SESSION XXIV

DRUG COMBINATIONS

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Upon successfully completing this session the student will be able to:

- Explain the prevalence of polydrug use among drug impaired subjects and identify common combinations of drugs abused by those subjects.
- Describe the possible effects that combinations of drugs can produce on the major indicators of drug impairment.
- Define the terms "Null", "Overlapping", "Additive" and "Antagonistic" as they relate to polydrug effects.
- Identify the specific effects that are most likely to be observed in persons under the influence of particular drug combinations.

A. The Prevalence of Polydrug Use

Studies have shown that polydrug use is on the rise throughout the country. In the Los Angeles Field Validation Study (1985), nearly three-quarters (72%) of the subject's who were evaluated were found to have two or more drugs in their blood samples. The most familiar drug of all, alcohol, apparently is an especially popular "mixer" with other drugs. Alcohol routinely shows up in combination with virtually everything else, and often DREs encounter subject's who have consumed alcohol along with two or more other drugs.

Cannabis is another popular "mixer", and frequently shows up in combination with Cocaine, PCP and various other drugs. The "speedball", a combination of Cocaine and Heroin, remains popular, despite the well-publicized hazards of this particular mixture.

Polydrug use among suspected drug impaired drivers continues to be very common. Data collected from DREs from throughout the U.S. and entered into the national DRE tracking database indicates that approximately 37% of all cases where toxicology was conducted resulted in two or more drug categories detected.

DREs should not be surprised to encounter virtually any possible combination of drugs. DREs may find more polydrug users than single drug users. This means that if the DRE is to do a good job at interpreting the results of evaluations, they must understand the mechanisms of drug interaction.

B. Possible Effects of Drug Combinations

When a person ingests two or more different drugs, each drug may work independently. What the body will **exhibit**, however, is a combination of those effects.

Four types of combined effects can, and generally will, occur when two or more drug categories are used together.

1. The Null Effect

The simplest way to explain the Null Effect is to say that no action plus no action equals no action. Some specific examples may help clarify this.

One of the first things a DRE does when examining a subject is to check for HGN. We know that many drugs **do not affect nystagmus**. For instance, if we examined a subject that was under the influence of a CNS Stimulant and nothing else, we would not expect to observe nystagmus. Likewise, if we examined someone who was under the influence of Cannabis and nothing else, no nystagmus would be present. What do you expect we would see when we check for nystagmus in the eyes of someone who has used a CNS Stimulant and Cannabis in combination? Since neither drug independently has any affect on nystagmus, the combination also would not affect nystagmus: nothing plus nothing equals nothing.

Another example of the Null Effect would be found when we check the pupil size of a subject who was under the influence of a Dissociative Anesthetic and a CNS Depressant. Dissociative Anesthetics generally do not affect pupil size; neither does a CNS Depressant. The combination of these drugs will not affect the size of the pupils.

The Null Effect, then, means simply this: **If neither drug affects some particular indicator of impairment, their combination also will not affect that indicator**.

2. **The Overlapping Effect**

The Overlapping Effect comes into play when one drug **does affect** some indicator of impairment and the other drug has **no effect whatsoever** on that indicator. This is a case of "something plus nothing equals something".

Consider once again the example of a combination of a CNS Stimulant and Cannabis. We've already seen that this combination produces a Null Effect as far as nystagmus is concerned. But what about when we examine the subject's eyes for a Lack of Convergence? Cannabis **does** produce a Lack of Convergence, a CNS Stimulant doesn't. Therefore, the subject who is under the combined influence of Cannabis and a CNS Stimulant will exhibit a Lack of Convergence due to the independent effect of the Cannabis. This is an instance where the effects of the two drugs "overlap".

Another example of an Overlapping Effect would be the pupil size of a person who has taken a Dissociative Anesthetic in combination with a Narcotic Analgesic. A Dissociative Anesthetic doesn't have any effect on pupil size. Narcotic Analgesics cause constricted pupils. Therefore, the combination would also cause the pupils to constrict.

The Overlapping Effect boils down to: **Action plus no action equals action**.

3. **The Additive Effect**

The Additive Effect occurs when two drug categories both affect some indicator of impairment in the same way. In combination, these effects reinforce each other.

Once again, think of the combination of a CNS Stimulant and Cannabis. What will we find when we check this subject's pulse rate? Cannabis produces Tachycardia, so does a CNS Stimulant. When the two drugs are taken together, we can expect to observe tachycardia because the drugs reinforce each other for that particular indicator of impairment. That is, the effect is <u>additive</u>.

The simplest way to express the Additive Effect is to say "something plus the same something produces that same something". One thing we can't say for certain is how much the two drugs will reinforce each other. Sometimes the reinforced effect is as simple as "one plus one equals two". But at other times, the combined effect is much greater than the individual contributions of the two drugs, e.g., on the order of "one plus one equals five". We use the term Additive Effect to cover all situations where two drugs impact on some indicator in the same way.

You have already noticed that we have used one particular drug combination, Cannabis and a CNS Stimulant, to furnish examples of all three kinds of effects covered so far. This drives home the important point that drug interactions are often complex, and involve a number of different mechanisms operating at the same time.

4. **The Antagonistic Effect**

The Antagonistic Effect occurs when two drug categories affect some indicator in exactly the opposite ways. This is a case of "action plus opposing action". For example, suppose we check the blood pressure of someone who is under the combined influence of a Narcotic Analgesic and a CNS Stimulant; what are we likely to find?

The fact is, we're likely to find just about anything at all. The Narcotic Analgesic, independently, tends to produce hypotension, the CNS Stimulant, independently, usually produces hypertension. The two drugs may offset each other, as far as blood pressure is concerned, and the subject's blood pressure may wind up normal. On the other hand, if the CNS Stimulant effects are starting to wear off and the Narcotic Analgesic is still active in the subject's body, we might find the blood pressure down. Conversely, if the CNS Stimulant is active but the Narcotic Analgesic effects have not yet reached their peak, we might find the blood pressure up. When we deal with an Antagonistic Effect, we simply can't predict what the outcome will be.

C. Identifying Expected Indicators of Specific Combinations

On the next page, you will find the Cumulative Drug Symptomatology Matrix. This lists all of the expected effects of each drug category on the major indicators of impairment, and summarizes the general indicators, time parameters and methods of ingestion for each category. This matrix will be useful in identifying how specific combinations of drugs will interact to produce a variety of Null, Overlapping, Additive and Antagonistic Effects.

INDICATORS CONSISTENT WITH DRUG CATEGORIES

	CNS DEPRESSANTS	CNS STIMULANTS	HALLUCINOGENS	DISSOCIATIVE ANESTHETICS	NARCOTIC ANALGESICS	INHALANTS	CANNABIS
HGN	PRESENT	NONE	NONE	PRESENT	NONE	PRESENT	NONE
VGN	PRESENT (HIGH DOSE)	NONE	NONE	PRESENT	NONE	PRESENT (HIGH DOSE)	NONE
LACK OF CONVERGENCE	PRESENT	NONE	NONE	PRESENT	NONE	PRESENT	PRESENT
PUPIL SIZE	NORMAL (1)	DILATED	DILATED	NORMAL	CONSTRICTED	NORMAL (4)	DILATED (6)
REACTION TO LIGHT	SLOW	SLOW	NORMAL (3)	NORMAL	LITTLE OR NONE VISIBLE	SLOW	NORMAL
PULSE RATE	DOWN (2)	UP	UP	UP	DOWN	UP	UP
BLOOD PRESSURE	DOWN	UP	UP	UP	DOWN	UP/DOWN (5)	UP
BODY TEMPERATURE	NORMAL	UP	UP	UP	DOWN	UP/DOWN/NORMAL	NORMAL
MUSCLE TONE	FLACCID	RIGID	RIGID	RIGID	FLACCID	NORMAL OR FLACCID	NORMAL

FOOTNOTE: These indicators are those most consistent with the category, keep in mind that there may be variations due to individual reaction, dose taken and drug interactions.

(1) Soma, Quaaludes and possibly some anti-depressants usually dilate pupils.
(2) Quaaludes, ETOH and possibly some anti-depressants may elevate.
(3) Certain psychedelic amphetamines may cause slowing.
(4) Normal, but may be dilated.
(5) Down with anesthetic gases, up with volatile solvents and aerosols.
(6) Pupil size possibly normal.

MAJOR INDICATORS	CNS DEPRESSANTS	CNS STIMULANTS	HALLUCINOGENS	DISSOCIATIVE ANESTHETICS	NARCOTIC ANALGESICS	INHALANTS	CANNABIS
GENERAL INDICATORS	Disoriented Droopy eyes (Ptosis) Drowsiness Drunk-like behavior Gait ataxia Slow, sluggish reactions Thick, slurred speech Uncoordinated *NOTE: With Methaqualone, pulse will be elevated and body tremors will be evident. Alcohol and Quaaludes elevate pulse. Soma and Quaaludes dilate pupils.	Anxiety Body tremors Dry mouth Euphoria Exaggerated reflexes Excited Eyelid tremors Grinding teeth (Bruxism) Increased alertness Insomnia Irritability Redness to nasal area Restlessness Runny nose Talkative	Body tremors Dazed appearance Difficulty w/speech Disoriented Flashbacks Hallucinations Memory loss Nausea Paranoia Perspiring Poor perception of time and distance Synesthesia Uncoordinated NOTE: With LSD, piloerection may be observed (goose bumps, hair standing on end).	Blank stare Confused Chemical odor Cyclic behavior Difficulty w/speech Disoriented Early HGN Onset Hallucinations Incomplete verbal responses Increased pain threshold "Moon Walking" Muscle rigidity Non-communicative Perspiring Possibly violent Sensory distortions Slow, slurred speech Warm to touch	Constricted pupils Depressed reflexes Drowsiness Droopy eyelids (Ptosis) Dry mouth Euphoria Facial itching Nausea "On the Nod" Puncture marks Slow, low, raspy speech Slowed breathing NOTE: Tolerant users exhibit relatively little psychomotor impairment.	Bloodshot, watery eyes Confusion Disoriented Flushed face Intense headaches Lack of muscle control Non-communicative Odor of substance Possible nausea Residue of substance Slow, thick, slurred speech **NOTE: Anesthetic gases cause below normal blood pressure; volatile solvents and aerosols cause above normal blood pressure.	Body tremors Disoriented Debris in mouth Eyelid tremors Impaired perception of time & distance Increased appetite Marked reddening of conjunctiva Odor of Marijuana Possible paranoia Relaxed inhibitions
DURATION OF EFFECTS	Barbiturates: 1-16 hours Tranquilizers: 4-8 hours Methaqualone: 4-8 hours	Cocaine: 5-90 minutes Amphetamines: 4-8 hours Meth: 12 hours	Duration varies widely from one hallucinogen to another. LSD: 4-6 hours Psilocybin: 2-3 hours	PCP Onset: 1-5 minutes Peak Effects: 15-30 minutes Exhibits effects up to 4-6 hours DXM: Onset 15-30 min. Effects 3-6 hours	Heroin: 4-6 hours Methadone: Up to 24 hours Others: Vary	6-8 hours for most volatile solvents Anesthetic gases and aerosols – very short duration	2-3 hours – exhibit effects (Impairment may last up to 24 hours, without awareness effects.)
USUAL METHODS OF ADMINISTRATION	Oral Injected (occasionally)	Insufflation (snorting) Smoked Injected Oral	Oral Insufflation Smoked Injected Transdermal	Smoked (PCP) Oral Insufflation (PCP) Injected (PCP) Eye drops	Injected Oral Smoked Insufflation	Insufflation (Historically, have been taken orally.)	Smoked Oral
OVERDOSE SIGNS	Shallow breathing Cold, clammy skin Pupils dilated Rapid, weak pulse Coma Shallow breathing	Agitation Increased body temperature Hallucinations Convulsions	Long intense "trip"	Long intense "trip"	Slow, shallow breathing Clammy skin Coma Convulsions	Coma	Fatigue Paranoia

D. Specific Examples of Drug Combinations: An Exercise for the Student

On the final five pages of this session, you will find examples of specific drug combinations. The expected results for the first two of these combinations (Cannabis and Stimulants, and Dissociative Anesthetic and Narcotic Analgesic) have been worked out for you. Study those examples, then complete the work sheets for the three remaining combinations.

CANNABIS AND CNS STIMULANT IN COMBINATION

IMPAIRMENT INDICATOR	EFFECT DUE TO CANNABIS	EFFECT DUE TO CNS STIMULANT	TYPE OF COMBINED EFFECT	WHAT WILL WE SEE
HORIZONTAL GAZE NYSTAGMUS	NONE	NONE	NULL	NONE
VERTICAL GAZE NYSTAGMUS	NONE	NONE	NULL	NONE
LACK OF CONV.	PRESENT	NONE	OVERLAPPING	PRESENT
PUPIL SIZE	DILATED OR NORMAL	DILATED	OVERLAPPING OR ADDITIVE	DILATED
REACTION TO LIGHT	NORMAL	SLOW	OVERLAPPING	SLOW
PULSE RATE	UP	UP	ADDITIVE	UP
BLOOD PRESSURE	UP	UP	ADDITIVE	UP
BODY TEMP	NORMAL	UP	OVERLAPPING	UP
MUSCLE TONE	NORMAL	RIGID	OVERLAPPING	RIGID

DISSOCIATIVE ANESTHETIC AND NARCOTIC ANALGESIC IN COMBINATION

IMPAIRMENT INDICATOR	EFFECT DUE TO PHENCYCLIDINE	EFFECT DUE TO HEROIN	TYPE OF COMBINED EFFECT	WHAT WILL WE SEE
HORIZONTAL GAZE NYSTAGMUS	PRESENT	NONE	OVERLAPPING	PRESENT
VERTICAL GAZE NYSTAGMUS	PRESENT	NONE	OVERLAPPING	PRESENT
LACK OF CONV.	PRESENT	NONE	OVERLAPPING	PRESENT
PUPIL SIZE	NORMAL	CONSTRICTED	OVERLAPPING	CONSTRICTED
REACTION TO LIGHT	NORMAL	LITTLE OR NONE VISIBLE	OVERLAPPING	LITTLE OR NONE VISIBLE
PULSE RATE	UP	DOWN	ANTAGONISTIC	DOWN/ NORMAL/UP
BLOOD PRESSURE	UP	DOWN	ANTAGONISTIC	DOWN/ NORMAL/UP
BODY TEMP	UP	DOWN	ANTAGONISTIC	DOWN/ NORMAL/UP
MUSCLE TONE	RIGID	FLACCID	ANTAGONISTIC	NORMAL/ RIGID/ FLACCID

WORKSHEET #1

KETAMINE AND LSD

IMPAIRMENT INDICATOR	EFFECT DUE TO D/A	EFFECT DUE TO Hallucinogen (Hall)	TYPE OF COMBINED EFFECT*	WHAT WILL WE SEE
HORIZONTAL GAZE NYSTAGMUS				
VERTICAL GAZE NYSTAGMUS				
LACK OF CONV.				
PUPIL SIZE				
REACTION TO LIGHT				
PULSE RATE				
BLOOD PRESSURE				
BODY TEMP				
MUSCLE TONE				

*Null; Overlapping; Additive; or, Antagonistic

WORKSHEET #2

CANNABIS AND CNS DEPRESSANT

IMPAIRMENT INDICATOR	EFFECT DUE TO CANNABIS	EFFECT DUE TO DEPRESSANT	TYPE OF COMBINED EFFECT*	WHAT WILL WE SEE
HORIZONTAL GAZE NYSTAGMUS				
VERTICAL GAZE NYSTAGMUS				
LACK OF CONV.				
PUPIL SIZE				
REACTION TO LIGHT				
PULSE RATE				
BLOOD PRESSURE				
BODY TEMP				
MUSCLE TONE				

*Null; Overlapping; Additive; or, Antagonistic

WORKSHEET #3

CNS STIMULANT AND CNS DEPRESSANT

IMPAIRMENT INDICATOR	EFFECT DUE TO CNS STIMULANT	EFFECT DUE TO DEPRESSANT	TYPE OF COMBINED EFFECT*	WHAT WILL WE SEE
HORIZONTAL GAZE NYSTAGMUS				
VERTICAL GAZE NYSTAGMUS				
LACK OF CONV.				
PUPIL SIZE				
REACTION TO LIGHT				
PULSE RATE				
BLOOD PRESSURE				
BODY TEMP				
MUSCLE TONE				

*Null; Overlapping; Additive; or, Antagonistic