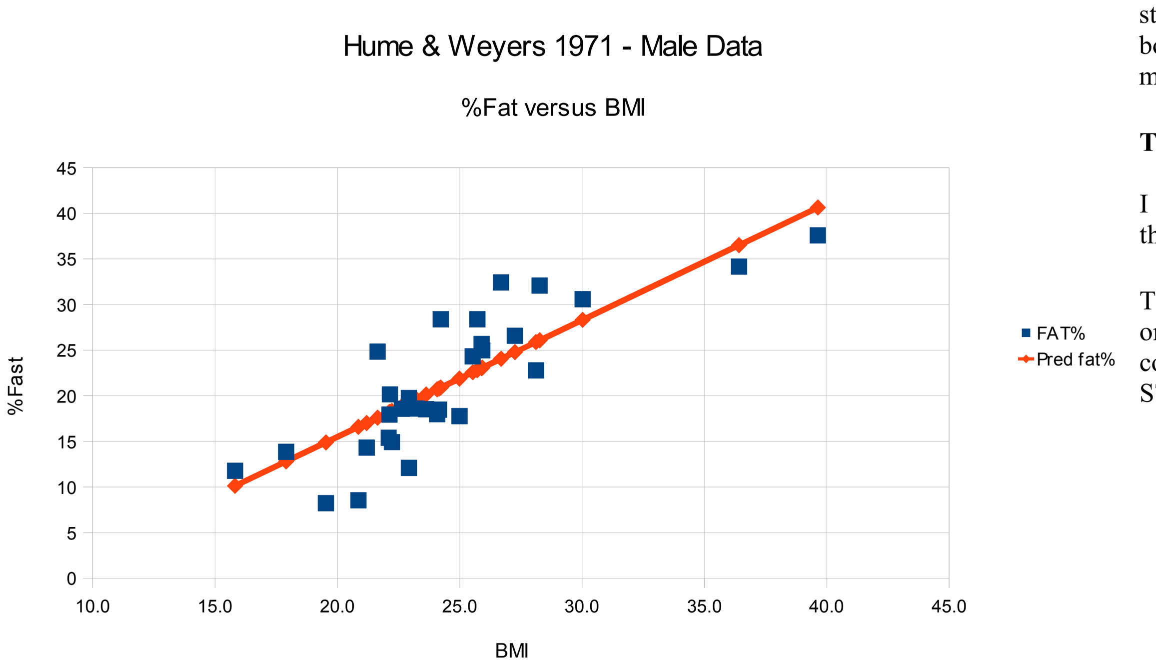
Substituting back the constants we have the maximum BMIs of 42.97kg/m² (male) and 36.15kg/m² (female). This has confirmed the assumption that the equations peak. However the original Hume and Weyers equations showed showed that for any given height, lean body mass increases with gross weight. The Hume and Weyers equations are:-

Male $LBM_m = 0.2668h + 0.4066w - 19.19$ $(r^2 = 0.908)$

Female $LBM_f = 0.4720h + 0.2518w - 48.32$ $(r^2 = 0.916)$

As can be seen both equations have good correlation. Copying the Hume & Weyers data into a spreadsheet I was able to derive lean body mass and body mass index and produced the following plots by linear regression. These are plots of Hume& Weyers data expressed as BMI and Fat%:



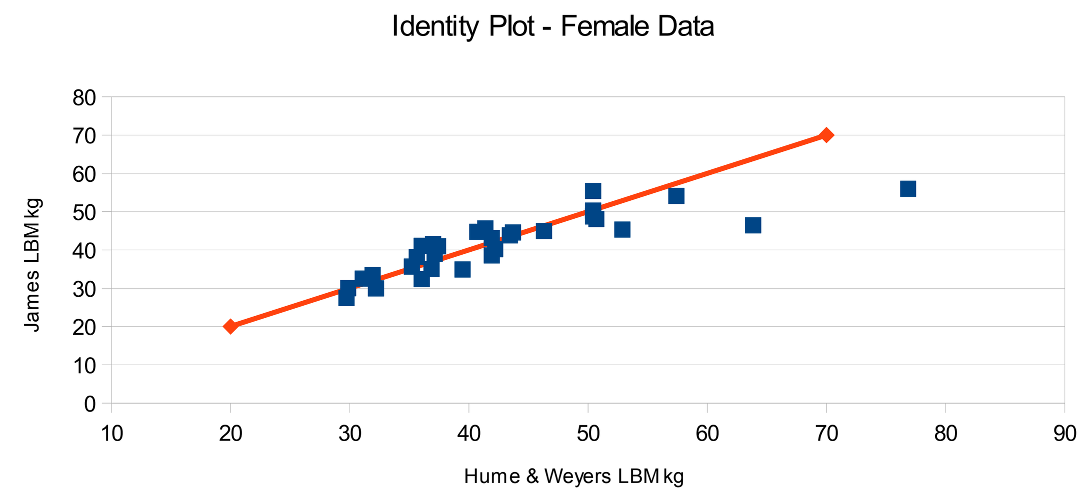


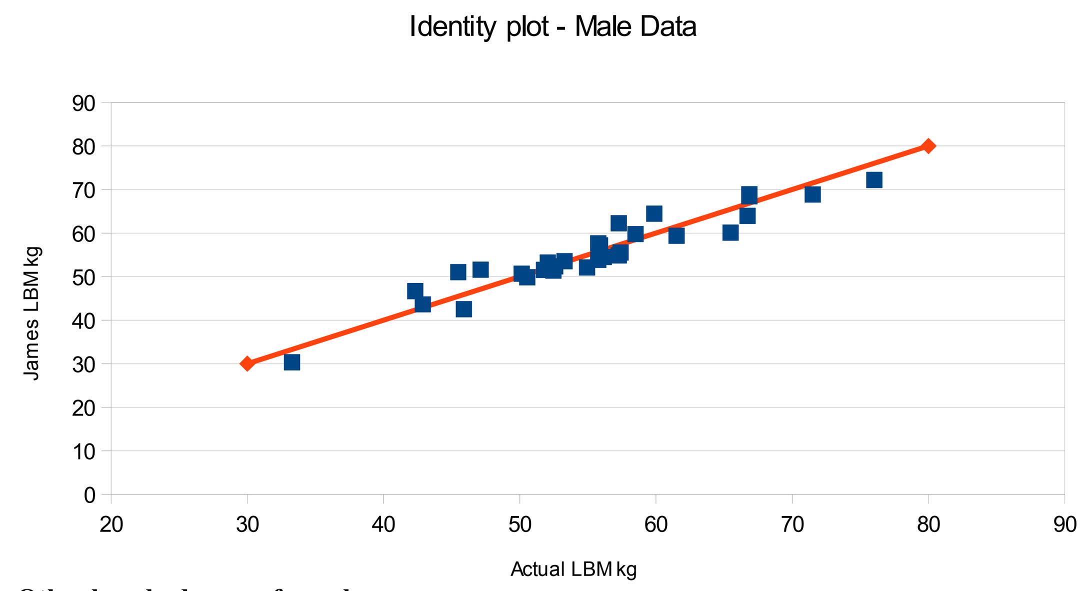
Obviously the data is not well grouped onto a straight line. The residual sum of squares using all the unsmoothed female data is 0.734 ('James' method) as opposed to 0.837. (The residual sum of squares differs from that published by Hume & Weyers and I can only presume that some form of data smoothing was used e.g. remove outliers. As such, however, the difference between the RSQs stands.)

Similarly one can plot the male data. Again the fit is poorer than the Hume & Weyers method, the residual sum of squares being 0.695 ('James' method) as opposed to 0.906.

Both plots have the appearance of a curve, not a straight line.

It is difficult to understand why the 'James' method came into regular use as there is much evidence that it is less accurate than the Hume & Weyers method. Using identity plots also shows up James' weakness, as all data should lie on a straight line, not a curve!





Other lean body mass formulae

Hume had published a previous paper in 1966[11]. This early attempt used antipyrine space and produced equations similar the the later paper but with residual sum of squares being 0.92 (male) and 0.69 (female) presuming the stated 'multiple correlation coefficient' to be the square root of the residual sum of squares.

Dual energy xray absorptiometry (DEXA) has been used by Janmahasation[10] in 2005 to produce his own formulae in an attempt to be more accurate than Hume & Weyers but in practice produced similar results. A more readable paper discussing the Janmahasation results was that of Han[12]. A notable feature of the paper was the vast number of subjects (373) and range of BMI(17 – 70). The equations are:-

Hume 1966(w kg, h cm)

Male $LBM_m = 0.3281w + 0.3393h - 29.53$ $(r^2 = 0.919)$

Female $LBM_f = 0.2957w + 0.4181h - 43.29$ $(r^2 = 0.686)$

Hume & Weyers 1971 (w kg, h cm)

Male $LBM_m = 0.2668h + 0.4066w - 19.19$ $(r^2 = 0.908)$

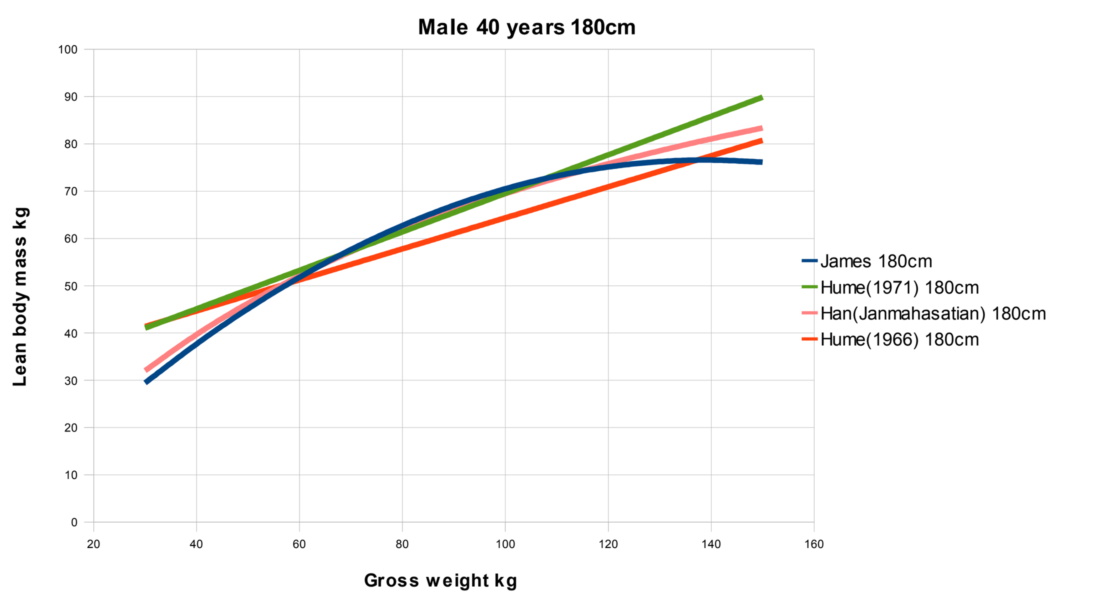
Female $LBM_f = 0.4720h + 0.2518w - 48.32$ $(r^2 = 0.916)$

Janmahasation / Han 2005 (w kg, BMI kg/m²)

Male $LBM_m = \frac{9270w}{6680 + 216*BMI}$ $(r^2 = 0.92)$

Female $LBM_f = \frac{9270w}{8780 + 244*BMI}$ $(r^2 = 0.94)$

To assess the various lean body mass equations I created a spreadsheet, summarized below:

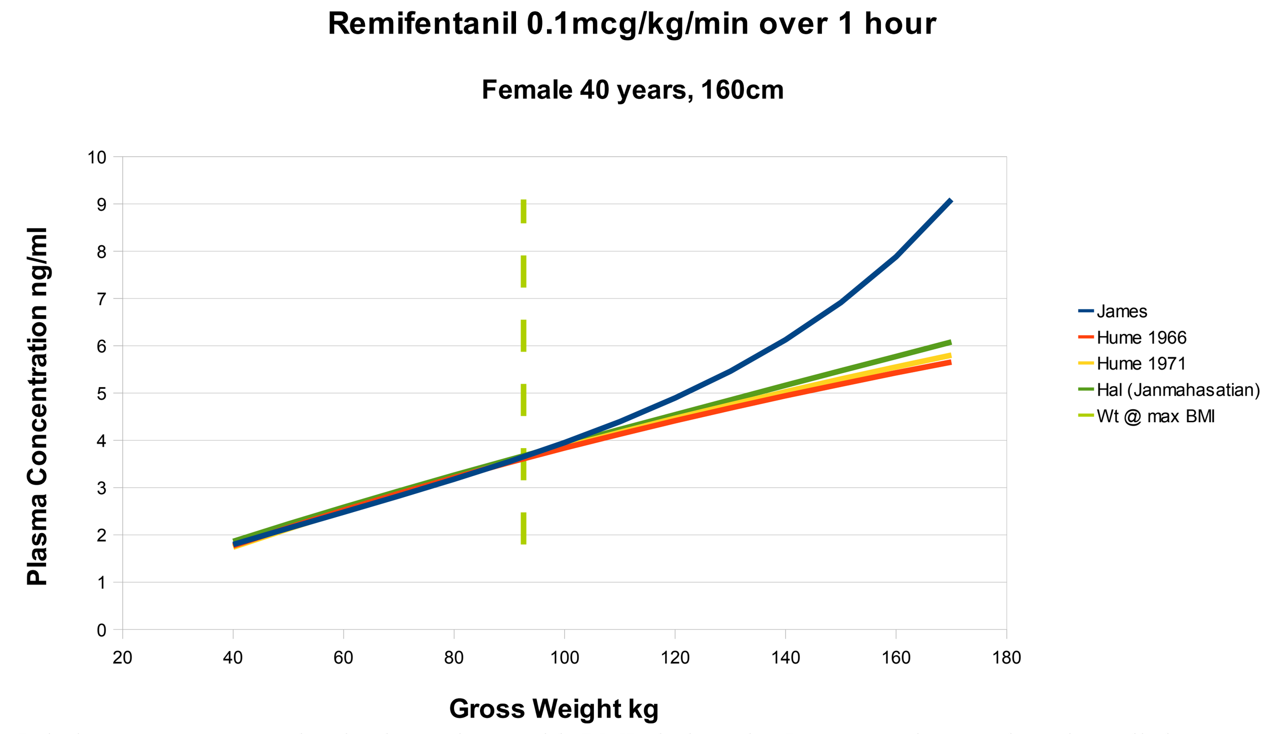


In both graphs it is obvious that both the Hume plots are straight lines and the 'James' line is distinctly curved. It is not very obvious that the Janmahasatian plot is also a curve. In females, as stated by Dordevic[13], the Janmahasatian formula, also derived from DEXA, returns lower lean body mass than Hume[11] (1966). However the Janmahasatian equations do offer similar lean body mass estimates to the Hume & Weyers[6] (1971) equations.

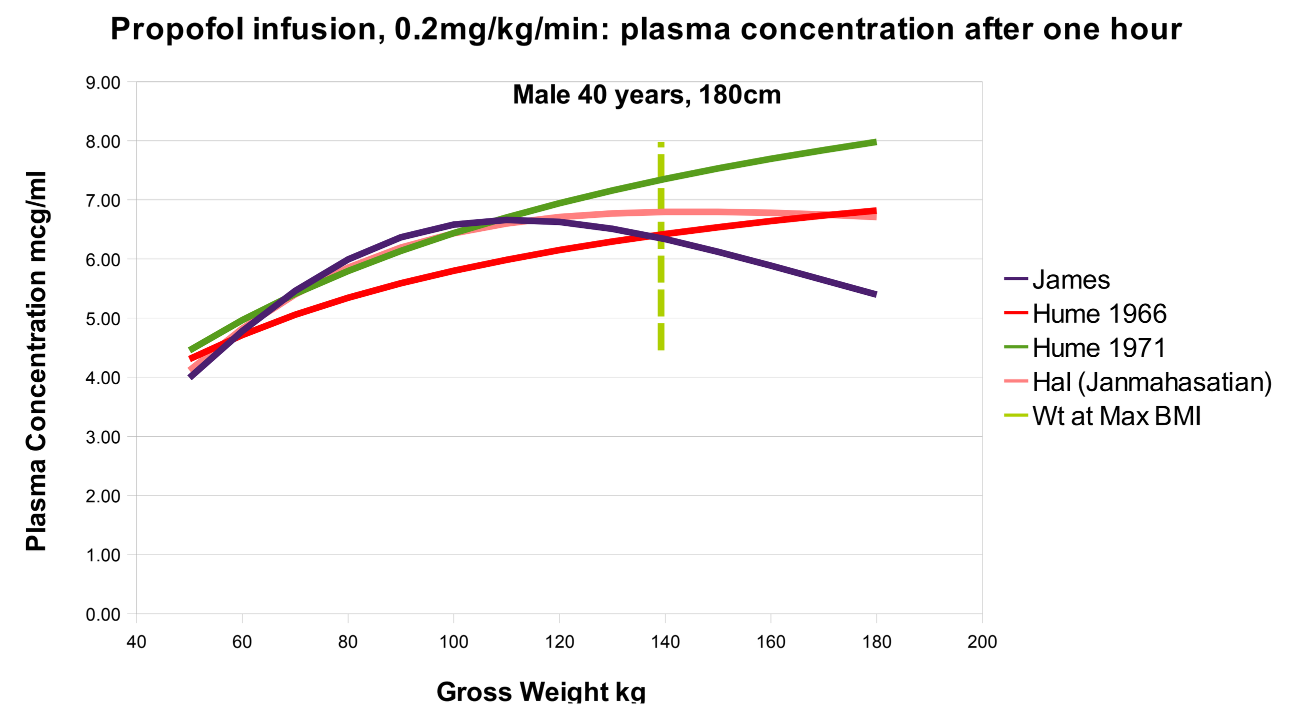
The effect of changing the lean body mass equations on propofol and remifentanil delivery.

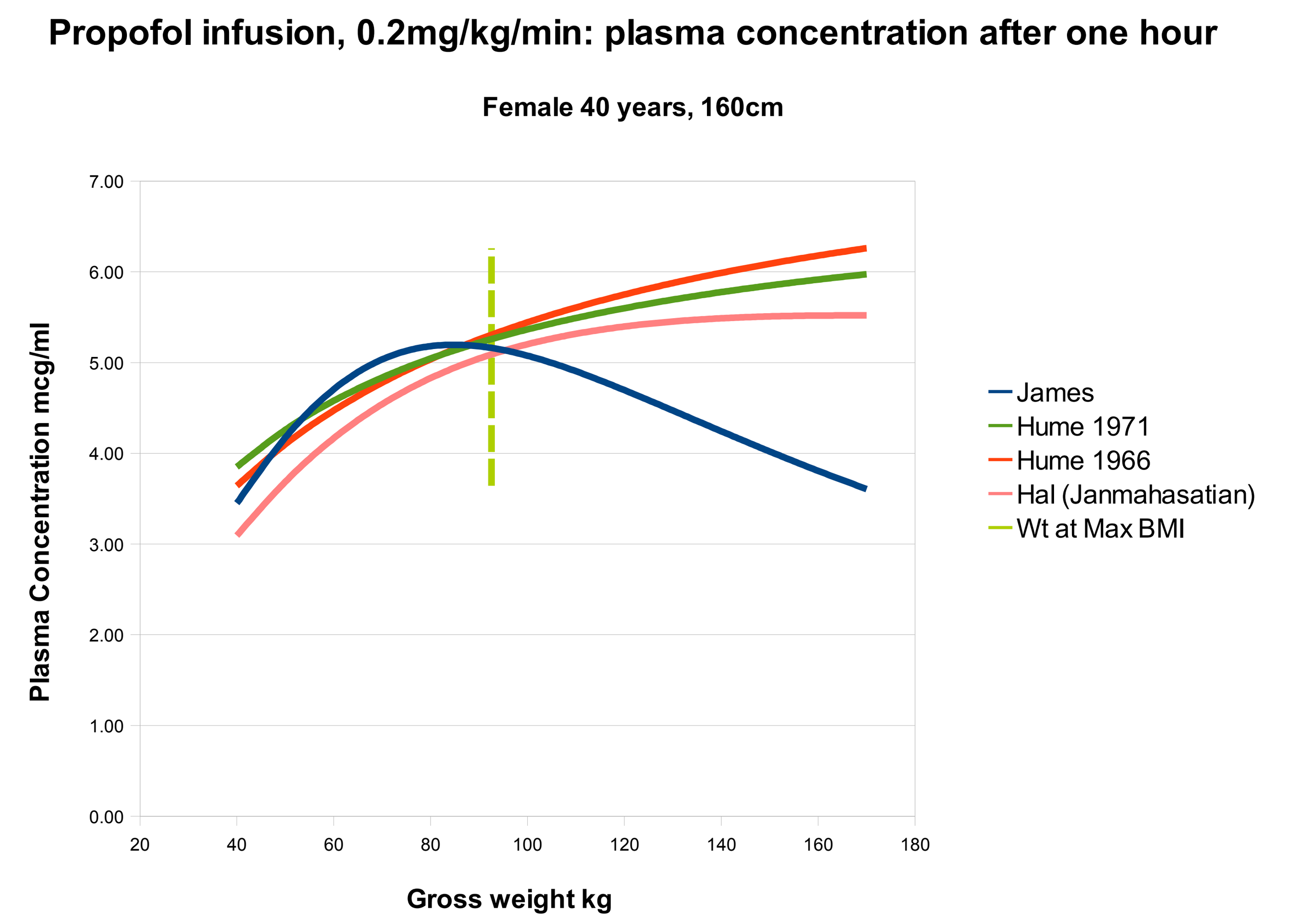
I assessed the theoretical effect of changing the lean boy mass equation in a simulator written for this purpose by myself, as I was not aware of other suitable products.

The simulator was written in Delphi for 32-bit Windows and featured extremely accurate fourth-order Runge-Kutta integration. The simulator was used in a constant infusion mode and the plasma concentration deduced after one hour. The drug models were copied from Steven Shafer's excellent STANPUMP[15] program for DOS (available from http://opentci.org/).



It is important to note that in the patients with BMIs below the James maximum, there is so little difference between the plots it is difficult to separate the lines. In these circumstances there is no practical difference between the LBM equation used. Above the James maximum, the James equations obviously overestimates the plasma concentration leading to potential underdosing. For propofol the plots are somewhat different:





For males, with the exception of the Hume 1966 equation, the plots are similar up to the James maximum. However it should be noted at this point that the predicted plasma concentration for the Janmahasatian equation 'flat-lines' and then starts to fall slightly. The female data is more consistent.

Most of us have used approximations for weight and height when patients present who have a BMI above the James maximum. The commonest approximation is to reduce the weight to the maximum allowed; a better approximation is to increase the height. However both result in overestimating the plasma (and hence effect) concentration. If patients present who are vastly over the James maximum BMI then the 'double concentration/half weight' method has been used; this results in a significant underestimate of the plasma concentration.

Conclusion

The original 'James' equation have benn found to be unfit for all but their original purpose – to illustrate a table of BMI values all in the range 20-26 kg/m². It is not suitable for estimating lean body mass in larger persons. The Hume & Weyers equations have been found to approximate the Janmahasatian equations for larger people and both should be suitable for use in target controlled anaesthesia. Therefore consideration should be given to modifying the current Schnider and Minto models to render them more usable for large people. Probably a simple substitution of the Hume & Weyers or Janmahasatian equation would suffice for Minto's remifentanil model.

The Schnider model for propofol would probably nedd to be modified and would be best achieved by a program such as NONMEM[14].

Declaration of Interest

I have received no support for this work, other than my salary as an NHS doctor!

References

1. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. Schnider TW, Minto CF, Gambus PL, Andressen C, Goodale DB, Shafer SL, Youngs EJ. Anaesthesiology 1998 May;88(5): 1170-82.
2. Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil. I. Model development. Minto CF, Schnider TW, Egan TD, Youngs E, Lemmens HJ, Gambus PL, Billard V, Hoke JF, Moore KH, Hermann DJ, Muir KT, Mandema JW, Shafer SL Anesthesiology86p10-23(1997 Jan)
3. Compiled by James W, Research into Obesity, HMSO 1976, p9. ISBN 11 450034 7.
4. http://opentci.com/doku.php?id=issues:obesity_and_lean_body_mass
5. SIVA UK Scientific meeting 2004. Delivery of Remifentanil by TCI in obese patients is influenced by the method of calculation of lean body mass. Dr Iain Glen, Knutsford
6. Relationship between total body water and surface area in normal and obese subjects. Hume R, Weyers E J Clin Pathol 24 p234-8 (1971 Apr)
7. Studies on body composition. III. The body water and combined nitrogen content in relation to fat content. Pace N, Rathbun EN. J Biol. Chem., 158, 685-691.
8. The relation of total body potassium to height, weight and age in normal adults. Boddy K, King PC, Hume R, Weyers E., J Clin. Path., 1972, 25, 512-517.
9. A comparison of the fat free mass of young adults estimated by anthropometry, body density and total body potassium content. Womersley J, Boddy K, King PC, Durnin JVGA. Clin Sci 1972; 43:469-475.
10. Quantification of lean bodyweight. Janmahasatian, S., Duffull, S.B., Ash, S., Ward, L.C., Byrne, N.M. & Green, B. Clin. Pharmacokinet. 44, 1051–1065 (2005).
11. Prediction of lean body mass from height and weight. Hume R., J Clin Path(1966), 19, 389.
12. Dosing in Obesity: A Simple Solution to a Big Problem. Han PY , Duffull SB, Kirkpatrick CMJ,Green B. Clinical Pharmacology & Therapeutics, 82 ,5, Nov2007, 505.
13. Lean Body Mass Assessment By Dual-Energy X-Ray Absorptiometry And The Method Of Hume. Dodevic D Stratrova SS. Journal of the Anthropological Society of Serbia Novi Sad, vol. 44, str. 27-32, 2009, UDK 572(05), ISSN 1820-7936
14. Non-linear mixed effects modelling. Available from http://www.iconplc.com/technology/products/nonmem/
15. STANPUMP. Available from http://opentci.com

All programs and several free downloadable papers (including this one) are available from my website: http://muirheads.co.uk/richard