PE1463/LLLL
Dr John Midgley submission of 6 March 2017

BULLET POINTS FOR DISCUSSION

These points are ordered with decreasing ease of performance (as to timescale to achieve). This ordering does not detract from the need to address each problem.

1) Reduce the extortionate cost of purchasing T3 tablets, which has been unjustifiably raised by monopoly providers in the UK. Permit patients to use natural dessicated thyroid (NDT) products if a favourable response to treatment justifies this.
2) Mandate robust calibration of all suitable assays against acceptable standards to achieve better harmonisation and comparability between assays from different manufacturers. Improve the accuracy of reporting placement within normal ranges by including a "percentage up scale" measurement in addition to actual figures. This corrects for the different ranges set by different manufacturers for the same test.
3) = Do not rely on TSH as a diagnostic tool for assessing treatments with either T4 or T4/T3 combination. Substitute with a FT3 measurement (do not measure if nonthyroidal disease present). Reduce the role of TSH to screening for hypothyroidism and noncompliance, and diagnostically to differentiate primary from secondary hypothyroidism (where the pituitary is at fault).

3) = Reduce the upper limit for TSH in such detection to lower the threshold for more complete testing and more timely treatment..

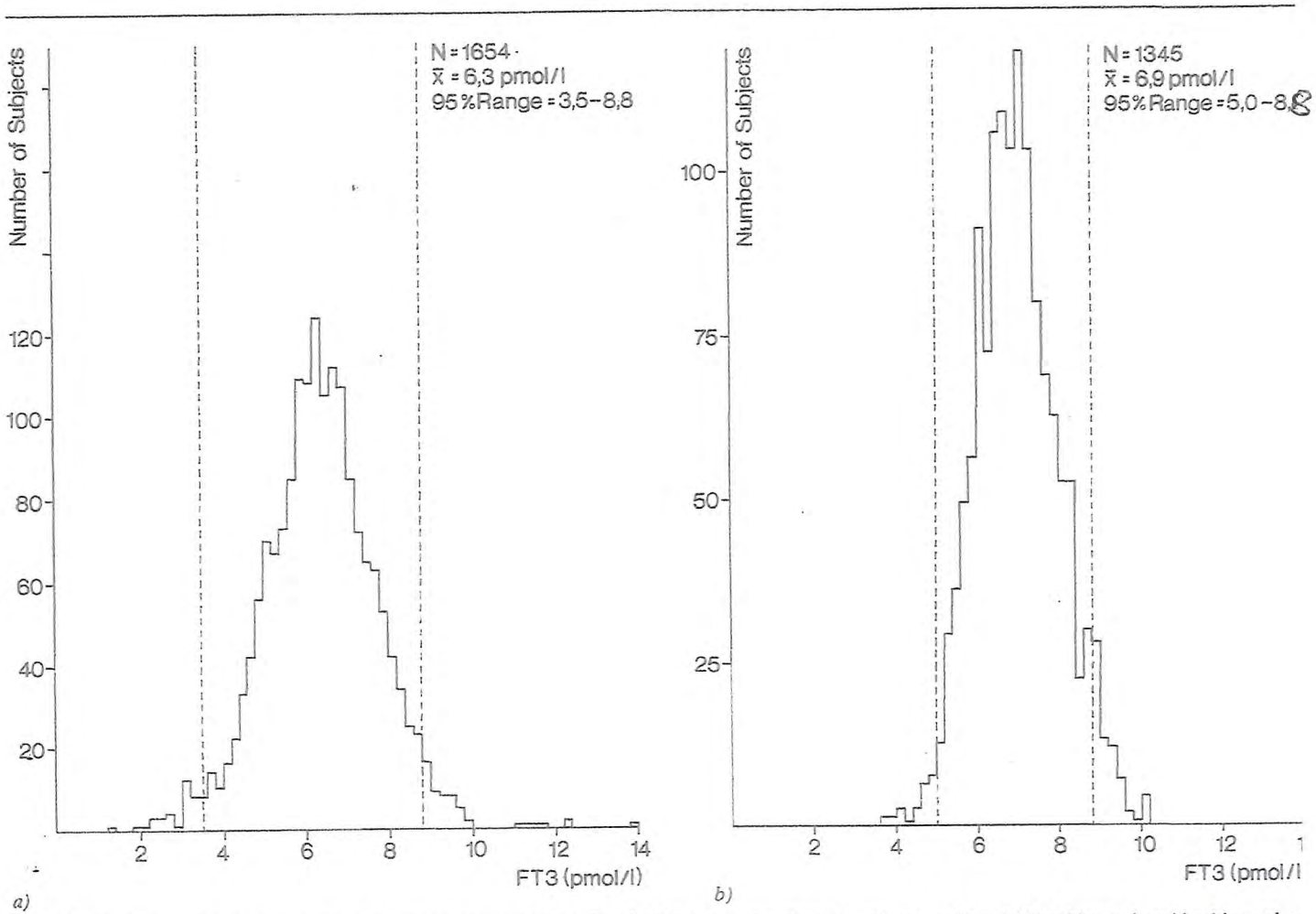
4) = Give patient presentation symptoms a much greater importance and relegate biochemical testing to a supporting rather than defining role in diagnosis. This is essential as it scientifically links the pre-test probability of dysfunction with the test outcome.

4) = Re-educate clinicians as to the meaning of the statistical approach to using the reference range in diagnosis rather than the present simplistic "goalpost" approach as to whether a patient's values are within or without the reference range. This "shoehorning" approach is mathematically and diagnostically invalid.

5) Measure FT4 and FT3 once in all healthy individuals before dysfunction occurs. Archive the results as in 2) above and use the results for guidance as a target if dysfunction occurs in future. Note: this does not necessarily apply to FT4.

6) Deriving from 5) use FT3/FT4 ratios in health, also using T4 dosage and conversion efficiency to act as a guide in assessing possible needs for T4-only therapy and T4/T3 combination in dysfunction.

7) Perform properly designed trials to determine benefits for patients of alternative T4/T3 combination therapy, likelihood of atrial fibrillation and osteoporosis, by first stratifying patients on T4-only therapy according to their FT4/FT3 ratios. The higher the ratio, the greater the likelihood of favourable responses to combination therapy and the smaller likelihood of undetectable TSH being an adverse indicator of overtreatment..



Figs. 3 a, b Distribution histograms for serum FT_3 concentrations for a) 1654 referred euthyroid subjects, and b) 1345 healthy euthyroid subjects abov 20 years old. The dotted lines in each graph refer to the 95% confidence limits of values in the respective populations. The mean FT_3 concentration fo the referred group was 6.3 ± 2.5 pmol/l (2 SD) and for the healthy group 6.9 ± 1.9 pmol/l (2 SD). Both populations were normally distributed.