REFLECTION

Drug Toxicity and My Dad's Ethnicity

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ABSTRACT

My Korean-American father experienced a severe drug eruption after receiving allopurinol for gout. Although commonly used as a first-line medication in the United States, in South Korea, allopurinol is only prescribed after human leukocyte antigen (HLA) testing due to the high frequency of an HLA allele associated with allopurinol-induced severe cutaneous adverse reactions. Given the complexity of the discourse around engaging race and ethnicity in medical practice, my father's experience led me to contemplate the current context of eliminating race from clinical decision making to address historical and ongoing injustices. Upon this reflection, I advocate for the separation of race and ethnicity to appropriately consider ethnicity when it may support quality and safety of care for all patients.

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Exhausted, I returned home after finishing my third year in medical school, imagining a relaxing summer weekend with my parents. I arrived to find my dad even more exhausted than I. He was breathing heavily, covered in a full body rash, soaked in sweat, face wrinkled with pain.

I got that gut feeling that my residents had taught us to recognize. My dad was "sick." Sick, but unwilling to seek care. Perhaps it was his fatigue, or the pain, or that my mother's face couldn't successfully conceal her fear, but we were finally able to convince my dad to visit the emergency department (ED).

I had just spent weeks in the ED as a student—on the side of the care team—and now here I was again, in a completely different role. My dad was diagnosed with a "severe inflammatory reaction with rash." He received intravenous methylprednisolone and acetaminophen, and soon felt his headaches and fatigue improve. Laboratory tests revealed only a slight eosinophilia and elevated liver function tests.

With his fever gone and symptoms slowly dissipating, my dad was discharged with a course of steroids. He felt much better. Mom, too. But I still felt worried. Didn't we need to know a clear diagnosis? My dad didn't have any known new exposures or potential sources of infection. The only "new" thing was starting allopurinol for gout, but that was well over a month before his ED admission.

Given the timeline of exposure, the ED team was less concerned about a drug-induced reaction. I think that because I knew *less* than the ED team, and because it was *my* dad, something still stirred in my mind. I was flipping back and forth from daughter to medical student and back again. "Could my dad's clinical picture be consistent with a delayed, severe cutaneous drug eruption?" At home, I continued in the role of the student—researching "the case." The student part of me was interested, but the daughter part was worried and scared.

While searching for literature on allopurinol-induced delayed cutaneous eruptions, I discovered some interesting data linked to our personal history. Our family is ethnically Korean, with multiple generations traceable back to the Korean peninsula. It is well-documented in the medical literature that ethnic Koreans and Han Chinese have a high frequency of human leukocyte antigen (HLA)-B*5801, an HLA allele strongly associated with allopurinol-induced severe cutaneous adverse reactions.[1] As a result, in South Korea, HLA testing is recommended before trials of allopurinol; HLA testing has been shown to be more cost-efficient than managing episodes of allopurinol-induced severe cutaneous adverse reactions.[2] In South Korea, because allopurinol has a relatively higher incidence of life-threatening drug reactions, febuxostat, a non-purine based xanthine oxidase inhibitor, is used alongside allopurinol as a first-line therapy for gout.[3] In the United States, the American College of

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Rheumatology also recommends HLA testing specifically for patients of Korean, Han Chinese, Thai, and African-American descent before initiating allopurinol, recognizing the higher frequency of the HLA-B*5801 allele in these populations.[4]

Weeks later, my dad followed up with his primary care physician, had HLA testing, and was found to be a carrier of HLA-B*5801. With a prednisone taper and cessation of allopurinol, my dad recovered over several months.

My mom and I recovered, too; after all, we had all seen a potentially life-threatening drug reaction. As a medical student and daughter, I found myself contemplating the appropriate use of race and ethnicity in medicine given the literature surrounding HLA-B*5801. I felt conflicted: while I agreed with medicine's intentional shift away from using race to guide clinical practice, I felt frustrated that greater consideration of ethnicity may have prevented my father's suffering.

Throughout the medical literature, "race" often acts as an umbrella term encompassing race, self-identified ethnicity, and genetic ancestry.[5] Although often grouped together, these frameworks can be disentangled.[5,6] Medicine has a thorny history with race. Race is a social construct based on perceived physical traits and has been used to justify and perpetuate discriminatory practices against non-White minorities.[6] Medicine's use of race in clinical settings has perpetuated racism and racial hierarchy, harming patients and furthering health inequities.[6,7] Alongside structural biases, race contributes to interpersonal biases in clinical interactions, from patient-clinician communication to patient perceptions of quality of care.[8,9]

Race, albeit socially constructed and flawed, is a composite characteristic capturing important epidemiologic information, such as social determinants of health, including racism and discrimination, and cannot be fully removed from modern medicine.[5] Self-identified ethnicity and genetic ancestry, which may be associated with race, may play a critical role in providing optimal care. Self-identified ethnicity can act as a composite marker of both biology and cultural practices, including genetic and environmental predispositions.[10] Genetic ancestry and population-specific genetic variants, such as apolipoprotein 1 among African-American populations and CYP2C19 variants impacting drug metabolism among Asian populations, have facilitated more effective screening and care delivery.[5] Components of race, particularly self-identified ethnicity and ancestry, can contribute to the holistic understanding of and care for a patient. It may be appropriate to adapt diagnostic considerations and management plans based on a patient's self-identified ethnicity and known ancestry.

In cases like my dad's, doctors may better manage a sudden rash and systemic symptoms by considering risks based on ethnicity, notably the increased likelihood of an allopurinol-induced reaction. Had my dad received his care in South Korea, where the standard of care is tailored to his ethnic background, he may have avoided the potentially life-threatening drug reaction altogether. Could considering self-identified ethnicity in clinical care help minimize harm and optimize benefits for patients? Failing to consider ethnicity and ancestry may lower quality and safety of care for patients from less represented populations.

To ensure we provide the best possible care, students, residents, and caregivers must learn respectful standards to determine patients' ethnicity and ancestry and appropriately weigh these factors in clinical decision making. Clinicians can learn to facilitate conversations that allow patients to feel comfortable and respected, by asking, listening openly, and clarifying without assumptions. It is critical to then thoughtfully and appropriately apply this information to generate management plans in the patient's interest. I believe medical schools can teach trainees how to helpfully seek relevant information related to ethnicity and ancestry—with regard for human history and the risk of misapplication. We can then be equipped to ensure individualized, nuanced care for each patient.

Since last summer, my dad's health and vitality have returned. He has successfully avoided drug reactions and gout flares, remaining allopurinol-free. My mom and I are thinking about caregiver roles and family roles with a little more perspective. Thinking of my dad, I am hoping to offer one more role: as a voice for awareness of ethnicity as a potential variable in caring for our patients.

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Key words: perspective; reflection; race; ethnicity; medical education

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