Clinical Pharmacology & Toxicology Pearl of the Week

Personalized Medicine

- Personalized medicine involves tailoring a treatment plan, including drug choice and dosage, to individual patients or subgroups of patients that share common characteristics.
- Personalized medicine considers the patient's personal factors, genetic factors, and environmental factors.
- The goal of personalized medicine is to improve patient-centered outcomes while reducing adverse effects of treatments.

Personalized Medicine: You are already doing it!

- ✓ Clinicians are already very adept at taking into account individual factors such as renal function and hepatic function into account when ordering medications.
- ✓ These commonly assessed features are taken into account regularly to decrease the risk of adverse drug events such as supratherapeutic drug accumulation and toxicity.
- ✓ Figure 1 breaks down personalized medicine into its separate pieces:

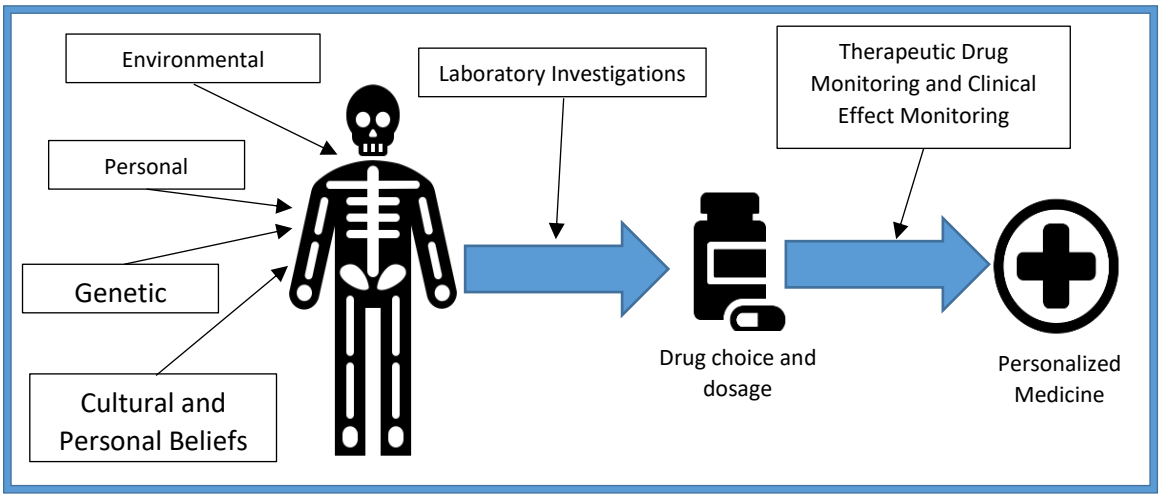

Figure 1: Factors involved in Personalized Medicine, adapted from Reference 2

Personal Factors

- ✓ Personal factors are **innate to the individual** and are generally non-modifiable.
- ✓ They include:
  - Age (particularly extremes of age)
  - Weight/Obesity
  - Gender
  - Ethnicity
  - Comorbidities
  - Allergies and Intolerances
- ✓ Personal factors can affect **drug dosing** (Ex: weight-based dosing) and **drug choice** (Ex: avoidance of beta-blockers in asthmatics, avoidance of anticholinergic medications in the elderly).

Environmental Factors

- ✓ Environmental factors are **external to the individual** and are often modifiable.
- ✓ They include:
  - Medications taken for co-morbidities
  - Herbals and supplements
  - Smoking
  - Recreational and illicit drug use
  - Alcohol use
  - Other foods and beverages

- ✓ Environmental factors can affect **drug choice** (Ex: avoidance of drugs with significant drug-drug interactions) or **drug dosing (**Ex: starting with a higher dose of warfarin for patients on CYP2C9 inducer carbamazepine).

Genetic Factors

- ✓ Genetic factors, or **pharmacogenomics**, are innate to the individual and are non-modifiable.
- ✓ They include:
  - Genetic polymorphisms related to **drug metabolism** (CYP-enzymes, p-glycoprotein)
  - Genetic polymorphisms related to **pharmacodynamics** (VKORC-1 and Warfarin, G6PD and Rasburicase)
  - Genetic polymorphisms related to **immune response** against certain drugs
  - Ethnicity and family history may play a role in the setting genetic polymorphisms that have yet to be identified in the genome
- ✓ Genetic Factors can affect **drug choice** (Ex: Tamoxifen in ER+ breast cancers) and **drug dosing** (Ex: decreased warfarin dosing in patients who have decreased VKORC-1 expression)
- ✓ Pharmacogenomics will be **discussed in more depth in subsequent Pearls of the Week.**

Cultural and Personal Beliefs

- ✓ A patient's autonomy and ability to choose treatments based on their core values and beliefs is of paramount importance in Canadian healthcare.
- ✓ Respecting a patient's wishes for avoidance of certain treatments, or even non-treatment, while providing full informed decision making of the options and expected outcomes aids in building a therapeutic alliance.

Laboratory Investigations

- ✓ Laboratory investigations goes **hand-in-hand with personal factors** that are innate to the individual.
- ✓ Common laboratory investigations include:
  - Liver function testing (INR/PTT, albumin)
  - Liver enzyme testing (ALT, ALP, GGT, Bilirubin)
  - Renal function testing (Creatinine/GFR)
  - Thyroid function testing
  - Echocardiography and ECG
- ✓ Laboratory investigations can affect **drug choice** (Ex: avoidance of NSAIDS in chronic kidney disease, spironolactone in low EF CHF, avoidance of QT prolonging agents in pre-existing long QT), **drug dose** (Ex: 2g/day acetaminophen in patients with chronic liver disease), and **dose frequency** (Ex: Vancomycin Q24-48 hours in CKD, daily gabapentin in CKD).

Therapeutic Drug Monitoring and Clinical Effect Monitoring

- ✓ Once a drug and dose has been chosen, **ongoing monitoring and dose adjustments often occur.**
- ✓ Most commonly, dosing is adjusted based on **patient reported or observed clinical effect and adverse effects.**
  - Ex: Increasing antidepressant dose, titrating betablocker therapy to heart rate, decreasing antipsychotic dose due to anticholinergic side effects
- ✓ Therapeutic drug monitoring is available to certain medications with the following characteristics:
  - Clinically established pharmacodynamic relationship between serum concentration and effect
  - Narrow therapeutic index
  - Dose optimization not possible based on clinical effects alone
  - Significant inter-individual pharmacokinetic variability
  - Duration of treatment and criticality of treatment justify dosing adjustments
  - Patient compliance may be of concern
- ✓ Therapeutic drug monitoring allows for titration of a dosage to a pre-determined therapeutic target.
  - Ex: Vancomycin, digoxin, amiodarone, phenytoin, valproic acid, lithium, tacrolimus

References:

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