FACULTY RESOURCE
CASE GUIDE

CASE: PEGGY
CASE DESCRIPTION:

Peggy is a physically healthy divorced 28-year old Puerto Rican ICU nurse in Washington DC, who is also a member of the U.S. Army reserves and a marathon runner. She presents to her primary care provider (PCP) for assessment of symptoms that began about a week after she returned from witnessing the 2013 Boston Marathon bombings a month ago where she also assisted her fellow runners who were injured. She appears anxious when describing her experience with the assistance efforts. Although she cries when describing the terror and chaos following the bombing and emergency care needed, she is methodical when describing her symptoms, including difficulty sleeping, nightmares, inability to concentrate, irritability, headaches, anxiety, and lack of energy - almost as if they are happening to someone else and not her. Peggy talked about her symptoms with her mother, who shared that she experienced similar symptoms after returning from the war in Vietnam where she served as a nurse. She explained to Peggy that such symptoms occurring in relation to a stressful experience are now identified as post-traumatic stress disorder (PTSD), and encouraged Peggy to see her PCP for evaluation. Among the PCP’s recommendations is a referral for psychotherapy and medication consultation, consideration of pharmacogenomic testing for guiding drug selection, and consideration of participating in clinical research to learn more about PTSD.

CASE OBJECTIVES:

- Describe post-traumatic stress disorder (PTSD) symptoms.
- Identify components of PTSD assessment.
- Explain the risk factors for PTSD including the influence of family history.
- State possible benefits and risks of recommended PTSD interventions.
- Summarize professional organization guidelines for pharmacogenomic testing for PTSD medication treatment.
- Identify ethical implications associated with PTSD treatment, including medication and genetic testing.
- Determine opportunities to further develop PTSD clinical research.
SUGGESTIONS FOR HOW TO USE G3C:

This is a clinical encounter of Peggy, a physically healthy 28-year-old Puerto Rican nurse, U.S. Army reservist, and marathon runner who presents to her primary care provider with symptoms suggesting post-traumatic stress disorder. Her symptoms began shortly after she returned home from running in the 2013 Boston Marathon where she witnessing the two bombings that took place near the marathon finish line and assisted fellow runners who were injured.

The learner should be instructed to enter the virtual clinic and begin by reviewing the case materials located in the client’s folder. When ready, the learner progresses to the client encounter and begins by selecting a question to ask the client from the list provided. Additional learner activities associated with the learner-selected questions are located below the client video. Supplementary case materials including those that the healthcare provider gathers during the encounter are identified by icons in the box to the right and can be viewed at any time during the case review. To gain further perspective on the case topic, the learner should also view the video commentary provided by an expert in the topic presented.

SUGGESTED SUPPLEMENTAL STUDENT ACTIVITIES:

Pedigree Construction

- Expand the three generation pedigree you drew for Peggy using My Family Health Portrait by using your imagination to include aunts, uncles and cousins on both sides of the family.
- Report if and why you think that one lineage (maternal or paternal side of the family) is more likely to increase Peggy’s risk for PTSD than the other lineage.
- Draw your own family history using standard pedigree nomenclature. Explain why it is important to use standard nomenclature and a systematic approach to obtaining family history information.

References:


Surgeon General’s Family History Tool
[http://www.hhs.gov/familyhistory/](http://www.hhs.gov/familyhistory/)

Although this tool can be used by health care providers, the primary purpose is for an individual to create a family history diagram based on their own family history. The health information and family history questions use lay language and are asked in the format one asks of an individual. For example, "How many sisters do you have?" The learner should answer the questions from the perspective of the person in the case study. For "Date of Birth" on the initial screen, subtract the age of the individual in
the case study from the current year to determine the year of birth and use 01/01 for the day and month of the individual’s birth. Unless stated otherwise, assume that all ages are in years, all relatives are full blood relatives (e.g., no half-siblings), and that no one is adopted, has a biological twin, or has parents who are related to each other than by marriage.

Diagnostic and Statistical Manual (DSM) of Mental Disorders Diagnostic Criteria

- Summarize the most current American Psychiatric Association DSM criteria for PTSD. How does this differ from the prior criteria?
- Name two findings which led to the revised DSM-5 diagnostic criteria.
- What is the dissociative subtype of PTSD?
- What are the diagnostic criteria for children less than 7 years of age?

References:
United States Department of Veterans Affairs, National Center for PTSD
http://www.ptsd.va.gov/professional/pages/diagnostic_criteria_dsm-5.asp

Pharmacogenomic Testing to Guide Psychotropic Drugs for Children and Adolescents

- Describe the key content of informed consent for a pharmacogenomic test. How might this apply to children and adolescents or other vulnerable populations?

References:


SUGGESTED CLASSROOM DISCUSSION POINTS:

Treatment options
Risks, benefits and limitations of PTSD pharmacogenomic testing
Ethical issues related to PTSD pharmacogenomic testing
Genetic/genomic research options pertinent to PTSD

1. PTSD: Post Traumatic Stress Disorder is an anxiety disorder triggered by experiencing or witnessing a traumatic event that causes recurrent disturbing psychological and physiological
or physical symptoms lasting at least one month. In the dissociative subtype of PTSD the individual experiences depersonalization and derealization. The prevalence of PTSD ranges from 7-12% among persons who sustained a trauma. Treatment includes medication, psychotherapy, exercise, and meditation.

2. Persons at risk for PTSD: military and emergency/trauma personnel and victims of war, natural disasters, crimes, violence (e.g., sexual or physical assaults, terrorism, family violence), or other serious events. Females are at higher risk for PTSD than males.

3. PTSD symptoms: symptoms usually start soon after a traumatic event, but may not appear until months or years later and may come and go over many years. Duration may be acute (less than 3 months) or chronic, or delayed (onset 6 months or more after the stressor). Symptoms lasting longer than 4 weeks, causing great distress, or interfering with work or home life may be indicative of PTSD. There are four types of PTSD symptom clusters:
   a. Intrusion (reliving the event)
   b. Avoidance (avoiding situations that remind a person of the event)
   c. Negative alterations in mood/cognition (changes in one’s beliefs or feelings)
   d. Alterations in arousal/reactivity (physiological distress such as feeling extremely tense/anxious/nervous [“all keyed up”])

4. Common physical symptoms associated with PTSD: gastrointestinal problems, gynecological problems, weight gain or loss, unexplained pain or headaches, skin rashes and other skin problems.

5. Common emotional or psychological symptoms associated with PTSD: lack of energy, feeling tired all the time, feeling depressed or “down,” anxiety, worry or panic attacks.

6. PTSD screening: brief screening questionnaires are available to identify adults and children who may be experiencing PTSD. A positive response does not always mean that a person suffers from PTSD but that further evaluation is warranted. Because depression or other mental health problems are often comorbid with PTSD, a structured interview may be required to determine the overriding condition to guide optimal treatment.

7. PTSD assessment: components include questioning the individual about symptoms that developed following the traumatic event such as re-experiencing or reliving the event, avoiding reminders of the event; feeling detached from people, emotionally "numb," depressed, jumpy, irritable or always "on guard;" having problems with anger, focusing or concentrating; losing interest in things that used to be important; and having difficulty falling or staying asleep. Because PTSD sufferers are also at high risk for alcohol, drug, or other substance abuse problems or may behave recklessly, assessment should also include questioning the individual about these behaviors as well as their coping behaviors, health history, and personal and family psychosocial history.

8. Risk factors for PTSD include:
   a. Environmental factors (childhood trauma, neglect, abuse; head injury; mental illness; alcohol or drug abuse; personality and cognitive factors, etc.)
   b. Social factors (family, school, work or other social interactions or isolation, etc.)
   c. Social support (from family, friends, colleagues, peers)
   d. Genetic and epigenetic factors (altering biological or behavioral outcomes)
   e. Family history of PTSD
   f. Gender (females are twice as likely as males to have PTSD)

9. Medication: various medications are used for treating PTSD. Most PTSD sufferers receive more than one psychotropic drug, with about 80% receiving a selective serotonin reuptake
inhibitor (SSRI). Other common medications used to treat PTSD include benzodiazepines and non-benzodiazepine medications, other sleep agents, and antipsychotics.

10. Benefits and risks of PTSD interventions: there is insufficient evidence to support the combined use of medications, psychotherapy, exercise, and meditation for PTSD, however the latter three have minimal risks and there combined use may potentially enhance the beneficial effect. The efficacy and side effects of medications differ among individuals due to gene-gene and gene-environment interactions. Determining the best medication or combination of medications with the least side effects for a given individual may be a frustrating and costly trial and error process.

11. Drug metabolism: individuals metabolize drugs differently, due to differences in inherited variants in specific genes, gene-gene interactions, environmental influences, and other factors. The CYP450 genes influence how an individual metabolizes SSRIs and many other drugs. CYP450 genetic testing (pharmacogenomic testing) is currently being used to help guide the choice and dose of SSRIs to improve the effectiveness of treatment for adults with PTSD and/or depressive disorder, however professional organization and institutions views of this testing vary (see below).

12. CYP450 variants are also commonly referred to as polymorphisms, single nucleotide polymorphisms (SNPs; pronounced “snips”), mutations, or alleles (referring to a different [alternate] copy of a gene, such as the gene for type A blood vs. the gene for type B blood, or the gene for blue eyes vs. the gene for brown eyes).

13. CYP450 is a complex of more than 40 liver enzyme families: the CYP1, CYP2, and CYP3 families are important in the metabolism of many drugs. Each CYP family has multiple subfamilies, denoted by a capital letter after the CYP family number, which is followed by another number designating the polypeptide that encodes for a specific gene, e.g., CYP2C9. The terms ‘enzyme’ and ‘gene’ are often used interchangeably when referring to CYP450. Many drugs used to treat PTSD are metabolized through the CYP 2D6, C29, C19 and C1A2 pathways and the SLC6A4 and HTR2A serotonin receptor and transporter gene pathways.

14. Professional organization and institutional views: as of September 2013, The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) working group discourages the use of CYP450 testing of adults beginning treatment with SSRIs for non-psychotic depression until additional information is available from clinical trials. Others, such as the Children’s Hospital of Cincinnati

15. PTSD ethical and social implications related to genetic testing include: informed consent, the value and relevancy to treatment, and reimbursement as well as stigmatization associated with having a psychological condition.

16. PTSD research: research opportunities related to trauma and PTSD may be identified through the U.S. National Institutes of Health (NIH) and other resources. Areas needing additional research include:

a. Comparison of various treatment modalities singularly and in combination
b. Determining optimal prevention and treatment strategies for various populations and situations (e.g., women, children, veterans; sexual abuse, natural disasters, civil and other violence)
c. Determining the most valid and reliable assessment tools
d. Elucidating the underlying genetic contributions, biological processes and physiological markers
e. Epidemiology studies (patterns, causes, and effects)
SUGGESTED READINGS AND RESOURCES:

Post Traumatic Stress Disorder (PTSD)

PTSD Overview

Department of Veterans Affairs Trauma and PTSD http://www.ptsd.va.gov/


PTSD Course Online http://www.ptsd.va.gov/professional/ptsd101/course-modules/what-is-ptsd.asp


PTSD for the Public http://www.ptsd.va.gov/index.asp

PTSD Risk Factors


Sartor, C., McCutcheon, V., & Pommer, N. (2011). Common genetic and
www.ncbi.nlm.nih.gov/pubmed/21054919

www.ncbi.nlm.nih.gov/pubmed/16100858

PTSD and Family History
U.S. Surgeon General's Family History Resources to Create Your Own Family History Diagram to take to your health care provider.
http://www.hhs.gov/familyhistory

PTSD and Veterans


Wounded Warrior project

Restore Warriors
http://www.restorewarriors.org/

PTSD Treatment Options
www.ncbi.nlm.nih.gov/pubmed/21664365

www.ncbi.nlm.nih.gov/pubmed/22941845

www.ncbi.nlm.nih.gov/pubmed/23720785


**Mental Health**

Coping with Stress [http://www.cdc.gov/features/CopingWithStress/](http://www.cdc.gov/features/CopingWithStress/)


**Pharmacogenomics**


Mayo Clinic Summary:
Cytochrome P450 (CYP450) tests
http://www.mayoclinic.com/health/cyp450-test/MY00135

Selective serotonin reuptake inhibitors (SSRIs)
http://www.mayoclinic.com/health/ssris/MH00066


Public Health Genomics
Center for Disease Control and Prevention, Public Health Genomics
http://www.cdc.gov/genomics/about/AAG/

Ethical Issues


Mental Health Clinical Research
National Institute of Mental Health Clinical Trials

Traumatic Stress Research Program

PTSD Genetics Research


www.ncbi.nlm.nih.gov/pubmed/21306736

www.ncbi.nlm.nih.gov/pubmed/21356219

www.ncbi.nlm.nih.gov/pubmed/22119520

Additional Resources Related to Pharmacogenomics
Ethics and Informed Consent
http://www.scu.edu/ethics/practicing/focusareas/medical/pharmacogenomics.html

Frequently asked questions about Pharmacogenomics
www.genome.gov/27530645

Personalized Medicine (Pharmacogenomics)
http://learn.genetics.utah.edu/content/health/pharma

Pharmacogenomics Data Base (PharmGKB)
http://www.pharmgkb.org/

PharmGenEd
http://pharmacogenomics.ucsd.edu

Peggy’s Family History (as described in the case; all healthy unless otherwise noted)
Peggy: age 28, divorced 2 yrs ago; no children; c/o symptoms of PTSD and/or depression; no prior hx of depression
Mother: Rosa, age 63, nurse in the Vietnam War - experienced PTSD at ages 25-28, responded to counseling and medications; experienced unpleasant side effects from the meds
Father: Pete, age 65
Siblings: one sister, Eva, age 26, lives in CA
Maternal Grandmother: Louise, 83, dementia since age 70; depression at age 71 (NOS)
Maternal Grandfather: Edgar, 85, “prostate problems”
Paternal Grandmother: Mary, died at age 67, r/t diabetes
Paternal Grandfather: George, died at age 70, MVA
Ethnicity:
Maternal: Puerto Rican
Paternal: English
Religion: Catholic

Pedigree

Abbreviations for family history:
c/o = complaining of
hx = history
r/t = related to
NOS = not otherwise specified
MVA = motor vehicle accident