INTEGRATING ADDICTION MEDICINE INTO ADDICTION TREATMENT

NYS OFFICE OF ALCOHOLISM AND SUBSTANCE ABUSE SERVICES

BUREAU OF CLINICAL RESOURCES

ADDICTION MEDICINE UNIT

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BACKGROUND

- THE CHEMICAL DEPENDENCE TREATMENT SYSTEM HAS HAD LIMITED EXPOSURE TO THE EFFECTIVE USE OF MEDICATIONS IN THE TREATMENT OF ADDICTIONS
  - TREATMENT OF WITHDRAWAL
  - ANTABUSE THERAPY
  - METHADONE MAINTENANCE - THE REAL START OF ADDICTION MEDICINE TREATMENT WITH THE WORK OF DR. DOLE AND DR. NYSWANDER IN 1963

BACKGROUND

- HISTORICALLY, ABSTINENCE - BASED AND DRUG - FREE TREATMENT MEANT THE ELIMINATION OF USE, AND/OR RELIANCE ON, MEDICATION
- THIS EXPERIENCE HAS CHANGED WHEN THE ADDICTION TREATMENT SYSTEM BEGAN TO TREAT PERSONS WITH CO - OCCURRING DISORDERS

BACKGROUND

- RECENTLY THE EXPONENTIAL GROWTH OF NEURO - SCIENTIFIC RESEARCH HAS INCREASED THE KNOWLEDGE OF THE INTERACTION OF NEUROTRANSMITTERS, NEURORECEPTORS AND DISEASE

BACKGROUND

- O'MALLEY ET AL IN 1992 AND 1996 CONCLUDED THAT PSYCHOLOGICAL TREATMENT AND PHARMACOLOGICAL TREATMENT STRATEGIES ARE COMPLEMENTARY INSTEAD OF COMPETITIVE

- EFFECTIVE TREATMENT DEPENDS BOTH ON MULTIMODALITIES AND ACCEPTABILITY TO THE PATIENT

BACKGROUND

- THE SUCCESSFUL INTEGRATION OF MEDICINE AND BEHAVIORAL TREATMENTS PROVIDES ONE KEY TO UNLOCKING THE FUTURE OF SUCCESSFUL ADDICTION TREATMENT

ADDICTION MEDICINES

- ACAMPROSATE
- ANTABUSE
- BUPRENORPHINE
- CLONIDINE
- LOFEXIDINE
- METHADONE/LAAM
- NALTREXONE
- NALMEFENE
- NEURONTIN
- SSRI'S
- ZOLFRAN
- ZYBAN
- VACCINES

ACAMPROSATE

- CALCIUM ACETYLHOMOTAURINATE
- TRADENAME: CAMPRAL®
- CHEMICAL STRUCTURE SIMILAR TO THE NEUROTRANSMITTER GAMMA - AMINOBUTYRIC ACID (GABA).
- GABA IS THE MAJOR INHIBITORY NEUROTRANSMITTER AND ACAMPROSATE STIMULATES ITS TRANSMISSION, THUS DECREASING THE CRAVING FOR ALCOHOL

ACAMPROSATE

- IT ALSO HAS A BINDING SITE ON GLUTAMATE RECEPTORS, GLUTAMATE BEING AN EXCITATORY NEUROTRANSMITTER.
  - INHIBITS GLUTAMATE'S RELEASE
- WHEN ALCOHOL COMSUMPTION IS STOPPED, THERE IS A HYPEREXCITABLE STATE THAT IS AT LEAST PARTIALLY DUE TO THE GLUTAMATE SYSTEM. AMCAMPROSATE MAY RESTORE RECEPTOR TONE THAT CAN TAKE UP TO 12 MONTHS.

ACAMPROSATE

- THUS, THERE IS ATTENUATION OF THE SYMPTOMS OF ACUTE AND PROTRACTED ALCOHOL WITHDRAWAL

ACAMPROSATE

- WELL TOLERATED WITH MAJOR SIDE -EFFECT BEING INTESTINAL CRAMPS AND DIARRHEA
- NOT METABOLIZED BY THE LIVER AND IS ELIMINATED 90% UNCHANGED IN THE URINE
- THERE HAVE BEEN NO DRUG - DRUG INTERACTIONS REPORTED
- DOSING WAS 2000MG DIVIDED INTO TWICE DAY DOSING IN THE EUROPEAN STUDIES

ACAMPROSATE

- WHITWORTH AND COLLEAGUES SHOWED A RELAPSE RATE OF 19% IN A 12 WEEK STUDY PERIOD (23% WITH REVIA).
  - PATIENTS STATED THAT THEY “SEEMED TO LOSE INTEREST IN ALCOHOL”
  - EUROPEAN STUDIES INVOLVING OVER 4000 SUBJECTS HAD GOOD RESULTS IN 11 OUT OF 12 STUDIES, THOUGH THE DROP OUT RATE WAS HIGH (~50%)

ACAMPROSATE

- UNIVERSITY OF LAUSANNE, SWITZERLAND SHOWED INCREASE EFFECTIVENESS IF ACAMPROSTATE WAS COMBINED WITH ANTABUSE AND NO ADVERSE DRUG INTERACTIONS WERE NOTED

ANTABUSE

- BIS (DIETHYLTHIOCARBAMOYL DISULFIDE)
- AVAILABLE SINCE THE LATE 1940'S
- "AVERSION THERAPY"

ANTABUSE

- MECHANISM OF ACTION IS THE BLOCKADE OF THE METABOLISM OF ALCOHOL (OXIDATION) AND AN ACCUMULATION OF ACETALDEHYDE (5 -10 X'S INCREASE)
- ACETALDEHYDE ACCUMULATION PRODUCES THE "ANTABUSE REACTION"
  - RANGES FROM A FLUSH AND THROBBING IN THE HEAD AND NECK, TO NAUSEA, VOMITING, BREATHING DIFFICULTY, CHEST PAIN, HEART FAILURE AND POSSIBLE DEATH.

ANTABUSE

- ANTABUSE SHOULD NOT BE GIVEN TO ANYONE WITH:
  - HISTORY OF SEVERE HEART DISEASE
  - PSYCHOSIS
  - ALLERGY TO ANTABUSE
  - PREGNANCY
  - PARALDEHYDE USE
  - METRONIDAZOLE USE

ANTABUSE

- ANTABUSE SHOULD BE USED WITH CAUTION WITH:
  - HISTORY OF DIABETES
  - HISTORY OF SEIZURES
  - HISTORY OF LIVER DISEASE

ANTABUSE

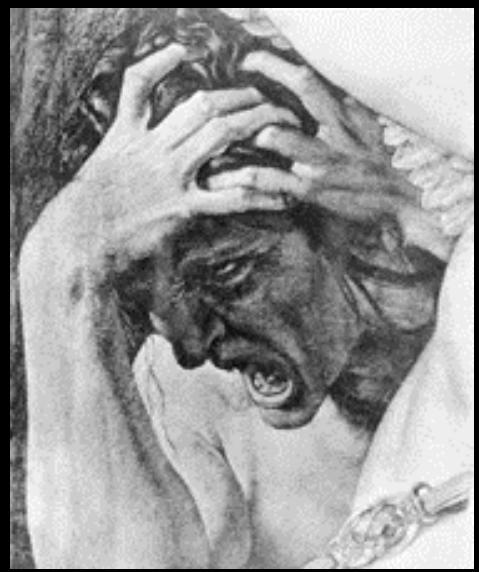
- ANTABUSE IS BEING STUDIED FOR TREATMENT OF COCAINE DEPENDENCE BY SEVERAL GROUPS INCLUDING:
  - CARROL ET AL - ADDICTION 1998
  - PETRAKIS ET AL - ADDICTION 2000

ANTABUSE

- CONCLUSIONS OF THE DISULFIRAM FOR COCAINE DEPENDENCE
  - 2 PILOTS AND 3 LARGER TRIALS ALL SHOW SIGNIFICANTLY MORE COCAINE FREE URINES: 51% VS. 35%
    - NO SERIOUS ADVERSE EFFECTS NOTED

BUPRENORPHINE - A NEW TREATMENT OPTION

- THEBAINE DERIVATIVE
  - MAKES THIS LEGALLY CLASSIFIED AS AN OPIATE
- PARTIAL OPIOID AGONIST
- INITIALLY USED AS AN ANALGESIC

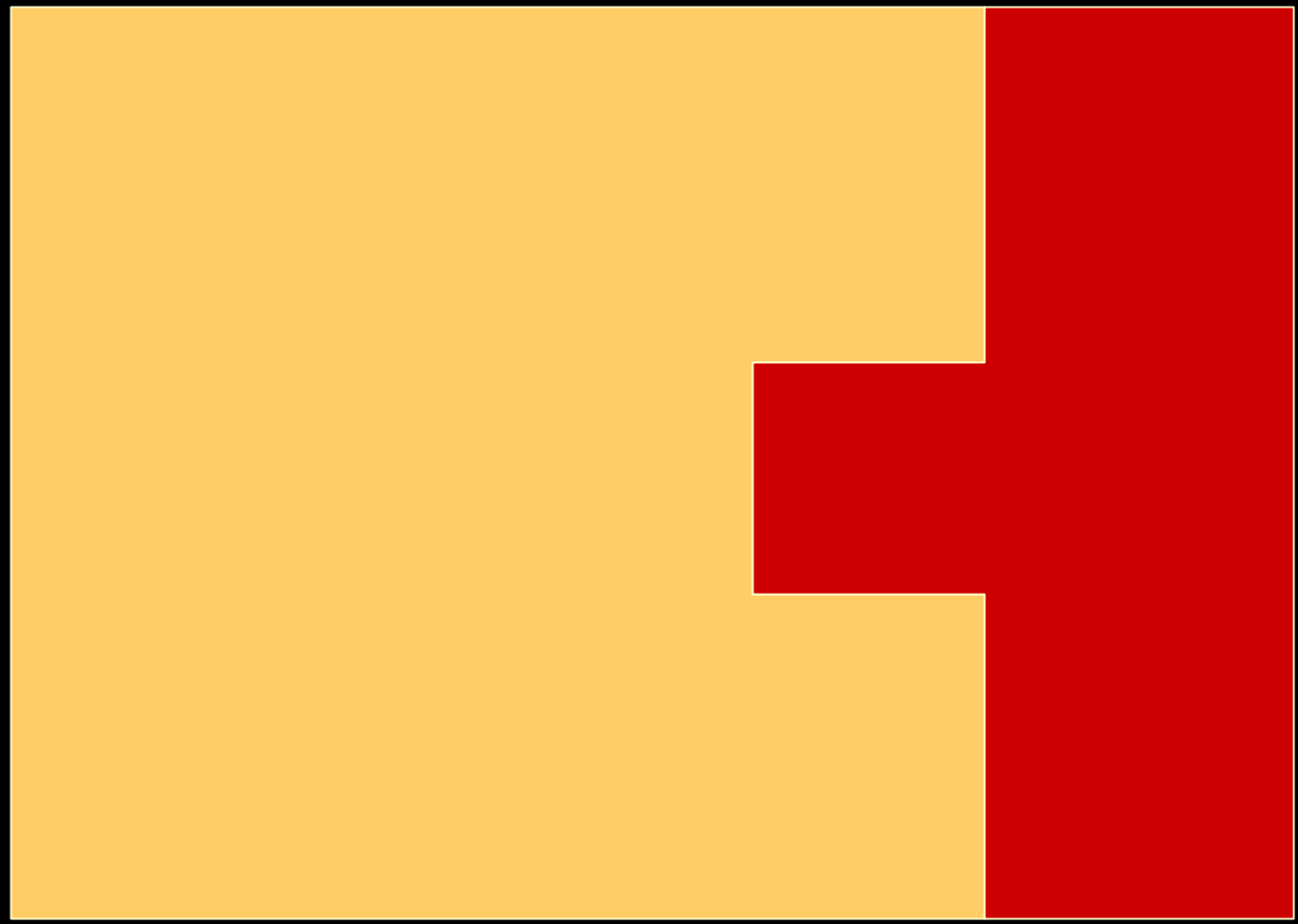


BRONSIO'S SCULPTURE OF PAIN

DEFINITIONS

- FULL AGONIST
  - DRUGS THAT ACTIVATE A RECEPTOR IN THE BRAIN
    - OCCUPY THE RECEPTOR AND TURN IT ON
    - INCREASING DOSES OF THE DRUG PRODUCE INCREASING RECEPTOR - SPECIFIC EFFECTS UNTIL A MAXIMUM EFFECT IS ACHIEVED
    - MOST ABUSED OPIOIDS ARE FULL AGONISTS

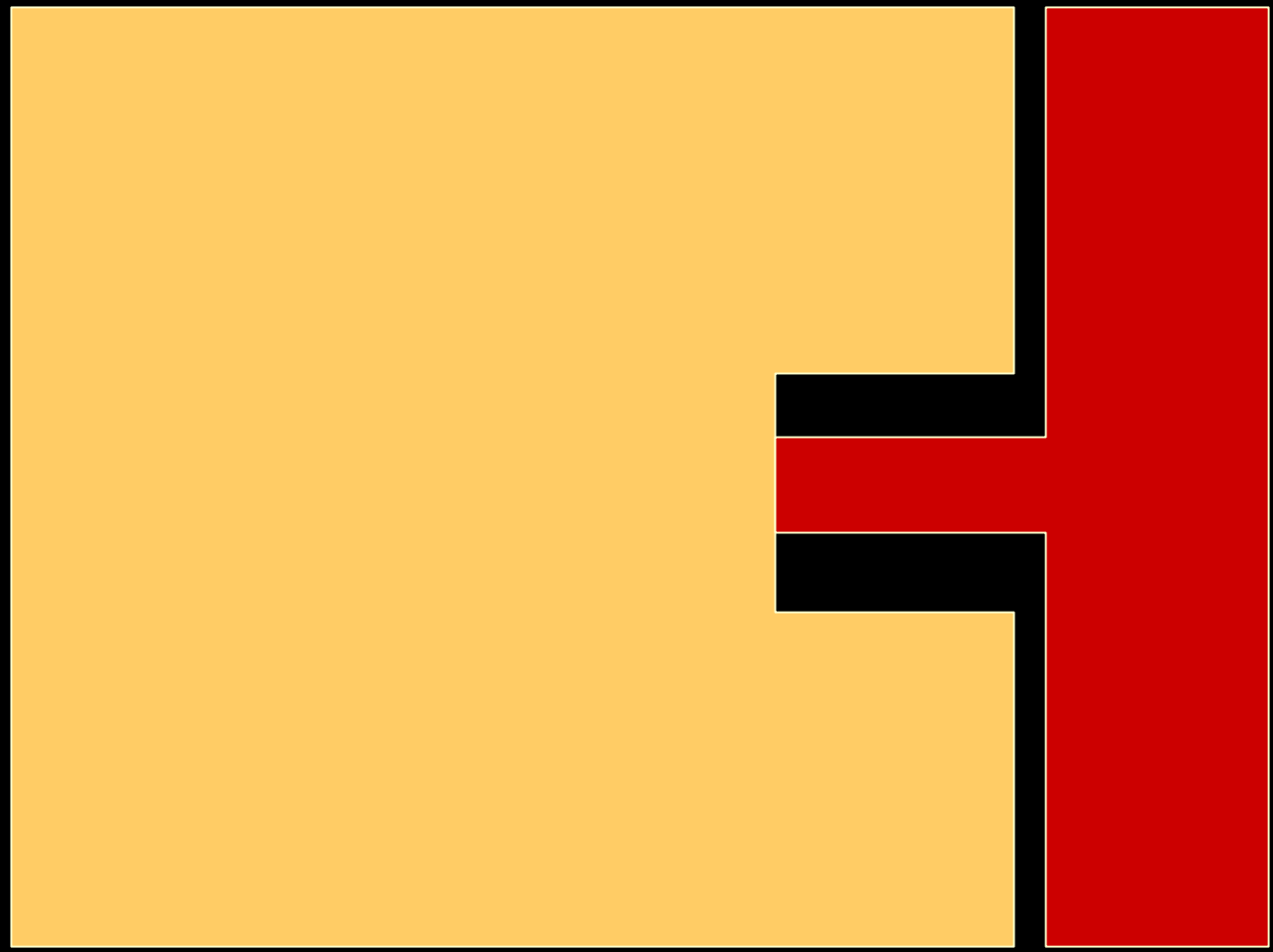
AGONIST



DEFINITIONS

- PARTIAL AGONIST
  - SIMILAR TO FULL AGONIST
  - BINDS TO AND ACTIVATES THE RECEPTOR
  - AT LOW DOSE, FULL AND PARTIAL AGONISTS ARE INDISTINGUISHABLE
  - AT HIGH DOSE, THERE IS NOT AS GREAT EFFECT AS THE FULL AGONIST

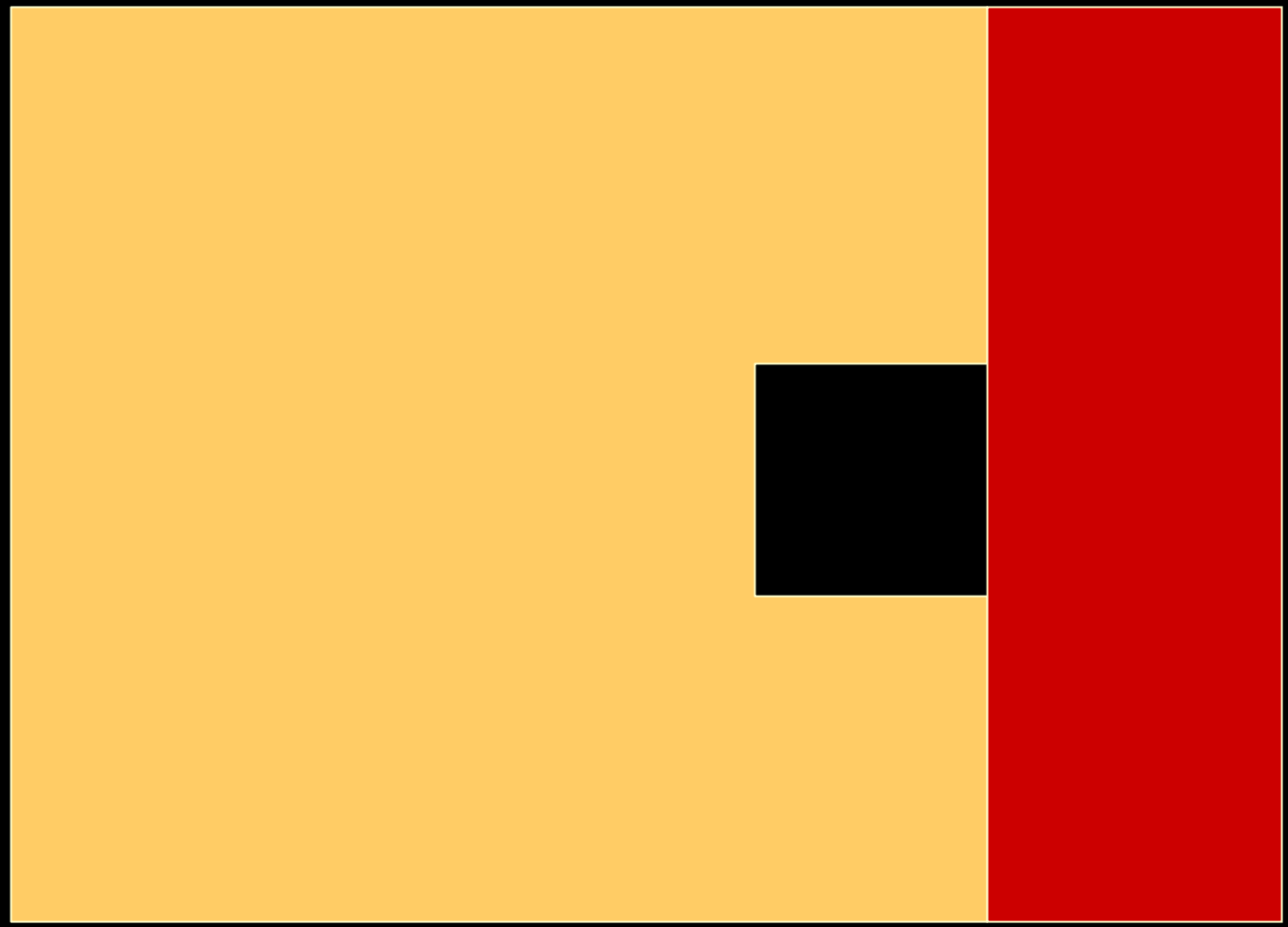
PARTIAL AGONIST



DEFINITIONS

- ANTAGONIST
  - BINDS TO RECEPTOR
  - EFFECTIVELY BLOCKS THE RECEPTOR
    - PREVENTS ACTIVATION BY AN AGONIST

ANTAGONIST



OPIATE RECEPTORS

- MU
- KAPPA
- DELTA
- EPSILON

OPIATE RECEPTORS

- MU
  - EUPHORIA
  - ANALGESIA
  - INDIFFERENCE TO PAIN
  - MIOSIS
  - RESPIRATORY DEPRESSION
  - INCREASE IN DOPAMINE

MU RECEPTOR

- MAYBE SUBSETS
  - MU-1 RESPONSIBLE FOR ANALGESIA
  - MU-2 RESPONSIBLE FOR RESPIRATORY DEPRESSION AND GI EFFECTS
- METHADONE AND HEROIN ARE EXAMPLES OF EXOGENOUS RECEPTOR STIMULANTS

OPIATE RECEPTORS

- KAPPA
  - ANALGESIA
  - DYSPHORIC AFFECT
  - DECREASE IN DOPAMINE
  - NO AGONIST AVAILABLE IN HUMANS
    - SIGNIFICANT HALLUCINATIONS

OPIATE RECEPTORS

- DELTA
  - ANALGESIA
  - WORKS THROUGH THE ENDOGENOUS ENKEPHALINS, ENDORPHINS AND DYNORPHINS

THERE ARE AT LEAST A DOZEN OTHER ENDOGENOUS PEPTIDES WITH OTHER SITES (EPSILON, LAMBDA)

EFFECTS DIFFER BY SPECIES, RECEPTOR AND DRUG DOSE USED

BUPRENORPHINE

- PARTIAL OPIOID AGONIST
  - AT LOW DOSE BEHAVES AS AN AGONIST
  - AT HIGH DOSES AS EITHER AN AGONIST OR ANTAGONIST
    - PARTIAL AGONIST AT THE MU RECEPTOR
    - ANTAGONIST AT THE KAPPA RECEPTOR
  - VERY HIGH AFFINITY FOR MU RECEPTOR
    - WILL DISPLACE MORPHINE, METHADONE

BUPRENORPHINE

- PARTIAL OPIOID AGONIST
  - DESIRABLE PROPERTIES
    - LOW ABUSE POTENTIAL
    - LOWER LEVEL OF PHYSICAL DEPENDENCE
    - SAFETY IF INGESTED IN OVERDOSE QUANTITIES
    - WEAK OPIOID EFFECT AS COMPARED TO METHADONE

BUPRENORPHINE

- PARTIAL OPIOID AGONIST
  - IF GIVEN TO A PATIENT MAINTAINED ON A FULL AGONIST, IT CAN PRECIPITATE AN ABSTINENCE SYNDROME DUE TO HIGH AFFINITY TO THE MU RECEPTOR
    - CANNOT EASILY OVERCOME THE BUPRENORPHINE EFFECT NOR CAN AN ANTAGONIST OVERCOME ITS EFFECT.

BUPRENORPHINE

- PHARMACOLOGIC USES
  - POTENT ANALGESIC
    - AVAILABLE IN MANY COUNTRIES AS A SUBLINGUAL TABLET (0.3 - 0.4 MG) CALLED **TEMGESIC®**
    - AVAILABLE IN THE U.S. AS AN PARENTERAL FORM CALLED **BUPRENEX®**
    - LOW DOSES FOR PAIN TREATMENT AS COMPARED TO ADDICTION TREATMENT (0.3 - 0.6 MG IM OR IV Q 6 HOURS)

BUPRENORPHINE

- PHARMACOLOGIC USES
  - TREATMENT OF ADDICTIONS*
    - PENDING IN THE U.S.
      - 2 & 8 MG SUBLINGUAL TABLETS MADE BY RECKITT & COLMAN CALLED **SUBUTEX®**
      - 2 & 8 MG SUBLINGUAL TABLETS WITH NALOXONE IN A 4:1 RATIO CALLED **SUBOXONE®**

*2/96 AVAILABLE IN FRANCE FOR OFFICE BASED TREATMENT - 50,000 PATIENTS

BUPRENORPHINE

- PHARMACOLOGIC USES
  - DOSES USED FOR OPIOID ADDICTION TREATMENT IS 1 -2 MG UP TO 16 - 32 MG
  - DURATION IS A FEW WEEKS TO YEARS?
  - TO REDUCE POTENTIAL FOR ABUSE THE COMBINATION TABLET WAS MADE
    - WORKS ON PRINCIPLE THAT NALOXONE IS 100 TIMES MORE POTENT BY INJECTION THAN BY THE SUBLINGUAL ROUTE
      - IF TAKEN S.L. BUP>>>>>>NALONXONE
      - IF TAKEN I.V. NALOXONE>>>>>BUP

BUPRENORPHINE

- SAFETY
  - IF SWALLOWED ACCIDENTIALLY BY A NON-PHYSICALLY DEPENDENT PERSON DUE TO POOR ORAL BIOAVAILABILITY THERE IS **VIRTUALLY NO OPIOID EFFECT**

BUPRENORPHINE

- SIDE EFFECTS
  - SIMILAR TO OTHER MU AGONISTS THOUGH LESS SO
    - NAUSEA
    - VOMITING
    - CONSTIPATION

*NO DISRUPTION IN COGNITIVE AND PSYCHOMOTOR PERFORMANCE

*NO HEPATIC TOXICITY

BUPRENORPHINE

- TERATOGENESIS
  - LIMITED REPORTS
    - ONE STUDY FOUND NO SIGNS OF PHYSICAL DEPENDENCY IN NEONATES OF HEROIN ADDICTED MOTHERS TAKING BUPRENORPHINE

BUPRENORPHINE

- DETERMINING APPROPRIATENESS FOR TREATMENT
  - A CANDIDATE SHOULD
    - HAVE AN OBJECTIVELY ASCERTAINED DIAGNOSIS OF OPIOID DEPENDENCE
    - BE INTERESTED IN TREATMENT FOR OPIOID DEPENDENCE
    - HAVE NO CONTRAINDICATION TO BUPRENORPHINE USE
    - BE EXPECTED TO BE REASONABLY COMPLIANT WITH SUCH TREATMENT
    - UNDERSTAND THE BENEFITS AND RISKS OF BUPRENORPHINE TREATMENT
    - BE WILLING TO AGREE TO FOLLOW SAFETY PRECAUTIONS FOR BUPRENORPHINE TREATMENT
    - AGREE TO BUPRENORPHINE TREATMENT AFTER REVIEW OF OTHER TREATMENT OPTIONS

CLONIDINE

- TRADENAME = CATAPRES®
- INITIAL INDICATION - TREATMENT OF HYPERTENSION
  - DECREASES NE RELEASE
    - DILATES BLOOD VESSELS
    - DECREASES BLOOD PRESSURE
- USEFUL IN TREATMENT OF OPIATE, ALCOHOL AND NICOTINE WITHDRAWAL

CLONIDINE

- SIDE EFFECTS
  - DECREASE IN BLOOD PRESSURE
  - DRY MOUTH
  - SEDATION

CLONIDINE

- WHEN USED FOR OPIATE WITHDRAWAL - LETHARGY, RESTLESSNESS, CRAVINGS ARE NOT REDUCED WELL
  - PATCHES AND PILL PROTOCOLS

CLONIDINE

- GLASSMAN ET AL SHOWED THAT CLONIDINE REDUCED THE INTENSITY OF CRAVING FOR TOBACCO

LOFEXIDINE

- SIMILAR TO CLONIDINE
- WORKS THRU THE NE SYSTEM
- LESS HYPOTENSION SEEN IN PATIENTS THAN THOSE TREATED WITH CLONIDINE

LOFEXIDINE

- CURRENT PHASE III TRIAL OF 3.2 MG LOFEXIDINE VERSUS PLACEBO IN AN OPIATE DEPENDENT POPULATION UNDERGOING WITHDRAWAL
- MAY BE TESTED FOR PREVENTION OF RELAPSE

METHADONE

- SYNTHETIC NARCOTIC DEVELOPED IN GERMANY IN WW II
- 1963 USED FOR OPIATE DEPENDENT PATIENTS
- 1972 APPROVED BY THE FDA FOR TREATMENT OF OPIATE DEPENDENT PATIENTS
- > 120,000 PATIENTS IN THE US IN MMTP

LAAM

- 1 - ALPHA - ACETYLMETHODOL ACETATE
- LONG ACTING, ORALLY ACTIVE ANALOLG OF METHADONE
- APPROVED FOR USE BY THE FDA IN 1993

THEORIES OF NARCOTIC ADDICTION IMPLICATIONS OF METHADONE MAINTENANCE

Prevents the *"off and on"* switch of fluctuating opioid blood levels that lead to euphoria alternating with cravings...

Continuous occupation of the endogenous ligand-opioid receptor system allow interacting physiological and behavior systems to become normal.

The patient is functionally normal.

Dole,Vincent P.
JAMA,
Nov 25,1988
Vol.260,No. 20

RATIONALE FOR OPIOID AGONIST MEDICATIONS

- OPIOID AGONIST TREATMENT
  - MOST EFFECTIVE TREATMENT FOR OPIOID DEPENDENCE
  - CONTROLLED STUDIES HAVE SHOWN SIGNIFICANT
    - DECREASES IN ILLICIT OPIOID USE
    - DECREASES IN OTHER DRUG USE
    - DECREASES IN CRIMINAL ACTIVITY
    - DECREASES IN NEEDLE SHARING
    - IMPROVEMENTS IN PROSOCIAL ACTIVITIES
    - IMPROVEMENTS IN MENTAL HEALTH

LAAM

- ADVANTAGES OVER METHADONE
  - SLOWER ONSET
  - LONGER DURATION OF ACTION
    - ADMINISTER 3 TIMES /WEEK SO LESS DIVERSION
    - 1.2 - 1.3 TIMES THE PATIENT'S USUAL METHADONE DOSE
- DISADVANTAGES
  - ROXANNE/FDA ISSUED BLACK BOX WARNING AS THERE IS THE POTENTIAL FOR CARDIAC ARRHYTHMIAS (TORSADES de POINTES)

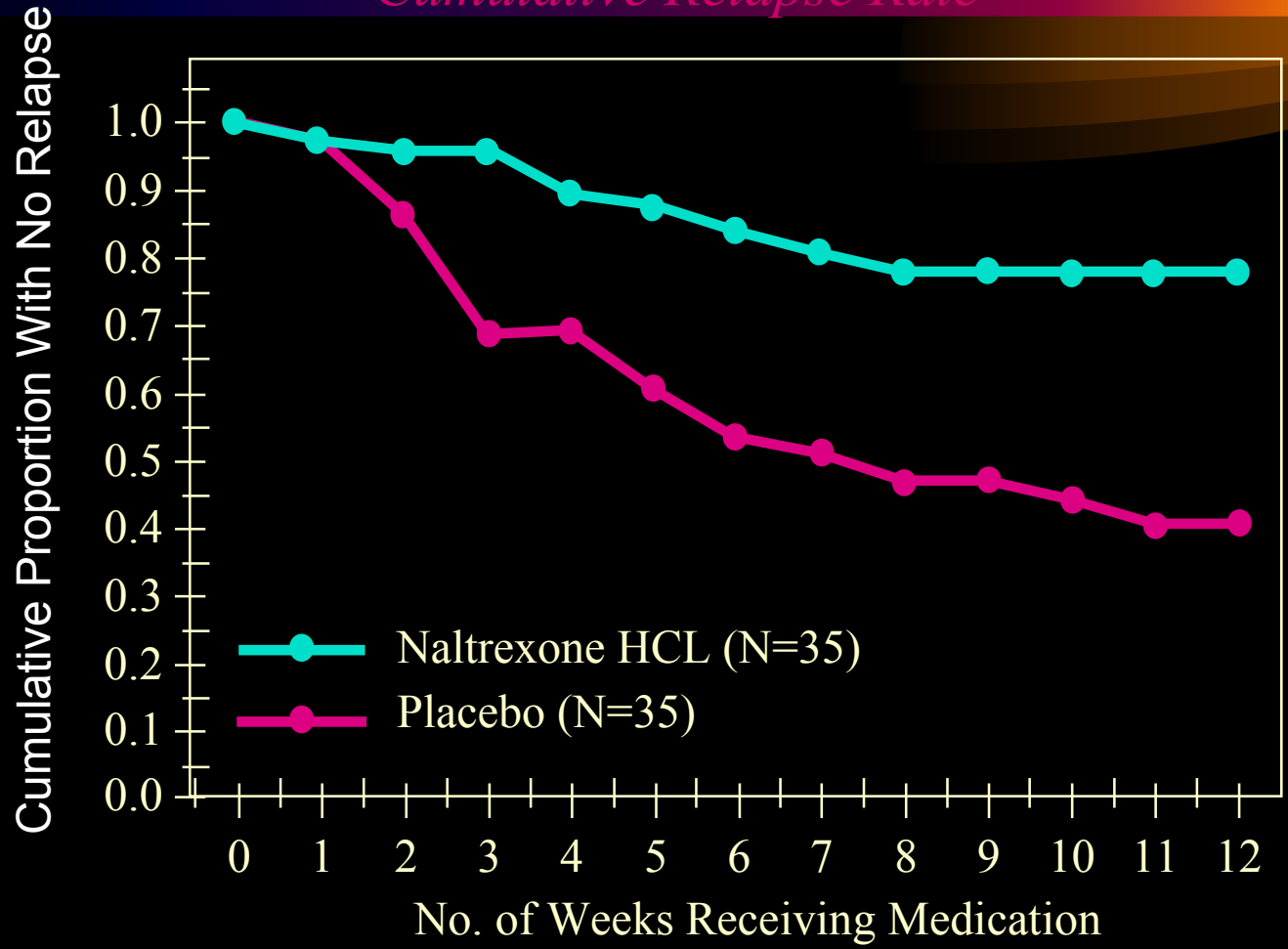
NALTREXONE

- FOR OPIATE ABUSERS
  - MARKETED AS TREXAN®
  - OPIATE RECEPTOR BLOCKER OR ANTAGONIST
  - LONG LASTING EFFECT AFTER ORAL DOSING (1- 3 DAYS)
  - NEW RESEARCH BEING CONDUCTED ON IMPLANTABLE SLOW RELEASE FORMULAS THAT LAST 6 - 8 WEEKS AND WILL IMPROVE COMPLIANCE AND THUS SUCCESS

NALTREXONE

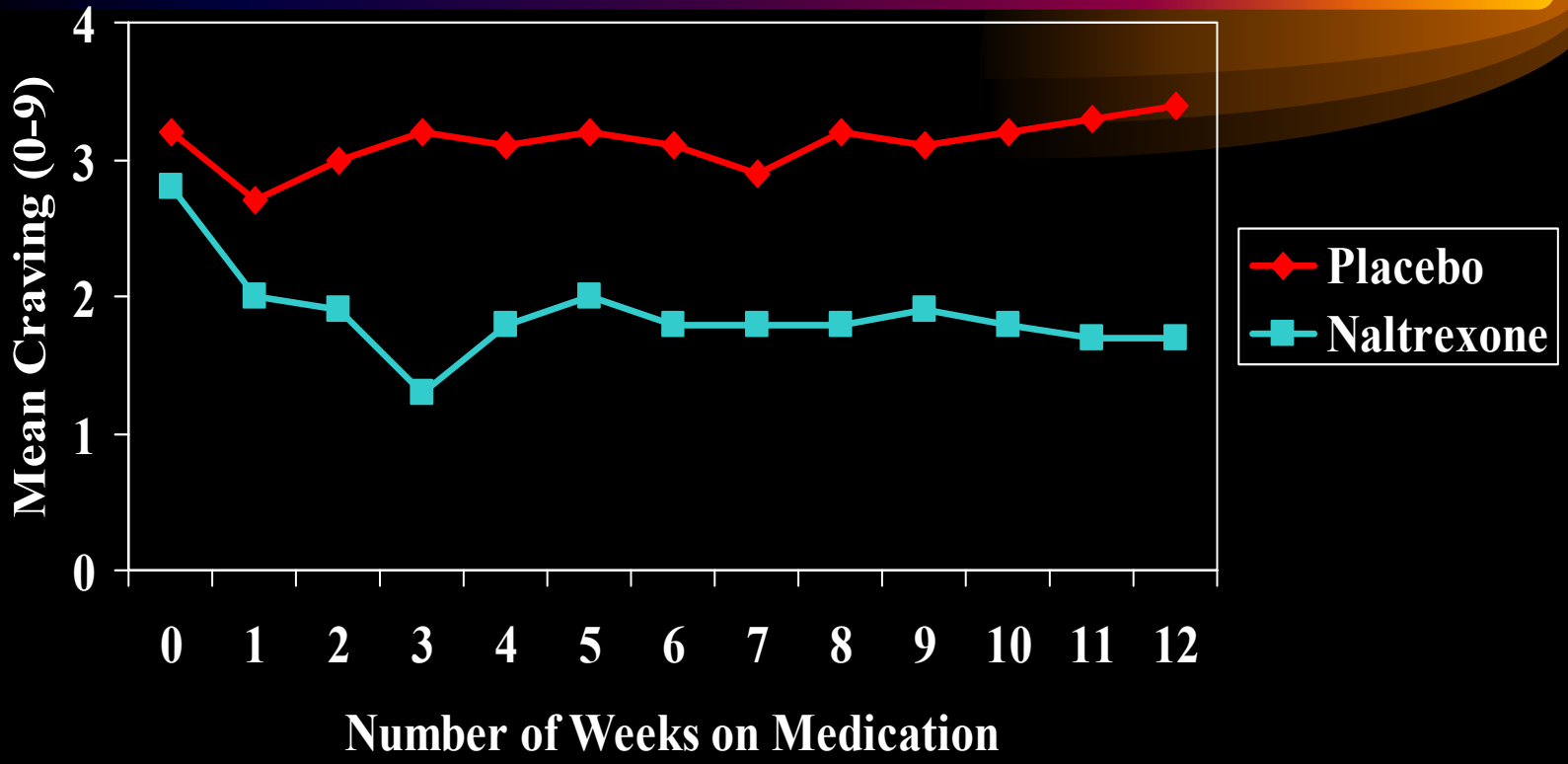
- FOR ALCOHOL ABUSERS
  - MARKETED AS ReVia® SINCE 1994
  - BLOCKS PLEASURABLE EFFECTS OF ALCOHOL(ATTENUATES STIMULATORY EFFECTS) AND REDUCES CRAVING
    - IN ONE STUDY, MEDICATION FOR 10 WEEKS; ABSTINENCE INCREASED FROM 37% IN CONTROL GROUP TO 89%.
    - IF SUBJECTS DID DRINK, THE NUMBER OF DRINKS DROPPED FROM 9.5 TO 2.5

NALTREXONE IN THE TREATMENT OF ALCOHOL DEPENDENCE



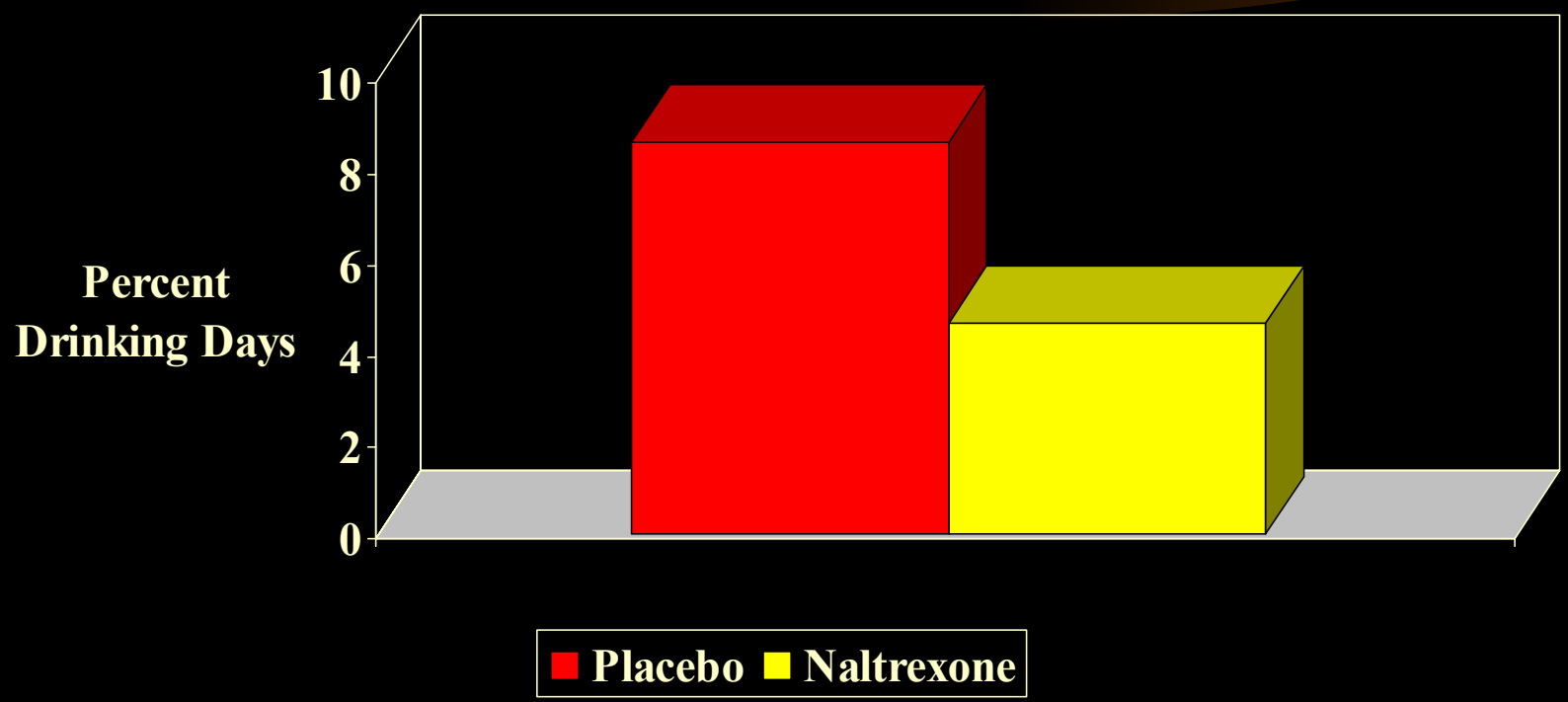
Volpicelli et al., 1992

MEAN CRAVING SCORES



Volpicelli et al., 1992

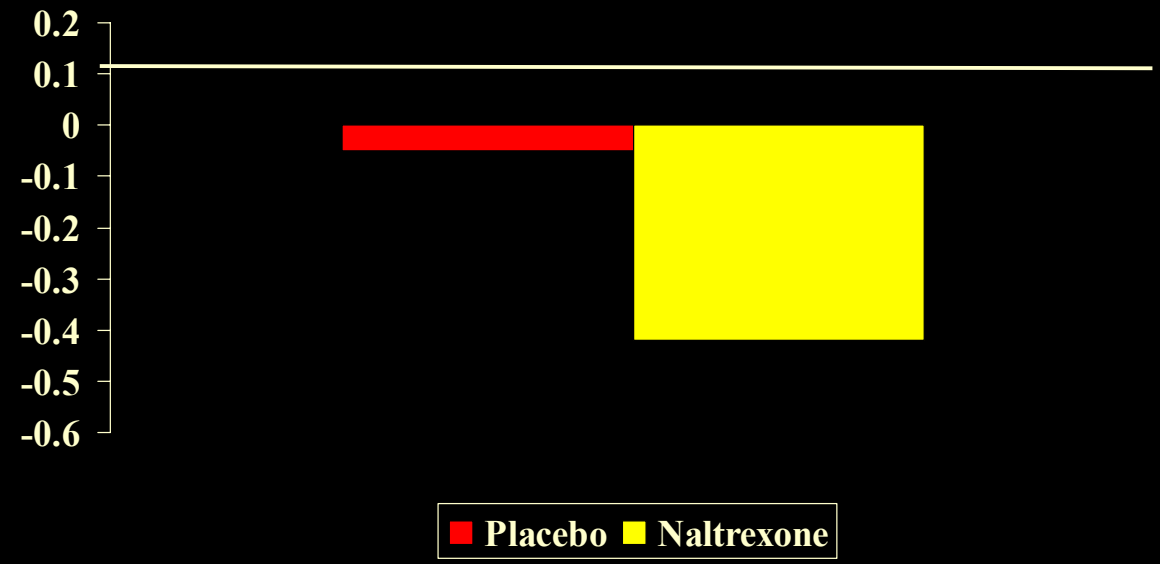
DRINKING DAYS WHILE ON MEDICATION



Volpicelli 1992, 1994

SUBJECTIVE “HIGH”

+1 = increased high
0 = no change in high
–1 = decreased high

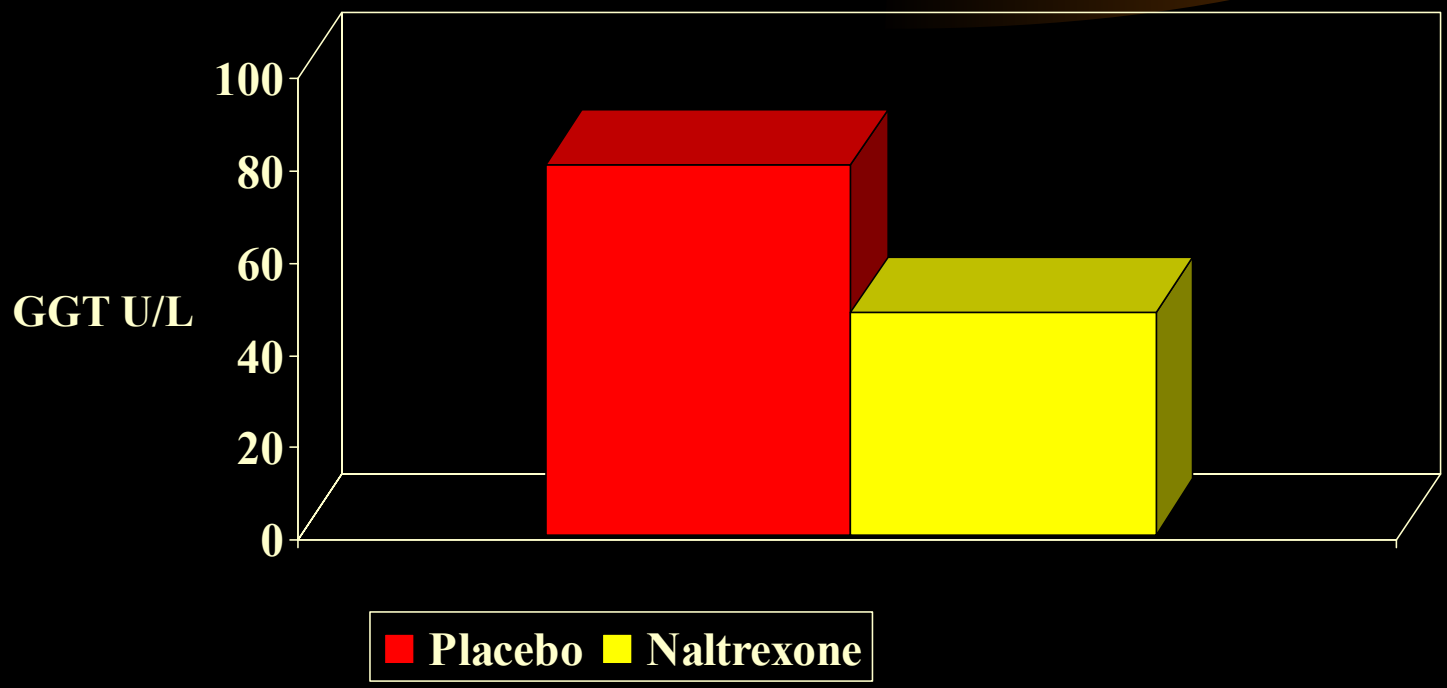


Volpicelli 1992, 1994

NALTREXONE

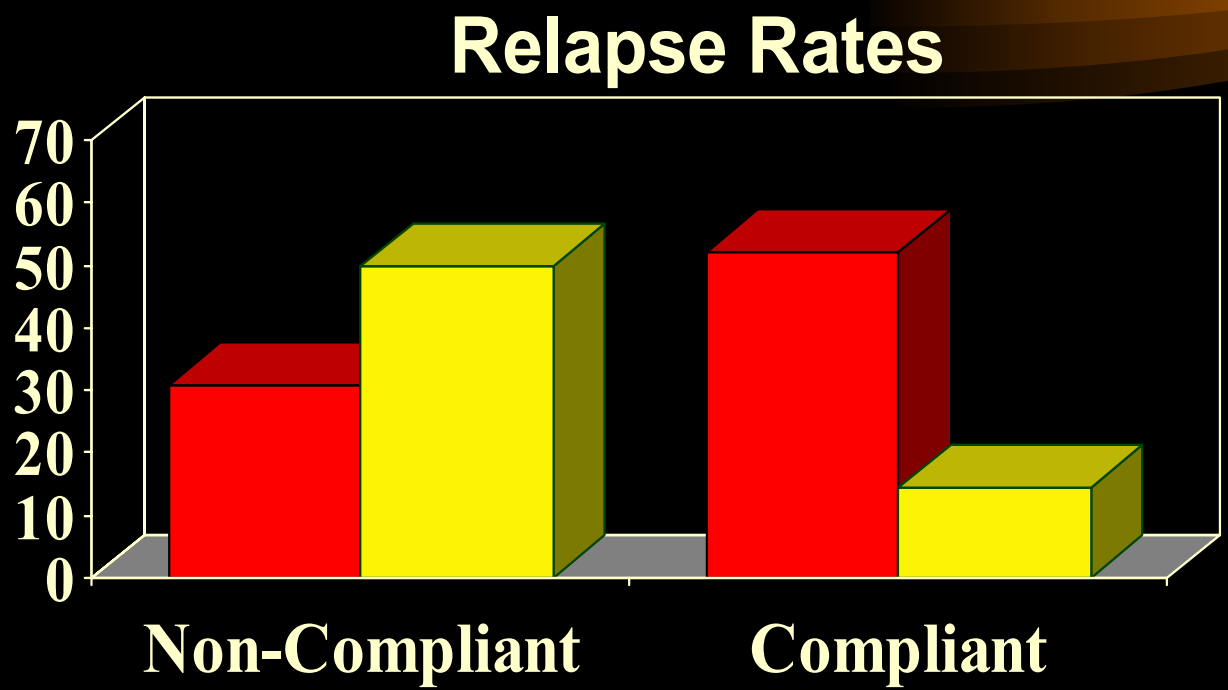
- SAFE
- MOST COMMON SIDE - EFFECT IS NAUSEA
- LIVER CAN BE AFFECTED AT HIGH DOSES
- COUNSELING AND SUPPORT GROUPS MUST ACCOMPANY THE USE OF THIS MEDICATION

GGT VALUES AT THE END OF THE STUDY



Volpicelli 1992, 1994

MEDICATION COMPLIANCE AND TREATMENT OUTCOME



Volpicelli et al., 1997

SIDE EFFECTS WITH 50 MG/DAY NALTREXONE

	Months 1-3	
	Naltrexone N=54	Placebo N=45
Headaches	20.4	11.1
Agitation/Anxiety	16.7	17.8
Nausea	13.0	4.4
Vomiting	0	2.2
Increased Sexual Desire	14.8	15.6

Volpicelli et al., 1995

SIDE EFFECTS WITH 100 MG/DAY NALTREXONE

	Months 1-3	
	Naltrexone N=119	Placebo N=61
Headaches	19.3	13.1
Agitation/Anxiety	10.1	13.1
Nausea	11.8 *	3.3
Vomiting	6.7	1.6
Increased Sexual Desire	5.9	6.5

Volpicelli et al., 2001

STARTING AND ENDING NALTREXONE TREATMENT

- THERE MAY BE FEWER SIDE EFFECTS WITH NALTREXONE WHEN INITIATED FOLLOWING ALCOHOL DETOXIFICATION
- SHORT-TERM NALTREXONE TREATMENT (3 MONTHS) MAY NOT BE AS EFFECTIVE AS LONG-TERM TREATMENT
- THE USE OF CBT THERAPY IN CONJUNCTION WITH NALTREXONE TREATMENT MAY PROVIDE SYNERGISTIC EFFECTS WHEN NALTREXONE IS STOPPED
- NALTREXONE MAY BE USED ON AN AS-NEEDED BASIS FOLLOWING A COURSE OF DAILY NALTREXONE

NALTREXONE

- DEPOT NALTREXONE - WORK BEING DONE BY COMER, COLLINS, NUWAYSER, KLEBER AND FISCHMAN

NALTREXONE

- CLINICAL TRIALS OF EFFECTIVENESS (RANDOMIZED AND PLACEBO CONTROLLED)
  - INITIAL WAS VOLPICELLI AND O'MALLEY
  - 6 FOUND NALTREXONE EFFECTIVE THOUGH RELAPSE DEFINITION DIFFERED (5 OR > DRINKS ON 1 OCCASION, 5 OR > DRINKING OCCASIONS IN 1 WEEK, ARRIVING AT CLINIC INTOXICATED)
  - 1 FOUND NALTREXONE NOT EFFECTIVE
  - META - ALANLYSIS: MODERATELY EFFECTIVE
  - NEJM KRYSTAL ET AL DEC 13, 2001
    - NOT EFFECTIVE IN MEN WITH CHRONIC, SEVERE ALCOHOL DEPENDENCE

NALTREXONE

- CLINICAL TRIALS - SPECIAL POPULATIONS
  - COMBINATION WITH SSRI'S, ACAMPROSATE, AND ONDANSETRON
  - EARLY PROBLEM DRINKERS
  - ALASKAN NATIVES
  - EATING DISORDER PATIENTS
  - PTSD PATIENTS
  - NICOTINE DEPENDENT PATIENTS

CONCLUSIONS

- ESPECIALLY EFFECTIVE IN SUBJECTS WITH A STRONG FAMILY HISTORY OF ALCOHOLISM, HIGH LEVELS OF INITIAL CRAVING, AND FOR SUBJECTS WHO RELIABLY TAKE THE MEDICATION
- SAFE IN DOSES OF 100 MG PER DAY
- EFFECTIVE IN A VARIETY OF TREATMENT SETTINGS INCLUDING PRIMARY SETTINGS WHERE MOTIVATION TO STAY IN TREATMENT AND TAKE MEDICATIONS IS SUPPORTED
- LONG-TERM TREATMENT (9 MONTHS) IS MORE EFFECTIVE THAN SHORT-TERM TREATMENT (3 MONTHS)

NALMEFENE

- CURRENTLY BEING USED IN ANESTHESIA TO REVERSE THE EFFECTS OF NARCOTIC PAIN RELIEVERS
- OPIATE ANTAGONIST (WORKS ON ALL OPIATE RECEPTORS)

NALMEFENE

- APPEARS TO LAST LONGER AND BE A MORE POTENT DOPAMINE BLOCKER THAN NALTREXONE
- FOUND TO REDUCE CRAVINGS AND PREVENT RELAPSE IN ALCOHOL DEPENDENT PATIENTS
  - STUDIES SHOW THAT PATIENTS RECEIVING NALMEFENE WERE 2.4 TIMES LESS LIKELY TO RELAPSE TO HEAVY DRINKING THAN THOSE IN THE CONTROL GROUP

NALMEFENE

- DR. BARBARA MASON'S WORK SHOWS IN A 12 WEEK TRIAL THAT PATIENTS TREATED WITH NALMEFENE WERE 2.4 TIMES LESS LIKELY TO RELAPSE WITH ALCOHOL THAN THOSE TREATED WITH PLACEBO.
- DR. ELIE NUWAYSER IS WORKING ON AN INJECTABLE, SUSTAINED RELEASE DEPOT FORM OF NALMEFENE.

NEURONTIN®

- AN ANTICONVULSANT
- GENERIC = GABAPENTIN
- USED FOR:
  - PAIN MANAGEMENT
  - ANXIETY DISORDERS
  - INSOMNIA

NEURONTIN

- DR. KIRK BROWN IS STUDYING THE USE OF NEURONTIN IN THE ALCOHOL DEPENDENT PATIENT AND HAS HAD GOOD RESULTS IN AMELIORATING THE INSOMNIA WITH TITRATING THE MEDICATION UP TO 1500 MG A DAY.

SSRI'S

- PROZAC® (FLUOXETINE) FOUND EFFECTIVE IN TREATING ALCOHOLICS WITH CO - OCCURRING PSYCH. DISORDERS (CORNELIUS ET AL 1997)
  - DECREASED ALCOHOL USE AND DEPRESSION
- ZOLOFT® (SERTRALINE) FOUND EFFECTIVE IN ALCOHOLICS WITHOUT DEPRESSION, DECREASED ALCOHOL USE, BUT NOT IN ALCOHOLICS WITH DEPRESSION, NO BETTER THAN PLACEBO (PETTINATI ET AL 2001)
  - ? CERTAIN TYPES OF DEPRESSION AND CERTAIN TYPES OF ALCOHOLICS

ZOLFRAN®

- AN ANTI - EMETIC USED IN CHEMOTHERAPY PATIENTS
- GENERIC FORM = ONDANSETRON
- SEROTONIN$_3$ (5-HT$_3$) ANTAGONIST

ZOLFRAN®

- SEROTONIN IS IMPLICATED IN ALCOHOLIC DRINKING BEHAVIOR, ESPECIALLY THE SEROTONIN 3 RECEPTOR AND ITS EFFECT ON DOPAMINE.
- IF THIS RECEPTOR COULD BE BLOCKED, THERE WOULD BE A DECREASE IN ALCOHOL INDUCED DOPAMINE RELEASE AND THUS A DECREASE IN ALCOHOLIC DRINKING BEHAVIOR (DECREASE IN THE DESIRE TO DRINK)

ZOLFRAN®

- WORK BY DR. BANKOLE JOHNSON SHOWED THAT EARLY ONSET ALCOHOLICS (EARLY ONSET OF AGE, BROAD RANGE OF ANTISOCIAL BEHAVIORS, AND HIGH FAMILIAL LOADING) DID WELL WITH ONDANSETRON AND NALTREXONE COMBINED, THOUGH THE INITIAL STUDY WAS SMALL.

ZYBAN®

- GENERIC FORM= BUPROPION HYDROCHLORIDE
- MARKETED FIRST AS AN ANTIDEPRESSANT
  - WELLBUTRIN® & WELLBUTRIN SR ®
- FIRST NON-NICOTINE MEDICATION APPROVED FOR SMOKING CESSATION

ZYBAN®

- APPEARS TO WORK THRU THE DOPAMINE AND NOREPINEPHRINE PATHWAYS TO REDUCE CRAVING
- CAN BE USED ALONE OR IN COMBINATION WITH NICOTINE REPLACEMENT MEDICATIONS
- SIDE EFFECTS
  - DRY MOUTH
  - INSOMNIA

ZYBAN®

- CANNOT BE USED IN PATIENTS WITH
  - SEIZURE DISORDERS
  - BULIMIA
  - ANOREXIA
  - PREGNANCY
  - ALLERGY TO BUPROPION
  - PATIENTS BEING TREATED WITH WELLBUTRIN

ZYBAN®

- ASSOCIATED WITH 57 DEATHS IN THE UK, BUT LINK IS UNCLEAR AS REPORTED IN JAN 2002
  - 14 CASES NOT TAKING ZYBAN® AT THE TIME OF DEATH

VACCINES AND NOVEL ADDICTION MEDICATIONS

- RECENT ADVANCES IN IMMUNOTHERAPY (TREATMENT WITH ANTIBODIES) AND ENZYMOLOGY (TREATMENT WITH PROTEINS THAT METABOLIZE THE TARGET SUBSTANCE) HAVE SUGGESTED NEW WAYS TO TREAT THE ADDICTED PATIENT

VACCINES AND NOVEL ADDICTION MEDICATIONS

- IMMUNIZATION WITH A CATALYTIC ANTIBODY
  - ANTIBODY THAT FUNCTIONS AS AN ENZYME BY INDUCING THE MOLECULE THEY FIND TO UNDERGO A CHEMICAL REACTION
    - THE ACTION FREES THE ANTIBODY FOR FURTHER BINDING

VACCINES AND NOVEL ADDICTION MEDICATIONS

- IMMUNIZATION WITH A COCAINE-PROTEIN CONJUGATE
  - BINDING OF COCAINE WITH THIS PROTEIN FORMS A LARGE PARTICLE THAT CANNOT PASS INTO THE CENTRAL NERVOUS SYSTEM

VACCINES AND NOVEL ADDICTION MEDICATIONS

- ADMINISTER BUTYRYLCHOLINESTERASE
  - A MAJOR COCAINE METABOLIZING ENZYME
  - ENDOGENOUS COMPOUND THAT DOES NOT NEED A FUNCTIONING IMMUNE SYSTEM

VACCINES AND NOVEL ADDICTION MEDICATIONS

- CONCLUSIONS FROM THE NIDA TRIALS
  - NO MAJOR ADVERSE EVENTS
  - VACCINES TOLERATED WELL
  - SOME ANTIBODIES PERSISTED BEYOND 12 WEEKS
  - IN ONE STUDY 5/8 OUTPATIENTS DID NOT USE COCAINE IN OVER 12 WEEKS

BEHAVIORAL APPOACHES

- 12 STEP PROGRAMS
- COGNITIVE BEHAVIORAL THERAPY
  - ID EXT. AND INTERNAL CUES/TRIGGERS
  - DEVELOP COPING MECHANISM
- MOTIVATIONAL ENHANCEMENT THERAPY
  - ASSIST PATIENT TO BE SELF MOTIVATED TO CHANGE AND CONTINUE CHANGE

*PROJECT MATCH (1997) NOTED NO DIFFERENCE IN TREATMENT OUTCOMES BETWEEN THE 3 APPROACHES

COMBINE

- COOPERATIVE AGREEMENT
- 11 SITE TRIAL (1375 PARTICIPANTS), 24 MONTHS
- DOUBLE BLIND
- PLACEBO CONTROLLED
- INTEGRATES MEDICATION TREATMENT (NALTREXONE, ACAMPROSATE AND COMBO) AND BEHAVIORAL INTERVENTIONS

COMBINE

- BEHAVIORAL/PSYCHOSOCIAL TREATMENTS
  - COMBINED BEHAVIORAL INTERVENTIONS
    - MEDICATION MANAGEMENT
    - MOTIVATION ENHANCEMENT THERAPY
    - COGNITIVE BEHAVIORAL THERAPY
    - MUTUAL - HELP GROUP PARTICIPATION
    - COMMUNITY REINFORCEMENT APPROACH
    - INVOLVEMENT OF SUPPORTIVE SIGNIFICANT OTHER

BARRIERS

- ????????????

BARRIERS

- LACK OF AWARENESS
- TOO EXPENSIVE
  - NALTREXONE $2.50 - $4.43 PER DAY
- INSUFFICIENT EVIDENCE REGARDING EFFICACY
- PHYSICIANS DO NOT PROMOTE USE
- COUNSELORS IN RECOVERY MAY HAVE ISSUES WITH ADDICTION MEDICINES

BARRIERS

- PATIENT COMPLIANCE WITH MEDICATION
- CORRECT DOSE
- SIDE - EFFECTS
- CANDIDATE SELECTION
  - TOOLS NEED TO BE RESEARCHED SO AS TO DETERMINE WHO WOULD BENEFIT

BARRIERS

- TREATMENT - COMMUNICATION WITHIN A PROGRAM
  - NEED FOR PHYSICIAN SERVICES AT ALL PROGRAMS FOR RX
  - NEED TO INCREASE COMMUNICATION BETWEEN PHYSICIANS AND COUNSELORS

BARRIERS

- TREATMENT - COMMUNICATION WITHIN A SYSTEM
  - NEED TO INCREASE COMMUNICATION BETWEEN PHYSICIANS AND OUTSIDE TREATMENT NETWORKS
  - PRIVATE MD'S NEED LINKAGE TO TREATMENT PROVIDERS
  - TREATMENT PROVIDERS NEED LINKAGE TO MD'S FOR AFTERCARE
    - NEED FOLLOW UP FOR SIDE EFFECTS, LAB TESTS, ETC

BARRIERS

- POTENTIAL FOR ABUSE OF MEDICATIONS
- POTENTIAL FOR DIVERSION
- NEED EVALUATION PROCESS FOR OUTCOMES
- MORE RESEARCH