A CLINICAL APPROACH TO BODY COMPOSITION IN WASTING

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INTRODUCTION

The term wasting is used by physicians as a clinical statement about loss of muscle mass and not even lean body mass in its entirety. Whatever the clinician may think, it is not possible to make, for example, an assessment about reduced liver nitrogen or protein in conjunction with protein energy malnutrition (P.E.M.) in the face of associated changes of fatty liver. Where there is sufficient evidence of wasting by inspection or by scrutiny of a weight chart, the diagnosis is often made without further confirmatory investigations. In patients with oedema or obesity the wasting is less overt and the need for further assessment arises.

Clinicians are interested in a precise, non-invasive anatomical definition of body composition. The combination of this need with that for a clinical assessment of nutritional status and metabolic state has become a challenge for technologists and, in particular, physicists. The opportunity to directly measure body composition has encouraged the clinician to ask for measures of nutrient intactness and distribution, in addition to anatomical and metabolic parameters of body composition.

As far as human nutrition is concerned, with body composition studies we are just beginning to move beyond the state we were at earlier this century with proximate food analysis for macronutrients, with little ability to measure micronutrients, let alone trace elements. Other than in a few centres, body composition studies have been limited to research projects. The development of hospital-based laboratories has enabled body composition measurements to be an integral part of a clinical assessment. Facilities such as our own (Stroud et al., this volume) have been established at relatively low cost and make routine studies more feasible. To be of practical value to the treating physician, results need to be reproducible and valid, even in the presence of oedema, obesity or osteoporosis. It is particularly in these clinical settings that indirect studies have failed to measure body compartments accurately in the wasted patient. This should not be a surprise, as many of the basic assumptions used are for "the reference man" and are not applicable to malnourished patients, or to the sick in general.

Recognition of the value of simultaneous assessments of body composition is seen with new developments such as the Dual-energy X-ray Absorptiometer (DEXA) (Rigg, 1988) which measures bone mineral density as well as directly measuring the percentage body fat. Although validation

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studies with In Vivo Neutron Activation Analysis (IVNAA) or other techniques are not available, DEXA is a modality which may be of great clinical benefit.

The economical practice of clinical medicine must consider cost, time, and space, as well as convenience. There is a need for inexpensive, portable instruments which are more accessible to the population most at risk. These populations are those in developing countries, as well as the underprivileged in our own societies.

Table 1. Types of Wasting

A. WASTING ALONE

Primary Malnutrition

- developing countries with limited food supply
- general community in developed countries (educationally and socioeconomically disadvantaged)
- eating disorders
- hospital or institutional settings

Chronic Wasting Disease

- Cardiac failure
- Infectious disease
- Liver failure
- Malabsorption
- Malignancy
- Neurological disorders
- Obstructive lung disease
- Renal failure

B. WASTING ASSOCIATED WITH OBESITY	As for Wasting Alone
C. WASTING ASSOCIATED WITH OEDEMA	As for Wasting Alone
D. WASTING ASSOCIATED WITH OSTEOPOROSIS	As for Wasting Alone

WASTING TYPES

Wasting is a consequence of protein-energy malnutrition (P.E.M.) when the body's need for protein and energy fuels or both cannot be satisfied by diet. Wasting can occur on its own, as in primary malnutrition where there is inadequate food intake, but wasting is also seen in chronic disease (Table 1). When wasting is seen in association with either obesity, oedema or osteoporosis it also occurs in the setting of either primary malnutrition or with chronic wasting diseases.

Primary Malnutrition

The extent of P.E.M. related to inadequate intake is illustrated by the World Health Organization's estimate of 300 million children worldwide with growth retardation related to malnutrition (WHO, Document WHA 36/1983/7). The emphasis has recently begun to shift from childhood to adult life with the recognition of an increasingly aging population in developing countries. It has been estimated that the number of people aged over 65 in developing countries will climb dramatically from 129 million in 1980 to well over 220 million by the year 2000. This is a far greater increment than the 167 million projected for developed countries, where in 1980 there were also 129 million elderly people (Andrews et al., 1986). With this rate of elderly population growth, the prevalence of chronic disease and wasting is likely to escalate and the need will arise for more sensitive low-cost technology to detect milder degrees of malnutrition.

In industrialized societies primary malnutrition is also seen, especially in the aged, the institutionalized and the underprivileged, who are at particular risk of inadequate food intake. Even in a hospital setting, wasting due to primary malnutrition occurs, for example in post-operative patients, unable to return to their usual dietary intake. Studies using body composition techniques are attempting to relate surgical risk to pre-operative nutritional status and weight loss (Windsor and Hill, 1988).

Table 2. Changes in Weight, Body Composition after 1 Year of Intervention

	Exercisers (n-47)	Dieters (n=42)	Controls (n-42)
Total wt (kg)	-4.0*	-7.2*	0.6
Non-fat body mass (kg)	0.1	-1.3*	0.8
Fat body mass (kg)	-4.1*	-5.9*	-0.3

* p<0.001 vs controls. Data from Wood et al, 1988

Chronic Wasting Disease

The wasting associated with chronic disease cannot be attributed solely to lack of adequate intake, as in primary malnutrition (Table 1). Cardiac cachexia is a term used to describe end-stage cardiac failure where although food intake may be reduced due to breathlessness, many other factors contribute to the severe wasting seen. In patients with cancer, factors such as tumor necrosis factor (TNF) and cachectin have been implicated in the wasting. TNF possibly plays a significant role in the pathogenesis of alcoholic liver disease (McClain and Cohen, 1989) and may account for some of the wasting seen. Lean body mass as calculated from total body nitrogen (IVNAA) was reduced in 13 patients with chronic obstructive pulmonary disease who were all underweight. The Nitrogen Index in each patient was calculated before dietary supplementation. This index is the measured nitrogen divided by the predicted nitrogen, as calculated by the following equation:

$$\text{Predicted Nitrogen} = \text{Constant} \times \text{HAS}^{2.6}$$

where the constant=0.42 for women and 0.50 for men. HAS is the mean of height and armspan in meters (Harrison et al., 1984). In these 13 patients the Nitrogen Index ranged from 0.4-0.7 compared with the normal range of 0.8-1.2. In addition to the reduction in fat mass seen by anthropometric techniques, a reduction in body protein, was able to be demonstrated.

Reduction in lean body mass and, therefore, muscle mass, will diminish the patient's functional capacity. Nutritional supplementation may increase lean body mass and aid diaphragmatic and respiratory muscle function, although in a recent study this was disputed. Otte et al.(1989) showed a weight gain in patients given nutritional supplementation. However, they did not show a significant improvement in other indices of well-being. This study did not have the benefit of direct body compositional measures for lean body mass and relied upon anthropometry to document changes in body protein. More direct methods of measuring total body protein such as I.V.N.A.A. are needed to determine whether weight changes are related to increased body protein, water or fat.

The changes in body composition in chronic disease are often complicated by the underlying pathology. A common example in industrialized societies is the vasculopath with risk factors like smoking. The vascular disease, which may be calcific, is associated with outcomes of immobility due to ischemic heart disease or to peripheral vascular disease. Cardiac decompensation and deformity related to stroke are additional factors which, because of their effect on body water, protein or fat, need consideration.

Table 3. The Wellcome Classification

Weight (percentage and standard*)	Oedema	
	Present	Absent
80-60	Kwashiorkor	Underweight
< 60	Marasmic kwashiorkor	Marasmus

* Standard - fiftieth centile Boston value

In Association with Obesity

Although it seems a contradiction in terms, wasting can occur in obese patients. First, although muscle mass and bone mass are usually increased in association with obesity, they can be too low for the level of obesity. Second, account needs to be taken of compartment changes other than fat, such as in muscle and bone. Third, sick obese patients are at greater risk than their less obese counterparts through underrecognition of reduced body protein, and cardiac decompensation with fluid overload. Garrow et al. (1988) recently reported an increased risk of post-operative morbidity in obese patients which was due to the occurrence of wound infection. This complication may be related to reduced non-fat mass in the obese patients and not simply to mechanical factors.

Wood et al (1988) assessed the loss of non-fat body mass in overweight men randomized to diet, exercise or to a control group (Table 2). Dieters lost approximately 1.3 kg of non fat-body mass, in addition to losing approximately 5.9 kg of fat body mass. Patients who exercised did not significantly alter their non-fat body mass despite a reduction in fat body mass.

In Association with Oedema

Alleyne et al. (1977) adopted the Wellcome classification (1970) in their book Protein-Energy Malnutrition. This classification divides

P.E.M. into four categories, based on the presence or absence of oedema and describes three clinical types of severe malnutrition - kwashiorkor, marasmus, and marasmic kwashiorkor. The recognition of lesser degrees or earlier accumulation of excess tissue fluid would be of great clinical value and would increase the understanding of the different types of P.E.M. The Wellcome classification (Table 3) is also based on body weight deficit and while using it as a simplistic classification, Alleyne et al acknowledged the inherent difficulties. Oedema may be associated with cardiac, renal, or liver disease and its presence may maintain the body weight at a normal level despite severe wasting. Thus, the diagnosis of malnutrition may not be suspected. Body composition studies with considerations of total body water and lean body mass as separate, measurable compartments allow for earlier recognition and classification.

In Association with Osteoporosis

Anorexia nervosa is one situation where loss of lean body mass is found with osteoporosis (see discussion of body composition in patient J.B. below). The Diagnostic and Statistical Manual (DSM-111) Criteria for Eating Disorders (APA, 1987) included loss of more than 25% of original body weight as a prerequisite for the diagnosis of Anorexia Nervosa. This diagnosis has been revised (DSM-111-R) (1987) and is now worded as "...weight loss leading to maintenance of body weight 15% below that expected." Neither description includes the loss of lean body mass or bone density or fluctuations in body water which may obscure the diagnosis.

Table 4. Limitations of Body Mass Index (B.M.I.)

- Presumes sedentary western life-style
- Presumes frame size
- Does not allow for effects of aging on bone density and height
- Makes no allowance for fat distribution
- Presumes normal body water

MEASUREMENT OF WASTING DISORDERS

One of the most basic anthropometric measures is that of body weight and the calculation of the Body Mass Index [wt(kg)/ht^2(m)] as described by Quetelet (1969) provides a reasonable guide to the contribution of fat to body composition in healthy subjects. But there are many circumstances in which these measurements cannot adequately assess body fatness (Table 4).

The most crucial of these is where the fluid balance is deranged, as occurs in cardiac failure as well as in renal and liver disease. In these patients, even assessment of skinfold thickness is hindered by subcutaneous oedema. Morbid obesity also poses large technical problems with skinfolds too large for precise measurement. Osteoporosis, while not necessarily associated with a reduction in lean body mass or body fatness, may reduce body weight and so factitiously reduce B.M.I. Unfortunately, few patients fit the "normal man" who is usually young, healthy, male and weighs 70kg. Amputees (whose missing limb will alter their weight without necessarily changing the measured height) and patients with collapsed vertebrae from osteoporosis are two such examples. Where more precision than can be expected from anthropometric measures is needed, further body composition studies are required.

Lukaski (1987) recently reviewed the available methods of assessing human body composition. In grading the precision of the various techniques at measuring non-fat mass and fat mass, he addresses the question of "...which existing method best meets the objectives of the proposed research". IVNAA was the only method to achieve a similar degree of precision as densitometry (underwater weighing). Coward et al. (1988) considered IVNAA to be "...the most significant development..." so far. By incorporating Burkinshaw's idea (Burkinshaw, 1985) of measuring multiple components of body mass and then deriving estimates of unmeasured components, IVNAA can give useful clinical information. In patients with wasting, however, many of the assumptions break down and more direct methods of measuring total body water and body fat are needed.

Table 5. Compartment Disorders of Interest in Wasting

1. Lean Body Mass
   - Metabolic mass - energy expenditure and requirement
   - Cellular function - eg. cardiac mechanics, skeletal muscle function

2. Fat
   - Energy stores
   - Drug distribution

3. Water
   - Water overload or reduction
   - Distribution of nutrients and drugs

4. Bone
   - Bone strength

CLINICAL INDICATIONS FOR BODY COMPOSITION STUDIES IN WASTING

Indications for body composition studies in wasting include the assessment of many complex chronic diseases where it is not sufficient to monitor only one component or a compartment in isolation. Wasting is rarely limited to the lean body mass and measures of body fat and bone mineral density are needed for completeness. Adequate documentation of the extent of the wasting gives a clear picture of the severity of the disease and, with sequential studies, the rapidity of progress of the disease can be assessed.

The compartments of interest vary with individual diseases (Table 5). Lean body mass may be important as a measure of metabolic mass when attempting to find the cause for wasting. Body composition studies allow earlier recognition of disorders such as the wasting that can occur in obese people or low-energy diets.

Any change in body composition, either reduction in lean body mass or increases in total body water will alter drug distribution. These changes can occur during growth spurts as in childhood and adolescence, as part of a disease process such as congestive cardiac failure or during normal aging. Steen (1988) showed that the most important cause of a decrease in body weight during the eighth decade of life is a reduced amount of extracellular water; this is considered to be part of normal

Table 6. Body Composition on a 24-year Old Man (D.C.) with Chronic Renal Failure and Chronic Pancreatitis - Before and After Pancreatic Enzyme Replacement

	Sept 88	May 89	Healthy range (if 1.62 m tall)
Weight (kg)	42.1	44.9	53-66
Height (m)	1.62	1.62	
BMI	16	17.1	20-25
IVNAA			
Total Body Protein (kg)	4.26	5.9	
Nitrogen Index	0.37	0.5	0.8-1.2
Impedance			
Total Body Water (%)	66(28L)	64(29L)	64-70(33-46L)
Lean Mass (%)	78(33kg)	78(35kg)	75-85(40-56kg)
Fat Mass (%)	22(9kg)	22(10kg)	15-25(8-16.5kg)

aging. However, any change in body water whether due to aging or to illness can drastically alter the volume of distribution of a drug and drug dosages need to be adjusted accordingly. Until a precise measure is readily available, dosages will be assessed with a large amount of guesswork (Gilman et al., 1985).

Clinical Examples of Wasting

The following two patients, one with chronic renal failure (D.C.) and one with anorexia (J.B.) highlight some of the complexities of studies in chronic diseases associated with wasting.

Patient D.C. is a 24-year old man with the problems of chronic renal failure due to focal glomerulosclerosis, chronic pancreatitis, poor pubertal development, fluid and electrolyte disturbances, and renal bone disease. IVNAA showed a reduced total body protein (Table 6) in September 1988. His malabsorption secondary to chronic pancreatitis was then treated with pancreatic enzyme replacement. The Nitrogen Index (usually between 0.8 and 1.2) increased from 0.37 to 0.50 after eight months treatment. Impedance measurements showed a gain in total body water of 1 litre, in lean body mass of 2 kilogram, and in fat mass of one kilogram. During this time his weight increased from 42.1 kg to 44.9 kg. In patients with end-stage renal failure who depend on either hemo- or peritoneal dialysis, weight changes are usually attributed to fluid retention. In this situation, it was invaluable to document an increased lean body mass and, hence, prevent attempts to reduce his weight to the "normal" level.

Patient J.B. is a 32-year old woman who has had anorexia nervosa with amenorrhoea for 15 years. In this eating disorder, a reduction in lean body mass and total body water as well as in bone mineral contribute to the large weight loss often seen. Osteoporosis is a particular threat in view of the poor dietary intake of calcium and protein together with the associated amenorrhoea and oestrogen deficiency state.

The patient J.B. had body composition studies using IVNAA, Bioelectrical Impedance, and DEXA (Table 7).

Table 7. Body Composition Studies in a 32-year Old Woman (J.B.) with Anorexia Nervosa

	June 89	Healthy range (if 1.57 m tall)
Weight (kg)	34.5	50-61.5
Height (m)	1.57	
B.M.I.	14.0	20-25
IVNAA		
Total Body Protein (kg)	4.65	
Nitrogen Index	0.55	0.8-1.2
Impedance		
Total Body Water (%)	70(24L)	55-60(27-37L)
Lean Mass (%)	85(29kg)	70-80(35-49kg)
Fat Mass (%)	15(5kg)	20-30(10-18kg)
DEXA - Total Body		
Bone mineral content (kg)	1.1386	
Bone mineral density (g/cm^2)	0.467	0.8-1.49/sq cm
Soft tissue mass (kg)	33.29	
Lean mass (kg)	29.2	
Fat content (%)	12.5(4.1kg)	20-30

Her body fat is reduced to 12.5% (by DEXA) which is below the healthy range of 20-30% for women. In addition, her Total Body Protein and calculated Nitrogen Index are far below that expected for her age and height. If her lean body mass (LBM) is estimated using the equation quoted by Forbes (1987):

$$\text{LBM (kg)} = \frac{\text{total N (g)}}{33}$$

an estimate of 22.54 kg is arrived at. This value is well below that measured with impedance and DEXA, and reflects the difficulties in using assumptions to derive unmeasured compartments. This raises yet again the question of which method should be used and also which constant is appropriate for a given clinical situation.

The reduced bone density does, however, place her at increased risk of fractures: indeed, she has already suffered two fractured ribs from minimal trauma. Longitudinal studies on this patient are needed to assess the rapidity of bone mineral loss and any possible improvement with therapy.

FUTURE DIRECTIONS

Hill and Beddoe (1988) quoted Beneke, 1878 "Nothing is measured with greater error than the human body". This is no longer true. In 1989, we have seen the advent of new technology such as Magnetic Resonance Spectroscopy (Chance and Veech, 1988), IVNAA and DEXA, together with total body water and potassium measures. Today, the ability to make simultaneous measurements of body composition is critical and is the way to the future. DEXA is a technique that allows several measures to be taken; however, the technique must be validated.

The possibility of measuring individual nutrients such as magnesium, zinc, essential fatty acids (Moonen et al., 1988), vitamins, or even total body cholesterol becomes more realistic as the technology improves. The accurate, direct measures of body compositional variables currently available make body composition studies a more integral part of contemporary metabolic medicine. Ultimately, by the introduction of low cost, portable units, the technology will become more and more a part of everyday clinical and public health practice.

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