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 considering individual factors such as renal function and hepatic function when ordering medications.
- ✓ These commonly assessed features are considered 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:

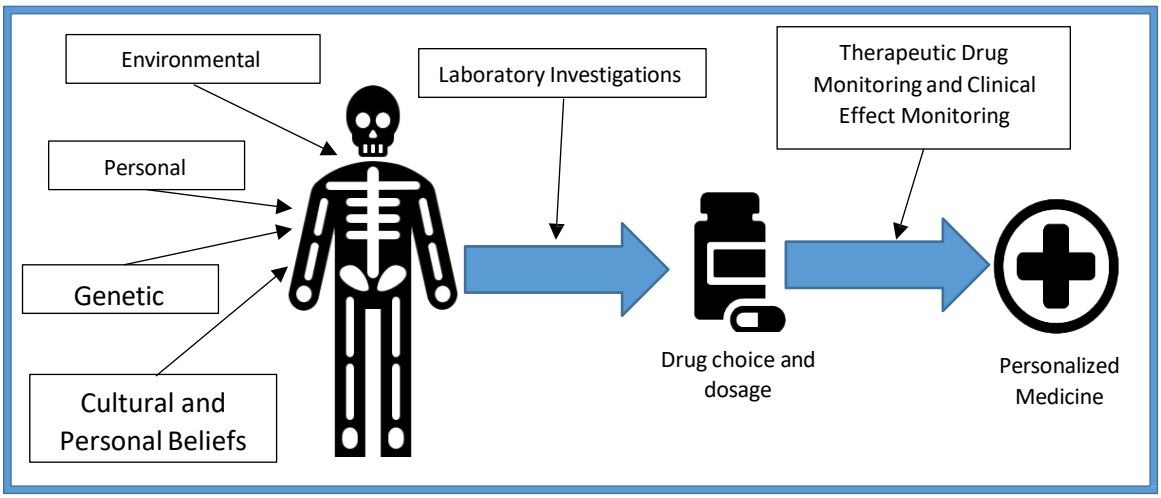

Figure 1: Factors involved in Personalized Medicine, adapted from Reference 2

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** (e.g., CYP-enzymes)
  - Genetic polymorphisms related to **pharmacodynamics** (e.g., VKORC1 and Warfarin)
  - Genetic polymorphisms related to **immune response** against certain drugs (e.g., HLA genes)
- ✓ Genetic factors can affect **drug choice** (Ex: Tamoxifen in ER+ breast cancers) and **drug dosing** (Ex: decreased warfarin dosing in patients who have decreased VKORC1 expression)

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 go **together 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:

1. Lewis S. Nelson et al, Goldfrank's Toxicologic Emergencies. 11th ed. New York: McGraw Hill Medical; c2019
2. Crettol S, de Leon J, Hiemke C, Eap CB. Pharmacogenomics in psychiatry: from therapeutic drug monitoring to genomic medicine. Clin Pharmacol Ther. 2014;95(3):254–257.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the Alberta Referral Directory (ARD) by searching "Pharmacology" from the ARD home page. Click HERE for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in Alberta Referral Directory (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found HERE.

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