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Letter to the Editor

Body Surface Area Misconceptions[1]

Thomas H. Slone[2]

1. MEASUREMENT OF BODY SURFACE AREA

Attempts at measurement of body surface area have been fraught with difficulty, and consequently have necessitated the making of gross assumptions. Despite the possible importance of surface area measurement to understanding clinical medicine and risk analysis, little progress has been made since the original attempts at measurement between 1879 and 1916.

Three methods have been used for surface area measurement: coating, surface integration, and triangulation. These methods are described in detail by Boyd.[1] Briefly, they are accomplished as follows: Coating involves making a cast of a subject, then flattening out the cast and measuring it. Surface integration involves using an instrument that takes linear measurements, such as a planimeter, and tracing it along the body so as to measure the body in nearly rectangular strips. The triangulation method is analogous to surface integration, but is accomplished by marking the body off into regular geometric segments, primarily triangles, and then measuring the segments. All three of these methods produce similar results.[1]

Because no significant modifications to these methods have been made since the early part of this century, all attempts at measurement have ignored the microscopic features of the skin which were not well known until scanning electron microscope (SEM) technology became widely used in the 1960s. Hence, the similar results reported by Boyd[1] are for methods which measure gross features only.

Mandelbrot[2] and others have shown that Euclidian (i.e., whole-numbered) dimensions are not always applicable to the physical world, and that intermediate (i.e., fractal) dimensions may be applicable. Though the concept of fractal geometry is not new, Mandelbrot[2] was responsible for naming it, synthesizing it from its numerous guises, and bringing it into general scientific recognition. Fractal geometry is a method for systematically measuring physical manifestations that are not easily measured with Euclidian geometry. The classic example that shows the need for fractal geometry is the measurement of the coast of Britain. The length of a coast is classically presumed to be a one-dimensional measurement, but consulting encyclopedias for the length of the coast of Britain gives many answers. The explanation for these different answers is that the coast is actually highly erratic and the length is related to the size of the "ruler" that is used to measure it: the smaller the ruler, the longer the length. This is symptomatic of fractal objects; if one could use an infinitesimally small ruler, one would measure the length of the coast of Britain as infinite. Hence, in Euclidian terms, coastal length is not a sensible concept. Fractal geometry solves this problem by assigning not a length to the coast, but a dimension, one that is intermediate between dimensions 1 (length) and 2 (area). The dimension is typically estimated by comparing the relationship between ruler size and measured size.

For a physiological example, Mandelbrot[2] and Goldberger and West[3] have shown that the lung is of a fractal dimension, and for good reason:

> From a functional viewpoint, the fractal geometry of the lungs may provide an optimal solution to the problem of maximizing surface area for diffusion of oxygen and carbon dioxide. Gas exchange in the lungs over this broad surface area is mediated by the interleaving of three fractal networks: pulmonary arterial, pulmonary venous, and bronchial alveolar. Fractal structure, in essence, provides a mechanism for converting a *volume* of dimension three (blood in large vascular tubes and air in the upper respiratory tract) into something approaching an alveolar-capillary surface *area* of dimension two, thereby facilitating gas exchange.[3]

Is the skin a fractal dimension? Goldberger *et al.*[4] have suggested that many organs appear to be fractal, including: blood vessels, intestines, and nerves. Gold-

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[2] Mail Stop: Barker Hall, 1 Cyclotron Road, Lawrence Berkeley Laboratory, Berkeley, California 94720.

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smith[5] has suggested that skin lesions may be a fractal dimension. Three criteria are commonly used to determine anatomical fractals: heterogeneity, multiple hierarchies, and self-similarity. An example of multiple hierarchies can be seen in a fern leaf: the first level is the entire leaf, the second level is the first level of branching within the leaf, the third level is the second level of branching, etc. Self-similarity can also be seen in a fern leaf: the appearance of any given branch of a fern leaf bears a strong resemblance to the entire leaf itself.

By examining SEM photography of the skin (e.g., Ref. 6), one can address these three criteria. Clearly the skin's surface is heterogenous; it consists of numerous desquamating scales, sweat pores, follicular orifices, and follicles with hairs. At least three hierarchies exist: flat or wavy (macroscopic), squamous (microscopic), and cellular. The skin, however, lacks any obvious self-similarity among these hierarchies.

The lack of self-similarity, coupled with heterogeneity, makes it difficult to calculate an accurate fractal dimension for the skin by analyzing SEM photographs. One would obtain different values depending on whether one is examining nearly flat nonfollicular areas or the three-dimensional follicles. Since much of the surface of the skin is obscured by secretions and foreign matter (e.g., sebum, yeasts, and bacteria), the analysis is further complicated. However, in defense of the possibility that the skin may be of a fractal dimension, it is worth noting that like the lung, the skin performs a function of converting volume into area; the efficient cooling of the human body is achieved, in part, by the dispersion of sweat over the squamous surface of the skin for evaporation.

Regardless of whether the skin is fractal, SEM photographs make it clear that early researchers were greatly underestimating the actual surface area of the skin. Much of the underestimation is due to the contribution of pores and follicles. Therefore, it is reasonable to assume that since other animals have a different distribution of pores and follicles than humans, they would have a substantially different relationship of surface area to other body measurements compared to humans. For example, eccrine sweat glands "are most numerous and best developed in higher primates. [I]n other mammals they are found only on a thickened epidermis in areas subject to wear."[7] Similarly, there is substantial variation in hairs and hair follicles among mammals.[7]

2. EXTRAPOLATION OF BODY SURFACE AREA

Meeh,[8] Rubner,[9] and Du Bois and Du Bois[10] are the papers principally cited among recent researchers for original measurement of body surface area. The uses of body surface area measurements have been in three areas: theoretical biology,[11,12] medical toxicology (e.g., Refs. 13 and 14), and regulatory toxicology (e.g., Refs. 15–23).

The U.S. EPA[15] in introducing regulations of chemical exposures in water, relied on Mantel and Schneiderman[16] for deriving the formula:

$$\text{Surface area} = \text{Constant} \times \text{Weight}^{2/3}$$

This relationship was initially proposed by Meeh,[8] but subsequently rejected by Du Bois and Du Bois[10] and by Boyd[1] for not taking height into account. The exponent in this formula has theoretical justification under Euclidian dimensions (which is not necessarily the case because the skin may be fractal) when density is 1.

Surface area has been used as an explanation for quantitative interspecies differences in carcinogenicity from rodents to humans.[15–17] The assumption made is that for a given chemical, the dose is proportional to the surface area in the two species, where surface area is derived from body weight as in the formula above. However a ¾ exponent best fits the data for interspecies toxicity data according to Travis and White.[18] Watanabe *et al.*[20] found that both ⅔ and ¾ fit the data for interspecies scaling. Travis and Morris[21] countered that numerous interspecies allometric measurements are related by ¾ power and hence given a choice of ⅔ and ¾ for interspecies carcinogenicity extrapolation, ¾ has supporting biological evidence. Davidson *et al.*[23] recognized, however, that ⅔ or ¾ have no inherent validity as exponents, primarily because of the many variables involved in extrapolation between species.

More recently, in an attempt to create consistency between regulatory branches of the U.S. government, the EPA[19] has proposed that all relevant regulatory bodies use ¾ as a scaling factor for regulation of carcinogens. The proposal to accept ¾ in place of the earlier ⅔[15] is based on closer agreement with empirical toxicity data,[18] and metabolic measurements. Due to the inadequacy of the data, the EPA[19] is careful to point out that the proposal to accept ¾ does not rule out the possible correctness of ⅔ or of some other value.

3. CONCLUSION

Proposals for interspecies extrapolation formulas that rely on surface area make two assumptions: that surface area is relevant, and that surface area has been measured accurately and correctly. There is insufficient evidence that surface area has ever been measured accurately; the methods have not taken into account the possibility that the skin is of fractal dimension nor have they measured microscopic features of the skin that account for a substantial part of the surface area. Thus, the justification for relying on surface area for interspecies extrapolation is weak and surface area has not been well measured. Therefore, it would be best to rely on empirical evidence (toxicity and/or metabolic measurements) which is not dependent upon surface area.

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