Hospice and Pharmacogenetics
Specialized Need of DD Population
Objective

- Apply the pharmacogenetics concepts to the hospice care team’s ability to individualize the pain medication regime resulting in optimal comfort
Social Work Perspective

• People with developmental disabilities are a vulnerable population
• This population is underserved by hospice (<8% compared to general population of 43%)
• Hospice & palliative care are about living well while dying
• Those who are developmentally disabled are entitled to the same consideration as the general population, whether curative or palliative.
Serving those with special needs

• In fact, individuals with Developmental Disabilities have the right to access the same care, including curative care (even when prognosis is poor), palliative care and hospice.
Foundation of Hospice

- Respect and dignity
- Comfort and quality of life with a special emphasis on managing pain and other distressing symptoms
- Support services of hospice care are available to the entire family and roommates
- Are comprehensive, provide compassionate care and are an experience of hope
- Will increase quality of life and may increase life expectancy
Hospice can be provided in:

- Private homes
- Hospitals
- Nursing Homes
- Community residences, group homes and assisted living homes and other residences
Hospice Services:

- Provided by an interdisciplinary team
- A resource and coordinating
- Developed in a individualized “Plan of Care”
- Assessment and care planning
  - 24 hour on-call nursing care
  - pain and symptom management
  - medical consultation
  - medications and medical supplies
  - therapy modalities
  - care giving assistance
  - complimentary therapies
  - spiritual counseling
  - full range of social services
  - grief and bereavement counseling
Specialty Hospice Providers

- Additional DD Training of all staff
- Additional DD Support for Grief of extended family including roommates
- Primary Choice of Aging Adults with DD children
- Understands that Behavior is Communication
- Assumes the ability to understand
Listening
Pharmacogenetics

- **Pharmacogenetics** is the study of how our genes affect our response to drugs. Every human has a genetic code that is unique to them alone.

- Variances in the genes that play a role in medications can:
  - Be of no consequence to the drug’s safety and efficacy
  - Render a medication useless
  - Result in a medication causing serious adverse reactions
**Pharmacokinetics**
- What the **body does to a drug**
  - Think metabolism, bioavailability
    - Converting Pro-Drug to active agent
    - Washing the active agent out of the body

**Pharmacodynamics**
- What the **drug does to the body**
  - Think therapeutic, sub-therapeutic or toxic

**Distribution**
Cytochrome P450 Enzymes

More than 50 enzymes in CYP450

CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5

90% of drugs are metabolized by these 6 enzymes\textsuperscript{1,2}

Links differences in gene structure (**inherited variation**) to drug metabolism and response

**SO WHY IS THIS IMPORTANT?**
Categories of people with specific CYP450 variants (polymorphisms)

- **Effective Metabolizer (EM):**
  - Normal Genetics
  - Two Good Copies of the genetic code required for metabolism

- **Intermediate Metabolizer (IM):**
  - Reduced enzymatic activity
  - 1 Good Copy and 1 Bad Copy of code required for metabolism
  - May render the drug a No Go or require a dose adjustment

- **Poor Metabolizer (PM):**
  - Complete lack of enzymatic activity
  - 2 Bad Copies code required for metabolism
  - Usually renders a drug a No Go

- **Ultra Rapid Metabolizer (UM):**
  - Higher than average enzymatic activity
  - 2 Bad Copies causing much higher than normal metabolism
  - May render the drug a No Go or require a dose adjustment
<table>
<thead>
<tr>
<th>Gene</th>
<th>EM</th>
<th>IM</th>
<th>PM</th>
<th>UM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2D6</td>
<td>53%</td>
<td>35%</td>
<td>10%</td>
<td>2%</td>
<td>47%</td>
</tr>
<tr>
<td>CYP2C19</td>
<td>36%</td>
<td>32%</td>
<td>4%</td>
<td>28%</td>
<td>64%</td>
</tr>
<tr>
<td>CYP2C9</td>
<td>57%</td>
<td>40%</td>
<td>3%</td>
<td>NA</td>
<td>43%</td>
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<tr>
<td>CYP3A4</td>
<td>87%</td>
<td>12%</td>
<td>1%</td>
<td>NA</td>
<td>13%</td>
</tr>
<tr>
<td>CYP3A5</td>
<td>1%</td>
<td>18%</td>
<td>81%</td>
<td>NA</td>
<td>99%</td>
</tr>
</tbody>
</table>
The Need for Pharmacogenetic Testing

• There can be wide variability in patient response to commonly prescribed medications:
  – Medication achieves goal and does not harm patient
  – Medication achieves goal, however, also causes an Adverse Drug Reaction
  – Medication does not achieve goal and causes an Adverse Drug Reaction
  – Medication does not achieve goal and does not cause Adverse Drug Reaction

Individualized Therapy

All patients with same diagnosis
(not all respond to therapy)

Severe overdosing
(toxicity)

Sub-therapeutic
(inadequate response)

Maybe just right?
(no such thing as a common dose)
Treat with conventional dose
Each person receives either a **GOOD** or **BAD** Genotype from both Mother and Father

**Effective Metabolizer** – Received **TWO GOOD**

**Intermediate Metabolizer** – Received **ONE BAD ONE GOOD**

**Poor Metabolizer** – Received **TWO BAD**

**Ultra Rapid Metabolizer** – Received **TWO BAD**
~60% of meds in top 20 list causing ADRs are linked to a genetic variation

122 drugs have FDA box warnings related to genetics
These Genes are responsible for the metabolism of approximately 85% of medications

<table>
<thead>
<tr>
<th>Gene</th>
<th>% of Effective Metabolizers</th>
<th>% of Intermediate Metabolizers</th>
<th>% of Poor Metabolizers</th>
<th>% of Ultra-Rapid Metabolizers</th>
<th>Variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D6</td>
<td>53</td>
<td>35</td>
<td>10</td>
<td>2</td>
<td>47%</td>
</tr>
<tr>
<td>BH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2C19</td>
<td>36</td>
<td>32</td>
<td>4</td>
<td>28</td>
<td>64%</td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2C9</td>
<td>57</td>
<td>40</td>
<td>3</td>
<td>NA</td>
<td>43%</td>
</tr>
</tbody>
</table>
CYP2D6

Cost of healthcare for chronic pain patients exceeds cost of treating patients with coronary artery disease, cancer and AIDS.

Opioid Medications

- 120M prescriptions for hydrocodone and oxycodone alone
- Opioid poisoning accounts for more fatalities than either heroin or cocaine
- Response rate of only 50% to 60% partly due to genetic variances in patients
- Increased regulatory oversight
<table>
<thead>
<tr>
<th>Clinical Fact</th>
<th>Economic Implication</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to opioids can vary as much as 40 fold among patients. Blood concentrations of opioids do not predict analgesia. Pain medications are involved in 30% of all adverse drug events involve pain medications.</td>
<td>Adverse drug events cost an average of $5.6M per hospital. Patients with adverse drug events average 8-12 additional hospital days at cost of $16,000 to $24,000</td>
<td>1,2</td>
</tr>
<tr>
<td>80% of patients reporting adverse drug reactions had impaired 2D6 metabolism</td>
<td>Adverse drug events cost an average of $5.6M per hospital. Patients with adverse drug events average 8-12 additional hospital days at cost of $16,000 to $24,000</td>
<td>3,2</td>
</tr>
<tr>
<td>51% of patients taking oral opioids experience at least one adverse event or adverse effect.</td>
<td>Adverse drug events cost an average of $5.6M per hospital. Patients with adverse drug events average 8-12 additional hospital days at cost of $16,000 to $24,000</td>
<td>4,2</td>
</tr>
<tr>
<td>29% of preventable adverse drug events were associated with analgesics</td>
<td>Increased length of stay by 2.2 days and costs by $3,244</td>
<td>5</td>
</tr>
</tbody>
</table>

References
2. Agency for Healthcare Research and Quality. Publication # 01-0020
CYP2C19, SULT4A1

23 Million Americans taking Behavioral Health medications
253.6 million prescriptions in 2010

Anxiety/Depression
- 63% of patients fail to achieve remission on first line SSRI therapy
- 16.3% withdraw due to drug intolerance

Schizophrenia
- 65,000 hospitalizations for schizophrenia and related disorders
- Average length of stay is 7.1 days
- Treating SULT4A1 positive Caucasian patients with olanzapine or quetiapine reduced the risk of hospitalization by over 80%
### Clinical Facts

<table>
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<tr>
<th>Clinical Facts</th>
<th>Economic Implications</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRD occurs in 10% to 50% of patients with diagnosis of depression</td>
<td>TRD increases medical costs: $6,852 annually versus $13,980 annually</td>
<td>1</td>
</tr>
<tr>
<td>TRD patients are 50% more likely to be hospitalized</td>
<td>TRD hospitalization increases medical costs: $6,512 annually versus $42,344 annually</td>
<td>2</td>
</tr>
<tr>
<td>Patients with depression diagnosis and PGx identified variants have 69% greater health care visits and 4 times greater disability claims</td>
<td>Depression diagnosis with PGx identified variants increased medical costs: $5,188 higher than patients with depression diagnosis and no PGx identified variants</td>
<td>3</td>
</tr>
</tbody>
</table>

References

3. Retrospective study of healthcare utilization that could have been avoided through PGx. Psychiatric pharmacokinetics predicts health resource utilization of outpatients with anxiety and depression. Transl Psychiatry 2013;3:e242
<table>
<thead>
<tr>
<th>Clinical Fact</th>
<th>Economic Implication</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenic patients have a 38% to 51% probability of readmission following initial hospitalization.</td>
<td>Re-hospitalized patients incur twice the medical costs compared to patients not requiring re-hospitalization</td>
<td>1</td>
</tr>
<tr>
<td>SULT Negative patient taking Olanzapine have 61% relapse vs 11% SULT positive</td>
<td>$7,786 no recent relapse verses $38,104 to 73,549 if recent relapse</td>
<td>1</td>
</tr>
<tr>
<td>SULT Negative patient taking Quetiapine have 58% relapse vs 12% if SULT positive</td>
<td>$7,786 no recent relapse verses $38,104 to 73,549 if recent relapse</td>
<td>1</td>
</tr>
<tr>
<td>74% of patients stop taking their prescribed antipsychotic medication at 18 months due to lack of efficacy or ability to tolerate the medication</td>
<td>Cost to treat relapse is $38,501</td>
<td>2,3</td>
</tr>
</tbody>
</table>

References
Practice Model

Genetic Code Variance Implications
- Pre-Disposition to Disease
- Understanding Current Disease

Response to Medications: Pharmacogenetics
- Safety
- Efficacy
- New Drug Development

- Disease Prevention

Personalized Medicine

Patient’s Unique Environment Characteristics

Patient’s Unique Physical Characteristics

Patient’s Unique Genetic Coding
Typical Agency Hospice Pain Management

- Pain is part of the hospice process
- Standard Pain Management for All patients unless contraindicated by terminal diagnosis
- Change and dosage adjustments as pain is uncontrolled
- Family Concern with comfort
- Patients unable to report pain levels
Pain in hospice patients is inevitable

- Prescription cost associated with pain medications that need adjusted and changed is potentially avoided with pharmacogenetics.
- As pain medication doses are increased higher risk for injuries such as falls associated with decreased awareness,
- Dosing patients accurately for the most effective pain management decreases this risk for patients with genetic variances.
- Non-Invasive Buccal Swab
- Results Available within 5 to 7 Days
- Lifetime Test – Your Genetics Remain The Same
- Variances Can Identify Possible Variances in family
## Drugs with Consensus Recommendations

<table>
<thead>
<tr>
<th>Gene</th>
<th>Phenotype</th>
<th>Drug</th>
<th>Consensus Based Action Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2D6</td>
<td>Intermediate Metabolizer • 35% of the population</td>
<td>oxycodone</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hydrocodone</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>codeine</td>
<td>Dose Adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>nortriptyline</td>
<td>Dose Adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>zuclopenthixol</td>
<td>Dose Adjustment</td>
</tr>
<tr>
<td></td>
<td>Poor Metabolizer • 10% of the population</td>
<td>codeine</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hydrocodone</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>oxycodone</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tramadol</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td>Ultra Rapid Metabolizer • 1 to 7 in every 100 people</td>
<td>codeine</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td>• 29% of North African and Ethiopian populations</td>
<td>hydrocodone</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td>• 6% of African American, Caucasian and Greek populations</td>
<td>oxycodone</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tramadol</td>
<td>Dose Adjustment</td>
</tr>
<tr>
<td>OPRM1</td>
<td>Poor Responder</td>
<td>Active Opioids</td>
<td>Dose Adjustment</td>
</tr>
<tr>
<td></td>
<td>Intermediate Responder</td>
<td>Active Opioids</td>
<td>Dose Adjustment</td>
</tr>
</tbody>
</table>
- Medicare and Medicaid
  Medical Necessity
- Commercial Insurance
  Prior Authorization Required
- Pilot Programs
  ViaQuest Hospice Pilot Program
- Self Pay
  One Panel is Approximately $850
- Takes guesswork out of prescribing

- When Behaviors are communication it allows clinicians to be confident pain is controlled

- Gives family peace of mind that pain is controlled

- Eliminates ineffective medications which may still be causing adverse reactions
For further information, please feel free to contact me directly:

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614-339-0802
Kathy.richard@viaquestinc.com