Designer Drugs & Treatment Implications: Will They Turn You into a Zombie? What Treatment Providers Need to Know about Synthetic Drugs

Vicki Staples, MEd, CPRP
ASU Center for Applied Behavioral Health Policy / Pacific Southwest ATTC
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Curriculum Development Collaborators

• Gulf Coast Addiction Technology Transfer Center
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What do you think?
Educational Objectives
At the end of this presentation, participants will be able to:

1. Identify the key characteristics and effects of synthetic drugs, most notably synthetic cannabinoids and synthetic cathinones.

2. Describe the current information available on the availability and patterns of synthetic drug use in the United States.

3. Explain strategies for communicating the dangers involved with synthetic drug use.
“Tales of Bath Salts and Zombie Cannibalism”

- Bath Salts made headlines in summer 2012 when a story of possible cannibalism was reported in Miami, FL
- The Miami-Dade Medical Examiner found no traces of bath salts, LSD, or synthetic marijuana in the perpetrator's system
- The sole psychoactive substance detected was cannabis (marijuana)
“Have your heard these stories about bath salts?”

• The man who slashed himself to remove the “wires” in his body
• The mother who left her demon-ridden 2-year-old in the middle of the highway
• The 21-year-old son of a family physician who, after snorting bath salts once, shot himself following 3 days of acute paranoia and psychosis, including hallucinations of police squad cars and helicopters lined up outside his house to take him away

KEY TERMS AND DEFINITIONS
How Psychoactive Substances Work

• Because of their chemical structure, alcohol and drugs have **dramatic effects** on neurotransmitters in CNS.

• Effects on:
  – Mental processes
  – Behavior
  – Perception
  – Alertness

## Commonly Used Psychoactive Substances

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol (liquor, beer, wine)</td>
<td>euphoria, stimulation, relaxation, lower inhibitions, drowsiness</td>
</tr>
<tr>
<td>Cannabinoids (marijuana, hashish)</td>
<td>euphoria, relaxations, slowed reaction time, distorted perception</td>
</tr>
<tr>
<td>Opioids (heroin, opium, many pain meds)</td>
<td>euphoria, drowsiness, sedation</td>
</tr>
<tr>
<td>Stimulants (cocaine, methamphetamine)</td>
<td>exhilaration, energy</td>
</tr>
<tr>
<td>Club Drugs (MDMA/Ecstasy, GHB)</td>
<td>hallucinations, tactile sensitivity, lowered inhibition</td>
</tr>
<tr>
<td>Dissociative Drugs (Ketamine, PCP, DXM)</td>
<td>feel separated from body, delirium, impaired motor function</td>
</tr>
<tr>
<td>Hallucinogens (LSD, Mescaline)</td>
<td>hallucinations, altered perception</td>
</tr>
</tbody>
</table>
“Designer” Psychoactive Substances

“Designer” Psychoactive Substances

Two classes:

1. **Stimulants**: mephedrone, MPDV, piperazines, “bath salts”

2. **Psychedelics**: 2C-B, mescaline, DMT, etc.

Differences in users:

1. Stimulant users similar to other ecstasy users; (shifting to mephedrone and MPDV due to shortage of Ecstasy?)

2. Psychedelic users started ecstasy use earlier; were more frequent users; used multiple substances; had more legal, mental health, and social problems.

# Examples of Major Stimulant Drugs

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DESCRIPTION</th>
</tr>
</thead>
</table>
| Mephedrone | 4-methyl-methcathinone; “Miaow”  
Similar to cocaine and MDMA (ecstasy) |
| Methylone | β-MDMA: 3,4-methylenedioxy-methcathinone; “Explosion”  
Similar to cocaine and MDMA (ecstasy) |
| MDPV      | 3,4-methylenedioxyprovalerone; MDPV; “NRG-1” (Brandt, 2010); “Ivory Wave”  
Stimulant with rapid onset; 2-4 hour duration of action |
| BZP       | 1-benzyl-piperazone  
Similar to amphetamine  
1/10 potency of d-methamphetamine |

## Examples of Major Psychedelic Drugs

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DESCRIPTION</th>
</tr>
</thead>
</table>
| 2C-I      | Phenethylamine, via PiHKAL; stimulant and hallucinogen  
Slow onset (1 hr); long duration of action (8-10 hr.) |
| 2C-B      | Phenethylamine, via PiHKAL; visuals  
Faster onset (1 hr.); shorter duration than 2C-I |
| 5-MeO-DMT | Tryptamine; naturally occurring (toad, shamantic brews)  
Smoked: almost immediate, very intense, short effect (<30 min) |
| DMT       | Tryptamine; naturally occurring  
Smoked: almost immediate, very intense, short effect (<20 min) |

A REVIEW OF SYNTHETIC CANNABINOIDS AND SYNTHETIC CATHINONES
Synthetic Drugs

• Not really “Spice,” “Bath Salts,” or “Incense”
• Chemically-based; not plant derived
• Complex chemistry
• Constantly changing to “stay legal”
• Need to prove “intended to use” to convict in some areas
Marijuana (Cannabis)

- Often called pot, grass, reefer, MJ, weed,
- A mixture of the dried, shredded leaves, stems, seeds, and flowers of *Cannabis sativa*—the hemp plant
- Most commonly used drug in the U.S.
- Delta-9-tetrahydrocannabinol (THC) is the main active ingredient in marijuana
- Common effects include: euphoria, relaxation, heightened sensory perception, laughter, altered perception of time, and increased appetite
- May also produce anxiety, fear, distrust, or panic, and can lead to severe mental health problems for some users.

Synthetic Cannabinoids (a.k.a. Spice)

- Wide variety of herbal mixtures
- Marketed as “safe” alternatives to marijuana
- Brand names include: K2, fake weed, Yucatan Fire, Skunk, Moon Rocks
- Labeled “not for human consumption”
- Contain dried, shredded plant and chemical additives that are responsible for their psychoactive effects.

SOURCE: NIDA. (2012). *NIDA DrugFacts: Spice (Synthetic Marijuana).*
Synthetic Cannabinoids (Spice)

- Mainly abused by smoking (alone or with marijuana); may also be prepared as an herbal infusion for drinking.
- The five active chemicals most frequently found in “Spice” products have been classified by the DEA as Schedule I controlled substances, making them illegal to buy, sell, or possess.

Synthetic Cannabinoids: The Major Compounds

a) Naphthoylindoles


b) Cyclohexylphenoles

\[ \text{CP-47,497-C8} \]

SOURCE: Agudelo et al. (2012). Effects of Synthetic Cannabinoids on the Blood Brain Barrier, Presented at 74th Annual CPDD.
The Emergence of Synthetic Cannabinoids

- **JWH-018/073** arrived early and have come and gone.
- **JWH-250** arrived a little later and has also cycled out.
- **JWH-081** was part of a second wave that has already completed its cycle.
- **JWH-122** was part of the same wave but has persisted in popularity and is part of the current scene.
- **AM-2201** was part of the same second wave and has gained in popularity, probably currently the most prevalent.
- **JWH-022** and **JWH-210** are showing signs of increasing popularity.
- Recent emergent drugs are the adamantoyl (**AM-1248**) and tetramethylcyclopropyl (**XLR-11** and **UR-144**) indoles which are ahead of the latest attempts to schedule these drug classes.

Timeline of Synthetic Cannabinoids and Spice Products

1964: THC isolated from Cannabis
1988: Synthesis of HU210
1995: Synthesis of JWH-018
2004: First Spice (K2) sold on the Internet
2008: First synthetic cannabinoids identified in Spice
2009: Spice banned in some European nations
2010: Spice banned in some US states
2011: Nine persons died in Sweden after consumption of "Krypton" (Kronstrand et al., 2011)

- Two young girls found intoxicated in US after smoking "Banana Cream Nuke" (Schneir et al., 2011)
- Two adolescents died in US after consumption of "K2" (Gay, 2010; Fisher, 2010)
- Three young boys found intoxicated in US after smoking "SpicyXXX" (Simmons et al., 2011)

Factors Associated with Spice Products’ Popularity

- They induce **psychoactive effects**
- They are **readily available in retail stores and online**
- The packaging is **highly attractive**
- They are **perceived as safe drugs**
- They are **not easily detectable** in urine and blood samples

Khat

• Pronounced “cot”
• Stimulant drug derived from a shrub (*Catha edulis*) native to East Africa and southern Arabia
• Use is considered illegal, because one of its chemical constituents, cathinone, is a Schedule I drug
• Khat found in the U.S. often comes in by mail from Africa

Synthetic Cathinones: “Bath Salts”

- Could be MDPV, 4-MMC, mephedrone, or methylone
- Sold on-line with little info on ingredients, dosage, etc.
- Advertised as legal highs, legal meth, cocaine, or ecstasy
- Taken orally or by inhaling
- Serious side effects include tachycardia, hypertension, confusion or psychosis, nausea, convulsions
- Labeled “not for human consumption” to get around laws prohibiting sales or possession

Synthetic Cathinones are $\beta$-keto (‘bk’) Analogs of Amphetamine

Methamphetamine

Methcathinone

4-Methylmethcathinone (Mephedrone)

3,4-Methylenedioxymethcathinone (Methylene)

3,4-Methylenedioxypyrovalerone (MDPV)
Sources and Continuing Availability

• A number of synthetic marijuana and bath salt products appear to originate overseas and are manufactured in the absence of quality controls and devoid of governmental regulatory oversight.

• The large profits from sales, plus the fact that these chemicals can be easily synthesized to stay one step ahead of control, indicate there is no incentive to discontinue retail distribution of synthetic cannabinoid products under the current statutory and regulatory scheme.

Federal Efforts to Ban Synthetic Drugs

• **Mar 2011**: Five synthetic cannabinoids were temporarily categorized as Schedule I substances under the CSA.

• **Oct 2011**: DEA exercised its emergency scheduling authority to control some of the synthetic substances used to manufacture bath salts; these synthetic stimulants are now designated as Schedule I substances.

• **Dec 2011**: House of Representatives approves the Synthetic Drug Control Act (HR 1254).

• **July 2012**: Congress passed and President Obama signed the *Synthetic Drug Abuse Prevention Act*.

Texas Poison Control Exposures and Effect of Controls

Synthetic Cannabis

Synthetic Cathinones

THE EFFECTS OF SYNTHETIC CANNABINOIDS AND SYNTHETIC CATHINONES
“People high on these drugs can get very agitated and violent, exhibit psychosis, and severe behavior changes...some have been admitted to psychiatric hospitals and have experienced continued neurological and psychological effects.”

(Dr. Rick Dart, AAPCC President)
Short-Term Effects of Synthetic Marijuana

- Loss of control
- Lack of pain response
- Increased agitation
- Pale skin
- Seizures
- Vomiting
- Profuse sweating
- Uncontrolled spastic body movements
- Elevated blood pressure
- Elevated heart rate
- Heart palpitations

In addition to physical signs of use, users may experience severe paranoia, delusions, and hallucinations.

Cannabis vs. Cannabinoids: Effects Seen in Clinical Cases

• **Most symptoms are similar to** cannabis intoxication:
  – Tachycardia
  – Reddened eyes
  – Anxiousness
  – Mild sedation
  – Hallucinations
  – Acute psychosis
  – Memory deficits

• **Symptoms not typically seen** after cannabis intoxication:
  – Seizures
  – Hypokalemia
  – Hypertension
  – Nausea/vomiting
  – Agitation
  – Violent behavior
  – Coma

Six States Report Cases of Kidney Damage Linked to Synthetic Marijuana

- Sixteen cases of kidney damage reported by CDC
  - All admitted to hospital
  - Five required hemodialysis
- Fifteen of the patients were male; ranged in age from 15 to 33, no history of kidney disease
- In early Feb 2013, UA-Birmingham reported 4 cases of previously healthy young men, whose acute kidney injury was associated with synthetic marijuana
  - Symptoms of nausea, vomiting, and abdominal pain
  - All four men recovered kidney function, and none required dialysis

# Clinical Symptoms of Synthetic Cathinone Use in Patients Admitted to the Emergency Department (N=236)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation</td>
<td>82%</td>
</tr>
<tr>
<td>Combative/Violent behavior</td>
<td>57%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>56%</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>40%</td>
</tr>
<tr>
<td>Paranoia</td>
<td>36%</td>
</tr>
<tr>
<td>Confusion</td>
<td>34%</td>
</tr>
<tr>
<td>Myoclonus/Movement disorders</td>
<td>19%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>17%</td>
</tr>
<tr>
<td>CPK elevations</td>
<td>9%</td>
</tr>
</tbody>
</table>

Bath Salts in Michigan Case Report – MMWR, May 2011

• First report to summarize epidemiology of bath salt ED cases
• Based on 35 people who had ingested, inhaled, or injected bath salts and subsequently visited a Michigan Emergency Department (ED) between 11/13/10 and 3/31/11
• Patients presented with hypertension, tachycardia, tremors, motor automatisms, mydriasis, delusions, and paranoia
• No relationship found between route of administration and severity of illness

Maine Reports Serious Infections Linked with Injection of Bath Salts

- Four cases of invasive Group A streptococcal infections
- Dangerous because it can cause infections of heart and bloodstream
- Two patients developed Streptococcal Toxic Shock Syndrome
  - Can cause rapid drop in blood pressure and organ failure
- One patient developed necrotizing fasciitis, a disease that progresses quickly, destroying muscles, fat, and skin tissue

THE EPIDEMIOLOGY OF SYNTHETIC DRUG USE
Number of Unique Types of Synthetic Drugs Identified Nationally: NFLIS (2010-2012)

(NOTE: Some 2012 NFLIS Lab reports will not be complete until March-April 2013)

Emerging Drug Items Identified in U.S. NFLIS Tox Labs: 2010-2012

(NOTE: Some 2012 NFLIS Lab reports will not be complete until March-April 2013)

Calls Received by U.S. Poison Control Centers for Human Exposure to Synthetic Marijuana, 2010 to July 2012

The number of calls in 2011 were more than double that in 2010

Past-Year Use of Illicit Drugs by High School Seniors (percent)

- Marijuana/Hashish: 36.4%
- Synthetic Marijuana: 11.4%
- MDMA (Ecstasy): 5.3%
- Hallucinogens: 5.2%
- Cocaine: 2.9%

SOURCE: University of Michigan, 2011 Monitoring the Future Study
Emergency Room Visits Related to Synthetic Marijuana

• In 2010, **11,406** ER visits were related to synthetic marijuana use
  • 78% male,
  • Mostly among teenagers (33%, 12-17) and young adults (35%, 18-25)

• Among patients aged 12-29, **59%** had no evidence of other substance use

• **76%** did not receive follow-up care upon discharge

• As a point of comparison, in 2010, there were **461,028** marijuana-related ER visits

Synthetic Cannabinoid Varieties 2010

- JWH-018: 63%
- JWH-073: 11%
- JWH-250: 13%

Synthetic Cannabinoid Varieties
2011

AM-2201
29%

JWH-250
12%

JWH-210
9%

JWH-122
12%

JWH-018
14%

Synthetic Cannabinoid Varieties 2012 (through 8/27/12)

AM-2201 53%

SYNTHETIC CANNABINOID 8%

JWH-210 9%

JWH-122 9%

Calls Received by U.S. Poison Control Centers for Human Exposure to Bath Salts, 2010 to July 2012

The number of calls in 2011 were over 20 times that in 2010

Synthetic Cathinone Varieties 2010

- Ethylcathinone: 32%
- Methcathinone: 37%
- Fluoromethcathinone: 16%
- MDPPP: 5%
- Naphyrone: 5%
- Butylone: 5%
Synthetic Cathinone Varieties

2011

FLUOROMETHCATHINONE 13%
BUTYLONE 11%

4-MEC 49%
4-MEPPP 3%
SUBSTITUTED CATHINONE 5%
PENTEDRONE 12%

Synthetic Cathinone Varieties 2012 (through 8/27/12)

- ALPHA-PBP: 64%
- BUTYLONE: 4%
- PENTEDRONE: 16%
- 4-MEPP: 3%

Challenges with Chromatography Screening

- Lack of availability of the reference standard for new drugs
- Variable quality of reference standards
- Lack of purity and labeled internal standards
- Chemical similarity of new drugs within a class requires great care with identification
- Sensitivity (correctly IDs the drug)

OTHER NOTABLE SYNTHETIC DRUGS – “NEW AND OLD”
MDMA (Ecstasy)

• 3, 4-methylenedioxy-methamphetamine
• Street terms: Adam, E, X, XTC, love drug, Molly
• A synthetic, psychoactive drug with both stimulant and hallucinogenic properties similar to methamphetamine and mescaline
• Adverse effects: enhanced physical activity, sweating, lack of coordination, mental confusion, jaw clenching, hyperthermia, and agitation

NIDA. (2010). *NIDA InfoFacts: MDMA (Ecstasy).*
Glimpses of the Current MDMA Situation

Results of Pill Tests Containing MDMA

- Australian EDRS reports drop in MDMA use from 52% in 2003 to 27% in 2011.
- Both Australia and UK report MDMA “drought.”
- Shift from PMK to safrole to make MDMA.
- Some experts predict return of high quality MDMA but from China, not BeneLux sources.

“Party Drugs” Identified by U.S. Toxicology Labs: 2005-2011

SOURCE: U.S. DEA, Office of Diversion Control, NFLIS data analysis by J.C. Maxwell.
2C-Phenethylamine

- A broad range of compounds that share a common phenylethanol-2-amine structure.
- Some are naturally occurring neurotransmitters (Dopamine and Epinephrine), while others are psychoactive stimulants (Amphetamine), entactogens (MDMA), or hallucinogens (the 2C-X series of compounds).
- 2C-X can be snorted or dissolved into a liquid and placed on blotter paper under the tongue.
- May last 6-10 hours; onset takes 15 min to 2 hours.
- Reports of seizures and renal failure.

Spread of 2C-Phenethylamine throughout the United States

Figure 5.1 2C-Phenethylamine Reports to NFLIS, by State, 2006

Figure 5.2 2C-Phenethylamine Reports to NFLIS, by State, 2010

Piperazines

- Frenzy, Bliss, Charge, Herbal ecstasy, A2, Legal Z, Legal E.
- Mainly available over internet and sold as ecstasy pills that are “safe.”
- Two classes: (1) benzylpiperazines (BZP) and (2) phenylpiperazines (TFMPP).
- Mimics effects of ecstasy (MDMA); dangerous with seizure disorders, psychiatric illness, or coronary disease.
- Adverse events included hypertension, reduced consciousness, psychotic episode, hallucinations, tachycardia, hyperthermia, coma. Could be toxic if combined with MDMA or amphetamines.

Benzylopiperazine (BZP) and trifluoromethyl-phenylpiperazine (TFMPP) identified in US Toxicology Labs (NFLIS).

<table>
<thead>
<tr>
<th>Year</th>
<th>BZP</th>
<th>TFMPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>274</td>
<td>106</td>
</tr>
<tr>
<td>2008</td>
<td>4,252</td>
<td>1,532</td>
</tr>
<tr>
<td><strong>2009</strong></td>
<td><strong>8,943</strong></td>
<td><strong>2,825</strong></td>
</tr>
<tr>
<td>2010</td>
<td>5,216</td>
<td>1,647</td>
</tr>
<tr>
<td>2011</td>
<td>3,536</td>
<td>1,225</td>
</tr>
<tr>
<td>½ 2012</td>
<td>1,082</td>
<td>367</td>
</tr>
</tbody>
</table>

SOURCE: U.S. DEA, Office of Diversion Control, NFLIS data analysis by J.C. Maxwell.
A Few Other Psychoactive Substances to Throw in the Mix...

- **Kratom** – opioid-like effects
- **Salvia divinorum** – hallucinogenic effects
- **Methoxetamine** – “legal ketamine”
Phencyclidine

- PCP, Angel Dust, Killer Weed
- Dissolved in embalming fluid ("Fry," "Amp," "Water, Water")
- Swallowed, sniffed, smoked on joints dipped in "Fry"
- Users report out-of-body strength

What is **DXM?** Dextromethorphan is a psychoactive drug found in common over the counter cough medicines.

Dextromethorphan (DXM)

- Dextromethorphan’s slang names include “Robo”.
- At high doses, may produce dissociative hallucinations (distance from reality, visual effects with eyes open and closed; perceptual changes, drug liking, mystical-type experiences similar to use of psilocybin.
- Can also produce tachycardia, hypertension, agitation, ataxia, and psychosis at high doses.
- Users of DXM engage in “dose dependent” behaviors in which they try to gauge the amount of the drug they take to produce the desired effects, which they call “plateaus”. Plateau is the mildest effect and the 5th plateau will guarantee a trip to the hospital.

Enter your weight in pounds: 150

Cough Syrup
Powder

Second Plateau
Strength: 2 mg/mL

You must drink between 85mL and 256mL of cough syrup to achieve your desired high!
CASE EXAMPLE, SAMPLE TREATMENT PROTOCOLS, AND CONCLUDING THOUGHTS
Case Example #1

You are a professional in a setting working with youth (e.g., counselor, educator, tutor, etc.). During your normal duties, you overhear a group of youth talking about their interest in trying bath salts or spice.

1. What messages would you want to communicate?
2. What strategies would you use to maintain trust but also being able to point out the possible dangers from using one of these synthetic drugs?
3. What initial assessment questions would you want to ask?
4. What alternative activities would you explore to using these drugs?
Synthetic Marijuana – Clinical Presentation

- Persistent depression
- Memory problems (can last for several weeks)
- Blunted affect
- Difficulty focusing
- Difficulty participating in clinical until stabilized
- Users also report elevated mood, relaxation, and altered perception
- Psychotic effects, such as extreme anxiety, paranoia, and hallucinations

Sample Clinical Treatment Protocol for Synthetic Cannabinoid Users

• Direct individual to emergency room via ambulance
• Consult a regional Poison Control Center
• Acute management consists of:
  – Supportive care with the use of benzodiazepines, if needed, to control agitation and anxiety
  – Observe until resolution of abnormal vital signs, vomiting, and psychiatric symptoms

Recognizing Bath Salt Intoxication

• Present with severe sympathetic stimulation:
  – Tachycardia
  – Hypertension
  – Hyperthermia
  – Seizures

• Present with profoundly altered mental status:
  – Severe panic attacks
  – Agitation
  – Paranoia
  – Hallucinations
  – Suicidal behavior

Sample Clinical Treatment Protocol for Synthetic Cathinone Users

- Supportive care
- Aggressive sedation with benzodiazepines (for agitation, seizures, tachycardia, and hypertension)
- Significant hyperthermia may require passive or active cooling
- Lab studies including electrolytes, renal and liver function tests, cardiac markers, and creatine kinase should be considered

What do you do if someone has taken a Spice Product or Bath Salts?

• Call your local poison center at 1-800-222-1222
  – 57 poison centers around the country have experts waiting to answer your call.
  – Experts can help you decide whether someone can be treated at home, or whether he or she must go to a hospital.

• Dial 9-1-1 immediately if they:
  – Stop breathing
  – Collapse
  – Have a seizure

In Summary: Key Points

• Despite widespread Internet availability and use among certain populations, health care providers remain largely unfamiliar with Spice products and Bath Salts.

• Research is needed to better understand the side effects and long-term consequences associated with the use of synthetic cannabinoids and synthetic cathinones.

• More toxicological identification of these new drugs, more information on the sources of them, as well as their distribution and patterns of use is needed to curtail future increases in use.
Resources for Continued Learning

- American Association of Poison Control Centers, www.aapcc.org
- Drug Enforcement Administration, www.dea.usdoj.gov
- European Monitoring Centre for Drugs and Drug Addiction, www.emcdda.europa.eu
- Refer to the *Synthetic Drugs Reference List* **
Thank you for your time!

For more information:
Jane C. Maxwell: jcmaxwell@mail.utexas.edu
**Beth Rutkowski: brutkowski@mednet.ucla.edu
Thomas E. Freese: tfreese@mednet.ucla.edu
Gulf Coast ATTC: http://www.attcnetwork.org/gulfcoast
Pacific Southwest ATTC: http://www.psattc.org