A Perspective on Drug–Nutrient Interactions

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1. SCOPE OF THE ISSUE

There are so many drugs available for use in the human condition, with continued approval of new agents, and expanded indications for existing ones (1). Likewise spending on pharmaceuticals in the United States continues to increase by 10–15% each year, driven by increased utilization as well as increased cost per prescription (1). According to a recent report, close to $141 billion of the estimated $1.4 trillion spent on health care annually in the United States are accounted for by prescription drugs (2). Beyond prescription medication, the wide availability of over-the-counter (OTC) pharmaceuticals and dietary supplements together with the increasing emphasis on self-care among people further increases consumption patterns of pharmacologically active substances. Recent estimates are that about 80% of Americans use medication, whether prescription, OTC, or dietary supplement products (3).

Although dietary intake may not be recognized in similar terms of increasing discoveries, it should be recognized that food intake habits have changed along with advances in nutrition and food sciences (4–6). Furthermore, our understanding of food components included in the diet, whether nutrients or phytochemicals, has expanded (7,8). This makes for an ever-widening potential for interactions between drugs and food, food components, or specific nutrients. The potential for interactions becomes that much more complex when patients with any underlying alteration in nutritional status are included. The working definition of a drug–nutrient interaction (DNI) used throughout this volume is that which results from a physical, chemical, physiologic, or pathophysiologic relationship between a drug and a nutrient, multiple nutrients, or food in general. The interaction is considered significant from a clinical perspective if therapeutic response is altered or nutritional status is compromised.

The potential number of interactions and permutations seems infinite. But it remains unclear what proportion of these have actually been identified, and more to the point, what number of the identified subset may be considered clinically significant. Clearly, if one is not looking for a DNI, one will not find it. For those interested in identifying specific interactions, a number of books over the years have dedicated some or all pages to DNIs (5,9–29). Some lists of DNIs are so brief they seem to question the legitimacy of the topic, others are so extensive one wonders how an interaction could ever be
avoided. With this mixed message, many clinicians simply discount the relevance of DNIs to their practice. A recent survey of health care providers found their knowledge of common DNIs to be wanting (30). This may in part explain why so few health care providers provide DNI counseling to the majority of their patients (31). These findings occur at a time when regulatory agencies expect DNIs to be addressed by clinicians in institutionalized settings. What is needed is a rational approach to evaluating the scientific basis and clinical relevance of existing DNIs to allow for appropriate recommendations. At the same time, this approach should set up a framework on which to build a database for the many interactions yet to be identified, evaluated, and documented. Although much has been done over the years, much more still needs to be accomplished.

2. HISTORICAL PERSPECTIVE

Through the ages, the use of food combinations or the addition of medicinal remedies to food were employed to preserve health or to manage disorders. Time has not slowed down either our penchant for food or the advancement of therapies used to manage disease. But more important than a historic review of the entire topic, is the evolution in relative importance placed on clinically relevant DNIs.

That disease and therapy could precipitate malnutrition was barely mentioned in a lengthy clinical review on nutritional assessment many years ago (32). A few decades later, the only clinically recognized DNIs were the more obvious intraluminal interactions between drug and food (33). It was still several years until the first major review recognizing the impact of food on drug absorption was published, finally stimulating clinical interest (34). As a result, any identified interactions between a drug and food were then treated with caution. The appreciation that not all interactions were clinically relevant developed more slowly. Even then, the idea that clinically relevant DNIs may involve more than simply physical interactions between food and drug also evolved slowly. This limited clinical focus occurred despite much earlier work on the impact of specific nutrients on drug metabolism (35) and the effect of drugs on nutrient metabolism (36,37). At about the same time, the overlap of heredity on the interaction between drugs and nutrients was recognized (38), and the effects of nutritional status on drugs began to be explored as well (39,40). Over the intervening decades, DNIs have been studied and discussed more formally, and presented in practical formats.

Dr. Daphne A. Roe was once referred to as the founder and “godmother” of the DNI issue (41). This noted physician spent a good portion of her tremendous professional energies in the arena of DNIs. She clearly understood that it was the responsibility of all clinicians to understand DNIs, and provided guidelines that included clinical aspects of DNIs. Besides contributing to the primary literature (42–46), she authored handbooks (10,20,21) and texts (13,14,17) on the subject. She also served as the editor of a journal dedicated to the topic—Drug–Nutrient Interactions: A Journal of Research in Nutrition Pharmacology and Toxicology (Drug–Nutr Interact), first published in 1982. A quick review of the periodical for its topics and authors reveal the breadth of original research activity and the quality of investigators in the field of nutritional pharmacology, many of whom remained active. They represented departments of nutrition, food science, and pharmacology in schools of medicine, pharmacy, and varied universities. The studies in the journal were supported by a variety of government and industry sponsors, as well as