

discussion of a systematic approach to disease nomenclature that incorporates the clinical or phenotypic diagnosis and the relevant etiologic factors, be they genetic or environmental. In the editorial, J.M. Friedman² suggests that the ACMG might develop an appropriate system.

In 1991, at the 8th ICHG meeting in Washington, I first proposed the use of a multi-axial diagnostic system (MADS) in clinical genetics³ similar to the DSM-III-R system used in psychiatry. I thought this was important as the clinical diagnoses, and even the ICD codes, were a mixture of etiologic, pathogenetic mechanisms and phenotypic diagnoses. For simplicity, only four major categorical axes (I, Phenotypic; II, Pathogenetic; III, Etiologic, and IV, Differential Diagnoses) were defined. The major advantages of such a system included improved diagnostic accuracy; greater reliability and homogeneity of the diagnostic categories, enhancing the comparison of diagnoses and achievements between different centers, states, regions, or countries; more comprehensive and specific definitions for controversial terms such as “syndrome” or “spectrum”; and its use for educating health professionals.

I recognized that the system would need periodic revisions to keep it consistent and conceptually accurate, in accordance with advances in genetics. A basic description was published in 1994⁴ after its presentation at the International Birth Defects Meeting organized by Bartsocas in Greece. In that meeting we pointed out how it could easily be updated in the future in accordance with the new molecular or biochemical information. Further updates were presented at the subsequent ICHG meetings in Brazil (1996) and recently in Austria (2001). In Vienna I stressed its usefulness for increasing the percentage of etiologic diagnoses established.⁵ In several other publications^{6–9} I have mentioned or further described this system. Therefore, after more than 12 years of using it, I couldn't be more in agreement with Robin and Biesecker and Friedman regarding the importance of using this kind of system in clinical genetics.

The principal goal of a clinical geneticist is to establish not only the phenotype and pathogenetic mechanism, if known, but to determine the etiologic diagnosis, which is the cornerstone for genetic counseling. This is Axis III in our MADS. In this axis we consider not only the classical Mendelian, chromosomal, polygenic/multifactorial, and environmental (teratogens) etiologies, but also the new, nontraditional etiologies or mechanisms that have been described in the past 10 to 20 years (contiguous gene syndromes or microdeletions, mitochondrial mutations, uniparental disomy, mosaicism, triple repeat expansions, etc.). Still new ones may yet be described.

There is no question that molecular information should be incorporated into the MADS. We all agree that syndromes that we thought were similar may have completely different gene mutations, and syndromes we suspected were different conditions have been shown to have sometimes similar mutations, or be allelic. The system I proposed allows the incorporation of this new information. I think it is a good idea to include modifiers of Axis I (the phenotype) such as age of onset and to systematically include the OMIM numbers for Mendelian dis-

Use of a multi-axial diagnostic system in clinical genetics

To the Editor:

In the July/August 2001 issue of *Genetics in Medicine*, Robin and Biesecker¹ suggest a multi-axis nomenclature system for medical genetics. The purpose of their proposal is to initiate

orders in Axis III as Robin and Biesecker suggest. In Brazil and Austria, I also insisted on the convenience of incorporating this kind of nomenclature into the ICD system. This idea was immediately envisioned by the late Dr. Frank Greenberg when he learned about the MADS. He asked me for further information in order to include our system in the ICD, as Robin and Biesecker suggest.

Although I don't agree with the dichotomy that Robin and Biesecker present of phenotypic versus etiologic and their proposed axes, I think further discussion and adoption of an international system will certainly be an important contribution to the field of clinical genetics.

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