acetoacetate hydrolase" (italics added) should have been written as *fumaryl*acetoacetate hydrolase (encoded by the *FAH* gene). The chapter ends with the most recent concepts on how to generate knockout and other transgenic mouse lines and on how to use "quantitative trait linkage (QTL) mapping" in the elucidation of pharmacogenetic disorders. These discussions are absolutely first-rate.

Part II of the book is almost twice as long as part I. Each chapter and section in part II is followed by short exercises designed to demonstrate a pharmacogenetic principle or to illustrate the application of concepts and techniques to pharmacological problems; these exercises are drawn almost entirely from observations (taken from the original literature) representing authentic clinical situations.

On the whole, part II is excellent. It is a bit disappointing, however, that, although the P450 cytochromes are discussed at some length (pp. 131–133 and elsewhere), there are no references citing the well-developed *CYP* gene–superfamily nomenclature system or the continuously updated Website (http://drnelson.utmem.edu/homepage.html) on this subject. It also is unfortunate that the *CYP2D6* alleles "A, B, C, D, L," et cetera (p. 169) are described in this book published in 1997, because a recommended standardized nomenclature system for all the human *CYP2D6* alleles was reported in early 1996 and has already become widely accepted. Furthermore, it would have been helpful to the student reader to learn that aldosterone synthase and steroid 11-β-hydroxylase (under "Glucocorticoid-Remediable Aldosteronism," pp. 222–225) are in fact P450 cytochromes encoded by the *CYP11B2* and *CYP11B1* genes, respectively.

It always has been debatable as to where to draw the line regarding inclusion or exclusion of a human disease as a pharmacogenetic defect. For example, if pyridoxine-responsive anemia, fructose intolerance, and lactose intolerance are included as "pharmacogenetic disorders," then why not acatalasemia, ceruloplasmin deficiency (Wilson disease), and Na^+-sensitive hypertension? Likewise, cystic fibrosis, vasopressin resistance, retinoic acid resistance/acute promyelocytic leukemia, and thrombophilia are included in the book, whereas other disorders (e.g., the CYP2A6-mediated coumarin 7-hydroxylase, NAD(P)H:quinone oxidoreductase, and microsomal epoxide hydrolase polymorphisms) are not included.

Last, I believe that the textbook could have been improved if the reader had been given the opportunity to ponder why, on an evolutionary basis, these human pharmacogenetic polymorphisms might have occurred in the first place (see Nebert 1997 and the references therein). It is now very clear that DMEs and the DME receptors that control the levels of DMEs first evolved for critical life functions (e.g., cell division, sporulation, mating, homeostasis, electrolyte balance, differentiation, apoptosis, and neuroendocrine functions); then, in animals, DMEs more recently expanded to include the role of detoxification of dietary products, evolving plant metabolites and, of course, drugs. Hence, the high allelic frequencies seen for many DME genes, among individuals within any one ethnic group, might represent the evolution of *balanced polymorphisms* that we presently cannot appreciate, such as improved rates of implantation, prenatal growth and development, postnatal health in response to dietary selective pressures, or even resistance to bacterial or viral infections. Allelic frequencies in DME genes that differ among ethnic groups also might reflect differences in diet that have evolved over thousands of years.

Two recent examples of clinical diseases correlated with mutations in a DME gene (encoding enzymes that have been commonly ascribed only to metabolizing drugs and other foreign chemicals) further underscore the tenet that DMEs often modulate critical life processes. Mutations and deletions in the microsomal aldehyde-dehydrogenase gene called "fatty-aldehyde dehydrogenase" (*FALDH*) have been shown to be the cause of Sjögren-Larsson syndrome, which is characterized by mental retardation, spasticity, and ichthyosis, indicating the importance of this enzyme in neurocutaneous homeostasis. Mutations in the *CYP1B1* gene appear to be responsible for primary congenital glaucoma (buphthalmos), implying that failure of the CYP1B1 enzyme to metabolize a specific endogenous substrate leads to this affliction. Perhaps this subject (i.e., the real reason for the existence of DME genes and these clinical polymorphisms) could have been used to replace the naive chapter 4 of part I, or it could have been used as a third, conclusion section.

All in all, however, this book is a worthwhile addition to the shelves of all colleagues in the field. *Pharmacogenetics* should serve, for the next several years, as an invaluable resource for helping to teach upper-level undergraduates, graduate students, and other students of such health sciences as medicine, pharmacy, and nursing.

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Reference

Nebert DW (1997) Polymorphisms in drug-metabolizing enzymes: what is their clinical relevance and why do they exist? Am J Hum Genet 60:265–271

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Am. J. Hum. Genet. 61:1462–1463, 1997

Oxford Medical Databases, version 2.0. By Robin Winter and Michael Baraitser. Oxford: Oxford University Press, 1996. £395.00 each.

The *London Dysmorphology Database* has been my favorite syndromology search program for many years, but I have never found it particularly easy to use. When I have been away from it for a few weeks, I always seem to forget exactly which key to push to make it do what I want. I was, therefore, anxious to tear open the shrink-wrap on this new Windows® implementation to see if my old friend was now friendlier.

The version of *Oxford Medical Databases* (*OMD*) that I

tested includes two CD-ROMs and a brief (and not particularly useful) manual. One CD-ROM contains the *London Dysmorphology Database* and the *London Neurogenetics Database*. The other CD-ROM includes >5,000 clinical photographs and radiographs that constitute the *Photo Library*, a component that is essential for any clinical geneticist but that must be purchased at additional cost.

The minimum system requirements are an industry-standard personal computer with an 80486 DX33 or better CPU running Windows 3.1® or Windows 95®, 4 MB of RAM (8 MB is highly recommended), 83 MB of hard-disk space, a VGA monitor (SVGA is highly recommended), a mouse, and a CD-ROM drive. The program installed easily on my machine, a 133-Mhz Pentium® with 16 MB of RAM and Windows 95®. *OMD* generally behaved well, although it interferes with some DOS programs that are loaded after it.

The new version acts pretty much as a Windows program should. This means that a user who is familiar with Windows but has never seen *OMD* before can do searches and print the resulting diagnosis lists, narrative summaries ("abstracts"), and references without consulting the manual or the on-line help. The printouts are nicely formatted, and one can modify their appearance as well as their contents. Abstracts and individual references (but not feature lists or reference lists) can be copied into other documents by means of the Windows clipboard; photos cannot be printed or copied.

Version 2.0 of *OMD* does not do anything that the previous DOS versions did not do, but everything is easier now that it was before. The interface is much more attractive, and I found some of the innovations to be very useful. For example, the keyword search includes simple check boxes for microdeletions, disomy, and mosaicism as well as for Mendelian patterns of inheritance. Tiny thumbnail photos adjacent to the syndrome abstract can be clicked to display full-size pictures of particular features.

The contents of the databases are unchanged from earlier versions, except for the addition of new information. *OMD* includes an abstract, a list of reported features in the standardized language of the database, and an extensive bibliography for each syndrome. The *London Dysmorphology Database* has >2,800 different syndromes, and the *London Neurogenetics Database* has >2,600, although there is much overlap between the two. Neither database includes chromosomal abnormalities, except for the microdeletion syndromes and some of the uniparental-disomy and chromosomal-mosaicism phenotypes. However, Oxford University Press also distributes Albert Schinzel's *Human Cytogenetics Database*, a companion product that provides similar information on phenotypes associated with constitutional chromosomal abnormalities.

The information in *OMD* is quite current to the time of publication. There are many references from 1995 included, and there are some from 1996 as well. In fact, the contents seem more up to date than the software. Although this version is well implemented in Windows, the system cries out for hypertext links to the World Wide Web. *OMD* would be much more powerful if the McKusick numbers were linked to *OMIM* and if the gene locations were linked to the human gene maps and the human/mouse homology database. Automatic updating of *OMD* over the Internet would also be a welcome addition.

Will *OMD* replace the clinical geneticist? I doubt it. The *London Dysmorphology Database* is an important diagnostic aid, much like a radiograph or an electrocardiogram. The nonspecialist can obtain useful information from such aids, but they are most valuable in the hands of the specialist. Considerable skill is required to formulate an effective search in *OMD*, and the clinical geneticist, who knows many genetic syndromes by name, can weed through a list of possible diagnoses much more quickly than someone who is not familiar with most of these conditions. Moreover, the clinical geneticist is trained to recognize differences in gestalt that distinguish between conditions with similar lists of phenotypic features. The *OMD*'s *Photo Library* is of considerable assistance for this purpose.

The *Oxford Medical Databases* remain a valuable diagnostic tool for clinical geneticists and a convenient source of current bibliographic information on dysmorphic syndromes. The improvements in version 2.0's interface make it much easier to use than its predecessors. Information technology is advancing as rapidly as genetics, however, and the next version of *OMD* should be even better.

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