JUST SAY KNOW!

by DM

MOLECULES REVISITED

In response to the "Molecular Madness" article in Flipside #92, Ivan Valencic from Bistrica, Slovenia writes:

"Maybe you have already realized that formulae for tryptamines in your issue number 92 issue are almost all wrong, and some substances, eg tryptophan, are not even tryptamines! Please consult the enclosed tables compiled by A. Shulgin, or him personally.

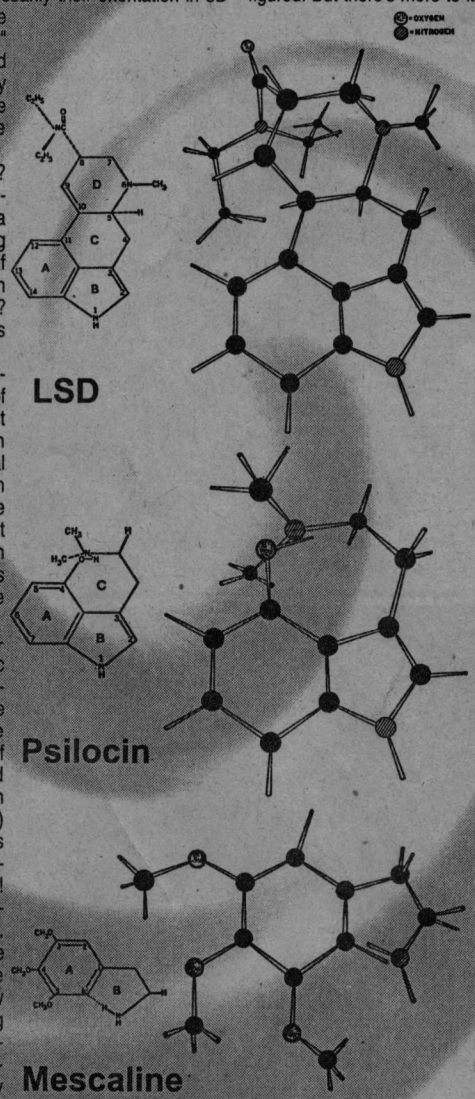
Sincerely, Ivan Valencic."

Well, this is a good lead in to what I was going to show you this issue. First off, the molecules were just fine as shown, it's just that there are a million different ways to show these things. Sure, in Shulgin's "Structure- Activity Relationships of Classic Hallucinogens and their Analogues" (the paper supplied by Ivan) the structure for DMT looks different. In fact, it's upside down! Well, that's ok, in these simple models of complex mechanisms the important things are the relationships of the parts to the whole, not necessarily their orientation in 3D space. (Like stated in that previous article, no attempt was made at showing dimensions in space, or for that matter, any "proper" orientation on 2D paper.) The way the molecules were arranged in that previous article were to show similarities in any arbitrary "family" of analogues. That's why "Tryptophan" was in with the Tryptamines, just to show the similarities. Again, these were designed to show similar traits within families.

But what about similarities that exist between the families? You may have noticed that LSD has a sort of "tryptamine" skeleton inside of it. This is the indole nucleus, a characteristic of a larger family of chemicals that both LSD and tryptamine belong to. Is there any similiarity, then, to the amphetamines? Well, if you really use your imagination there is. Can these similarities in structure be used to predict the activity of these compounds? That is indeed the 6 million dollar question. One that is perhaps still unanswered.

The bottom line is that we still don't understand how particular substances like LSD work. Researchers can look at a lot of biochemical and electrophysiological effects in animals; agonist activity at 5HT[1A] receptors causing decreased serotonin release (the "presynaptic" or "anti- serotonin" hypothesis), partial agonist at post- synaptic serotonin receptors, some interaction with dopamine and other receptors, but no one can come close to putting together these disparate facts into an explanation that accounts for the subjective effects in humans. Ah, but that is an entirely different part of the problem. We do know which groups of chemicals cause these effects and attempts have been made to understand what if anything they have in common.

Solomon Snyder and Elliott Richelson in their pioneering presentation "Steric Models of Drugs Predicting Psychedelic Activity" try to tackle the problem of explaining these relationships. (Coincidentally, this paper was presented at the same meeting, (at UCI in 1969, a workshop organized by the Psychopharmacology Research Branch of National Institute of Mental Health) that Dr. Shulgin presented "Chemistry and Structure- Activity Relationships of the Psychotomimetics" and in fact first defined the term "Psychotomimetic." See the side bar.) Snyder and Richelson dig deep and look at the 3D relationships of molecular structures. If you think the 2D molecules as presented last time didn't look "right" just check of these models! And again, they're models - actually crude stick molecule figures, that attempt to present 3D relationships on a 2D surface. We now know that temporal considerations must also be accounted for, which only make the models more and more complex. What Snyder and Richelson have done is to show how these molecules might arrange themselves in space, according to their charges, bonding characteristics and electronic configurations. Their hypothesis was that within steric classes of compounds, psychedelic potency was related closely to the energy of the highest occupied molecular orbital (HOMO), an index of the electron donating capacity of the resonating electrons of the molecule. They noted that models of known psychedelic compounds of three major classes (tryptamines, phenylethylamines and amphetamines) can all approximate a conformation simulating in part the major ring structures in LSD.



In the more potent derivatives, certain structural features might permit the stabilization of the hypothetical "active" conformation, perhaps enabling the prediction of psychedelic activity. Basically, this stabilizing and thus potentiating action is easily demonstrated in the three figures. LSD at the top is by far the more potent, with a configuration that includes plenty of "stabilizing" atoms. The electrons in the outer "D" ring can resonate with the electrons of the indole ring to produce a more energetic HOMO. This arrangement is of a higher energy order than in the tryptamines, which is reflected in their relative psychedelic potency. The most potent tryptamines, (represented here by psilocin, the active principle in magic mushrooms) are the ones that can approximate the "C" ring of LSD. With psilocin, an amine group is attracted to a hydroxyl group and physically permits hydrogen bonding between the two groups, thus stabilizing an eight membered ring which in 3 dimensions resembles the "C" ring of LSD. DMT lacks this arrangement and is far less potent than psilocin. Mescaline, is by far the lest potent of the three in this discussion. But it is active. The side chain of the phenylethylamine folds down toward the ring, thus resembling the indole nucleus (rings "A" and "B" of LSD) and providing the stabilization needed for a more energetic HOMO.

We have to remember that this is a model that tries to explain any activity at all. There are a lot of other things that effect potency as well - enzyme activity and metabolism are also very specific to molecular structure.

Ok, well that's all fine if you're a chemist, right? Of course, and there are other theories besides the one presented above. I guess the point is that I made a long answer out of a simple question - but you gotta admit (if you didn't followed at all, just look at the pictures!) that it's a pretty cool idea.

THINGS GO BETTER WITH COKE...

On to other things. I came across this interesting information about Crack Babies that just begs to be shared with the world. I don't know about you but I've always had a problem with the notion of babies being born "addicted" to drugs. Many of you who have experienced addiction know that you can pretty much kick that monkey off your back in less than a week. The real problem is killing the desire to get high. Well, that little baby isn't gonna take the rent money to cop some dope! So after a week or so, that kid should be clean. Well, that's what I figured. But there's more to it. You have to look at the mechanisms of addiction to really see what is going on.

Cocaine (any way you choose: blow, crack, freebase, etc) disrupts the normal balance of at least three essential neurotransmitters: norepinephrine, serotonin and dopamine. Serotonin is responsible for regulation of sleep. Cocaine tends to depress neurotransmission of serotonin and can lead to insomnia, jitteriness and general paranoia. The general purpose of Norepinephrine (nor- adrenaline) is to prep the body for emergency. Cocaine greatly increases its neurotransmission, producing increased heart rate, higher blood pressure etc. Continued levels of this intense stimulation can lead to respiratory failure and cardiac arrest. Dopamine, then, is where the addiction liability stems from.

Dopamine is responsible for what we feel as euphoria and pleasure. In general, as our bodies use these neurotransmitters, they are absorbed and recycled again and again. Cocaine acts to block the reabsorption of dopamine, this prolongs its activity in the brain nerve synapses causing a rush of euphoria. Then your dopamine is, however, metabolized and excreted before it can be recycled. As you deplete your supply of available dopamine, your craving for cocaine goes up and up. Your ability to experience pleasure is dramatically altered. The body's ability to naturally feel good is impaired and the only way to even feel alright is to use more cocaine to blockade the reabsorption of what little dopamine may still be left in your body. Some researchers believe that chronic use of cocaine may cause permanent depletion of these neurotransmitters and irreparable damage to the brains dopamine receptors.

In contrast, heroin works on a class of neurotransmitters called endorphins ("endogenous morphine"). Endorphins are the body's natural way of dealing with stress, a situation very similar to one with dopamine. When you use heroin you flood your body with endorphins. A superior sense of well being and calm results. Your body is fooled and feels that its natural production of endorphins is redundant, and shuts down. In due time your body is not producing its own endorphins, and heroin becomes a must. Without it you start to feel every pain that used to be so conveniently covered up. Your backs starts aching first, then every joint in your body - no endorphins to lubricate the pain away from everything that moves. The opiates, however, don't seem to cause a permanent depletion of these neurotransmitters. Your body eventually reacts to the pain, with its own defense system - production of endorphins.

Well, I strayed from the topic there a little. What does this have to do with Crack Babies? Well, can they possibly inherit permanent dopamine depletion from their mothers? Most researchers think not. In fact, idea of "Crack Babies" may be nothing more than a myth, as you will read shortly.

The real dangers with cocaine use for the average person are most likely not the long term depletion of dopamine. The over- stimulation factor associated with heart failure is a serious concern, as is the effects of smoking the hot and harsh vapors of crack or the irritation of the cocaine "hydrochloride" salt to your nasal membranes. The biggest danger is the most common one, getting busted by the law. The "war on drugs" is filling prisons with all kinds of drug users. In Georgia, a woman recently got a life sentence for selling an undercover cop $40 worth of cocaine!

But you're gonna do it anyway, I know how you are. I knew this guy once that would go on and on about the advantages of smoking freebase over snorting powder - basically pumping the fact that it is more effective when smoked and has a neutral Ph factor, not an acid salt like cocaine hydrochloride. Wait a minute, you say, what the hell is the difference between the powder, the freebase and crack. Well, let me explain.

Basically, "freebase" cocaine is what you typically know as the powder form of "cocaine hydrochloride" separated from its acid radical. You simply remove the "hydrochloride" part.

The presence of the radical gives cocaine its water solubility - and it's acidic Ph. Remove the radical and you get an un- soluble form, with a neutral Ph. You don't want to sniff freebase because it won't dissolve in your nose, but the melting point is some 100 degrees lower than the hydrochloride, making it a much better medium for smoking. Crack is basically a lazy ass way of freebasing. The difference between these forms is easily seen if you actually do a simple "freebasing" yourself. Remember folks, it's illegal to possess cocaine (U.S. Code of Federal Regulations, Title 21 Parts 329.1 and 1308.12, 1987), so don't try this at home!

HOW TO FREEBASE COCAINE

Freebase is usually a much cleaner form of coke than what you start with. You will shortly see that freebasing can actually help to purify your cocaine. Ok, here's what you'll need to do a simple freebasing: one test tube or small bottle with a screw on cap. It should hold about 50ml of water. Two eyedroppers, razor blades and a mirror. Chemistry wise, you'll need some ammonium hydroxide (regular household ammonia, without any detergents) and some solvent. The preferred solvent is ethyl ether, but it is hard to come by. Unless you want to distill some automobile starting fluid, it's best to use petroleum ether. This is easily had at the hardware store as "Naphtha," or if all else fails, it is had at Ralphs as Coleman stove fuel or lighter fluid. Of course, you'll also need a gram of cocaine.

After you get this stuff together, you are ready to become an clandestine chemist! First, grind up the gram of coke and put it into the test tube with about 25 ml (1 1/2 inch) of distilled water. Put the cap on and shake it up really good. Cocaine dissolves readily in water. The liquid should be clear. Usually whatever your coke is cut with will also dissolve - but not always. If there's anything left undissolved in the water you can bet it's crap. Without doing much at all, you've already started to purify your coke!

Next you get your eyedropper full of ammonia, and drop about 4- 5 drops into the test tube. A milky white precipitate will immediately form. This is the freebase. What you've done is taken the slightly acidic water/cocaine solution and made it basic by adding the ammonia. You could have used just about any other base, such as lye, to do so, but ammonia is easy to come by and is already in solution. Once the acid radical is removed, you have freebase cocaine which is not soluble in water. It is soluble in petroleum ether.

Now you pour about 15ml (or 3/4 of an inch) of the petroleum ether into the tube. This stuff is flammable (especially ethyl ether!) so unless you want to burn yourself up like Richard Pryor did, don't smoke while doing this! Put the cap on and shake vigorously for a few minutes. The freebase is soluble in the ether and will dissolve into it. Most of your standard cocaine "cut" is water soluble and will remain in the water. This is especially true for the really common sugar cuts, such as lactose or mannitol. Other cuts such as methamphetamine or procaine, will "base through." In other words, they also become water insoluble freebases and end up in the ether.

Once the solutions in the test tube have settled, you will notice that there are two layers - water and ether/cocaine. Take another eyedropper and suck up as much of the ether as you can. Carefully drop this out onto a clean surface such as a mirror or ceramic plate to evaporate. Once evaporated you should be left with a fluffy white residue. If it doesn't quite dry to a powder, it's probably because some cut has based through. For example, methamphetamine as a freebase is an oil (ask your biker friends about "Amp Oil"), not a solid. If it was mixed in with your cocaine at all, it will prevent the cocaine from drying into fluffy white crystals. In either case, scrape up the residue, let it dry as completely as possible and you're done.

To get the best yield from your expensive coke, you will want to extract the water solution at least 2 or 3 more times with ether, or until you get no more residue when the ether evaporates. You'll also want to add another drop or two of ammonia to the water to see if anymore freebase precipitates. It's best to not add too much ammonia to the water in the first step. Too much ammonia this will make your freebase slightly alkaline and not neutral, the much preferred condition. When you are satisfied that you have extracted all the freebase there is, you are done. The left over water is full of the water soluble cut, so remember that your yield will always be less than 100%.

To make crack, we modify our procedure a little bit. Dissolve your cocaine into the water as above, but instead of adding ammonia to the solution you will be substituting for another common base - baking soda. As you add the baking soda a precipitate should form as before. You are pretty much done except to evaporate the water down until nothing is left but a waxy rock of crack. A gentle heat carefully applied to the test tube will get this done quicker. This is indeed a lazy way to freebase, but you do end up with a nice hard, smokable substance.

STRAIGHT AND ALERT

Well, that's about it for this months column. Just remember - the ONLY sane reason for using drugs, is for recreational purposes. You might be scratching your head now, thinking - *"then everything I know is wrong?"* It is. You really should take a lesson from the pure straight edge philosophy - and that is simply, anti- obsession. If you're going to use drugs - don't become obsessed. Using coke until dopamine depletion is a waste of time - so is maintenance heroin/methadone use. Following a doctors orders for years of prescription Valium or Elavil etc or whatever is down right drug abuse. Legal or illegal, if you HAVE to take drugs, then you HAVE problem. Using medication to cover- up a real problem is really a stupid idea. If you have a medical problem, don't let the doctor hide it with drugs. You need to seriously consider alternatives in your lifestyle - diet, exercise, stress reduction etc... Drugs do a great job of glossing over - but rarely actually cure anything. Their real effective and most rewarding effects come from recreational use. But, take your drugs seriously. You can easily hurt yourself. Know what you're doing be it street corner bags of dirt or brand name pharmaceuticals. You can have the best times of your life on drugs but be smart about it. Don't die and remember to keep it recreational, not obsessional.

CHEMISTRY AND STRUCTURE-ACTIVITY RELATIONSHTPS OF THE PSYCHCOTOMIMETICS

by Alexander T. Shulgin, Ph.D.

This meeting is a discussion of the psychotomimetics, and since no one has yet defined the word, and I am the first to speak, I will define it. The first voice heard is the one that is argued against later.

The definition of the word is worthy of a few minutes. This entire group of materials can be arranged in a variety of ways. They could be, for example, considered from the point of view of their site of action. Thus, if you will classify a chemical as active at a cellular level or at a molecular level, you can argue that this is its primary site of action, and all such materials can be classified depending upon their action at this specific site. Secondarily, they have an action upon man, which is incidental to its classification. A material may be primarily cytolytic, and only incidentally cure some bacterial infection in man.

Quite separately, you can take all of the compounds assembled in the U.S. Pharmacopoeia and arrange them on the basis of their action on the human organism. The primary classification would describe the action on the intact individual, and only secondarily would it suggest how this action came to be. For example, a material may be a contraceptive and it is classified as such in the drug manuals. It is incidental whether it is a contraceptive because it inhibits ovulation or because it disturbs the cervical mucosa.

I would like to suggest a third way of organizing these materials. The psychotropic materials, as a special entity in the drug classification, can only be defined by their effect upon the interrelationships between people. This definition involves relationships such as mood, which, after all, have no absolute value. One can only evaluate a change in mood relating one person to another in his society, or even to himself at some separate time. One has a tenuous assignment of sanity, for sanity is a statistical thing. You have to have three people to decide which one is insane. It is a minority concept. The specific terms, sanity, insanity, psychosis and psychotomimetic, must be defined at a social or human level of interaction. This classification describes the general term "psychotropic," which is literally from the Greek for the mind or the soul, and the turning or changing of it.

One is confronted with an apparent paradox regarding sanity in the definition of psychotomimetics. When one changes from a real environment to a different environment, and this second environment seems as real as the first but is different from the first, then there seems to be no absolute way of determining which of the two real worlds is the "real" real world.

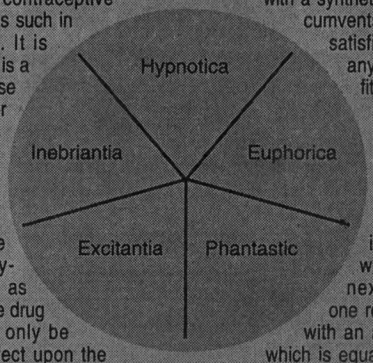
The psychotropic chemicals were subdivided into five groups some thirty or forty years ago by Lewin (1927). These form a useful way of cataloging psychotropic chemicals. They are presented in a circular form which allows a convenient classification of chemicals, for many of these drugs have more than one action.

The first of his classifications was an area known as "Excitantia," literally, chemicals that cause excitement and stimulation. Included here are such synthetic materials as amphetamine, methedrine and Ritalin. Here also are such natural materials as caffeine and khat.

The adjacent and very closely allied classification is entitled "Inebriantia." Here one finds inebriants which cause intoxication in the social sense, rather than in the pharmacological sense. There is a host of organic compounds known to all: ethanol, chloroform, ether, the various materials that have an initial phase of excitement and that cause mental distortion and mental depression, leading quite smoothly into the area of "Hypnotica," the third classification.

This region is best characterized by the barbiturates. In this area one finds the first challenge to the meaning of the real world. There is a replacement of reality with amnesia or confusion. Here, in addition to the sedatives and anesthetics, there are drugs such as atropine, scopolamine, benactyzine, phencyclidine, and other delusional and mentally deranging psychotropic chemicals that will be discussed later in this meeting.

Adjacent to "Hypnotica" is the area entitled "Euphorica," best illustrated by the opiates, in which there is a replacement of the unremembered and unrecalled "not" world with a synthetic substitute that circumvents all problems. This satisfies the user without any constructive benefits.



The last of Lewin's classifications, the one which fascinated him most, is the "Phantastica." This is the area which we will discuss during the next two days. Here, one replaces a real world with an alternate real world which is equally real and yet different. We must return to this philosophic argument: How can one determine which of these two is the "real" real world? There are people in South America, for example, who use the native drug *ayahuasca*, and who live as much of their lives as possible in a drug-modified world. They consider that state the real world, and it is only when the body becomes purged of these chemicals that they inhabit what we accept as our real world. They consider our world an idyllic heaven, but they soon return to their drugged state which is their real world, whereas ours is the escape world. Which of these two exclusive states is real? The class of "Phantastica," thus defined, is presented as a working definition of the term "psychotomimetic." The word psychotomimetic is from "psychoto," implying the origin of psychosis, and "mimetic," meaning the imitation of it. This is, admittedly, a controversial definition because in many ways these compounds do not imitate psychosis, but produce some recognizable symptoms. They have been called the hallucinogens as another synonym, but this is questionable, as hallucinations are rare things. They have been called psychedelics, but this name reflects some anticipation of virtue. Whatever they are, these are the classes of compounds which cause a change of reality but still allow recall.

(reprinted from Psychotomimitic Drugs, D.H. Efron Phd, Raven Press NY 1970)

THE MYTH OF THE 'CRACK BABIES'

(The Boston Sunday Globe January 12, 92 pg 69)
By Ellen Goodman

They are called "a biological underclass" and "a lost generation." Those are just two of the milder name tags attached to the children we have come to believe were permanently damaged by their mothers' use of cocaine.

The poster in maternity clinics conjure up the same image of the prenatally doomed: "Some people who smoke crack never get over it." The schools too have been put on emergency alert: "The crack babies are coming, the crack babies are coming."

Indeed, the phrases "crack babies" and "crack kids" are shorthand for monster-children who are born addicted. These are the kids destined to grow up without the ability to pay attention or to learn or to love.

But just when the name has stuck, it turns out that "crack baby" may be a creature of the imagination as much as medicine, a syndrome seen in the media more often than medicine.

Three years after the epidemic of stories about these children began, six years after hospitals began to see newborns in deep trouble, researchers are casting doubt on the popular demon of the war on drugs. The very phrase "crack baby" is, in any literal sense, a misnomer. Cocaine is rarely taken by itself. It's part of a stew of substances taken in a variety of doses and circumstances. No direct line has been drawn from the mother's use of cocaine to fetal damage.

Alcohol and tobacco may do as much harm to the fetus as cocaine. So may poor nutrition, sexually transmitted diseases, and the lack of medical care. Most important, it appears that the children born to cocaine-using mothers are not hopeless cases, permanently assigned to the monster track. Dr. Ira Chasnoff, who did some of the original work identifying the problem babies of mothers who took cocaine in combination with other drugs, has done a two-year follow-up study about to be published. It says, in his words, "Their average developmental functioning level is normal. They are no different from other children growing up. They are not the retarded imbeciles people talk about."

"Alcohol and tobacco may do as much harm to the fetus as cocaine. So may poor nutrition, sexually transmitted diseases, and the lack of medical care."

This is not, he cautions, a green light for taking drugs during pregnancy. Drugs remain a serious health problem, and cocaine specifically contributes to premature birth and small head size. While the children in his study - children who have been offered some help - now function normally as a group, they are at risk individually.

But, says Dr. Chasnoff, "As I study the problem more and more, I think the placenta does a better job of protecting the child than we do as a society." The need now is to widen the lens from nature to nurture, and from the environment of the unborn to that of the born.

Another researcher who has taken a responsible second look at the "crack baby" syndrome is Claire Coles of Emory University. She believes these children, labeled by their drug of origin, are in fact "often victims of gross neglect, not brain damage."

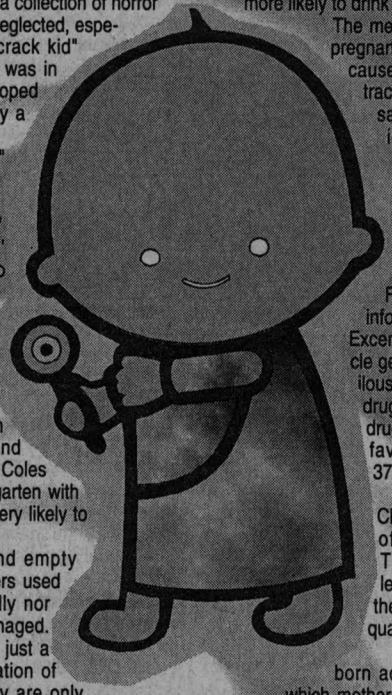
The worst damage that drugs may do is to the world a child inhabits after birth. Coles has a collection of horror stories about children growing up neglected, especially by cocaine addicts. One "crack kid" who couldn't concentrate in class was in fact hungry. Another poorly developed "crack baby" was being "raised" by a 5-year-old sister.

The myth of the "crack baby" became a media hit, Coles believes, because "crack is exotic and happening mostly in 'marginal' populations among 'bad people' who are not like 'us.'" It is easier to think about crack than alcohol or tobacco. There is more than a touch of racism in the attention.

But perhaps the worst effect of this distortion is the sense of hopelessness dispensed with the title "crack kid." Hopelessness on the part of mothers, teachers, and even the children themselves. As Coles warns, "If a child comes to kindergarten with that label, they're dead. They are very likely to fulfill the worst prophecies."

So, no more convenient and empty names. The children whose mothers used cocaine are neither universally nor permanently nor uniquely damaged. The so-called "crack kids" are just a portion of our growing population of children in deep trouble. They are only children, like so many others, growing up with a treacherous mix of nature's and nurture's woes.

If you need a label, call them kids who need help.
- Ellen Goodman is a Globe columnist.



"SMOKING OUT COCAINE'S IN UTERO IMPACT"

(Science- News November 1991)

Despite many reports of cocaine's ill effects on the developing fetus, scientists lack definitive evidence specifically linking cocaine to adverse reproductive effects (SN: 9/7/91, p.152). Using a powerful statistical technique, a Canadian research team has found that cocaine by itself causes very few problems during pregnancy.

Gideon Koren of the University of Toronto and his colleagues identified 20 previously published cocaine studies that involved pregnant women and yielded mixed results. Those studies often relied on small samples of cocaine users -- a problem that limited each study's statistical power.

To home in on cocaine's reproductive risks, his team turned to a method called meta-analysis, which statisticians use to assess data by pooling a number of similar studies. Koren and his colleagues identified women in the 20 studies who used cocaine during pregnancy but did not use other illicit drugs or alcohol, and compared them with those who reported no drug or alcohol use during pregnancy. They found no statistical link between prenatal cocaine use and premature delivery, low birthweight or congenital heart defects in babies -- problems often thought to result from cocaine.

The meta-analysis suggests that confounding factors -- such as other drugs, alcohol and smoking -- may account for the fetal growth retardation or prematurity commonly ascribed to cocaine, the researchers assert in the October "Teratology". Koren says women who use cocaine tend to smoke more cigarettes than women who use other illicit drugs and are more likely to drink alcohol and take additional drugs.

The meta-analysis did reveal a chance that a pregnant woman's cocaine use by itself might cause malformations of the genito-urinary tract in a small number of infants. Koren says this effect may trace to cocaine-induced constriction of the placental blood vessels.

A QUICK FIX FOR THE DRUG WAR

by Patricia Edmonds
Seattle Times. June 3.

Focus: Drug war in general. Good information on Crack Babies.

Excerpt: Still, those interviewed for this article generally agreed on one thing: its a perilous mix when leaders try to make war on drugs, law on drugs and political hay on drugs at the same time. On this point, a favorite cautionary tale concerns the 375,000 crack babies.

The story begins with Ira Chasnoff, a Chicago pediatritian, and his 1988 study of 154,856 births in 36 hospitals. Through interviews and tests, he learned that in 11 percent of the births, the babies had been exposed to some quantity of some drug during pregnancy.

Chasnoff did not say the babies were born addicted, or afflicted. He did not say which mothers used cocaine daily and which used marijuana one weekend. He said: some quantity of some illegal drugs was used during pregnancy. Then Chasnoff did the arithmatic. If there was drug exposure in even 10 percent of the 3.75 million births in the U.S. annually, that would be 375,000 babies.

"That," Chasnoff said, "is as far as it went".

[...goes on to detail how William Bennett used this study to show that there were 375,000 crack babies in the U.S./year...]

BIAS AGAINST THE NULL HYPOTHESIS: THE REPRODUCTIVE HAZARDS OF COCAINE

by Koren G., Graham K., Shear H., Einarson T.
Department of Pediatrics, University of Toronto, Ontario Canada. Lancet 1989 Dec 16;2(8677):1440-2 Dec 16, 1989

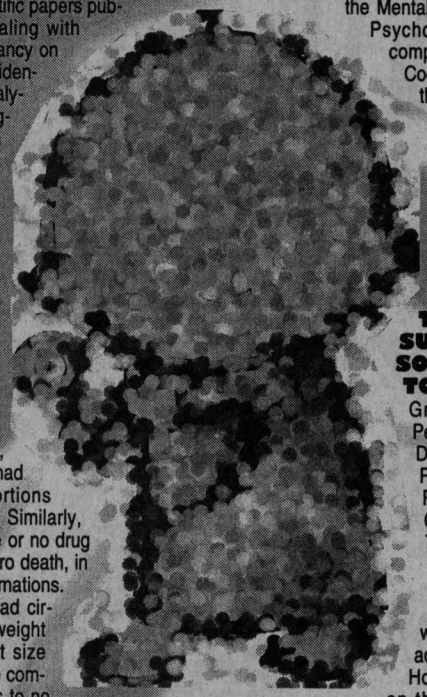
To examine whether studies showing no adverse effects of cocaine in pregnancy have a different likelihood of being accepted for presentation by a large scientific meeting, all abstracts submitted to the Society of Pediatric Research between 1980 and 1989 were analysed. There were 58 abstracts on fetal outcome after gestational exposure to cocaine. Of the 9 negative abstracts (showing no adverse effect) only 1 (11%) was accepted, whereas 28 of the 49 positive abstracts were accepted (57%). This difference was significant. Negative studies tended to verify cocaine use more often and to have more cocaine and control cases. Of the 8 rejected negative studies and the 21 rejected positive studies, significantly more negative studies verified cocaine use, and predominantly reported cocaine use rather than use of other drugs. This bias against the null hypothesis may lead to distorted estimation of the teratogenic risk of cocaine and thus cause women to terminate their pregnancy unjustifiably.

RELATIONSHIP BETWEEN GESTATIONAL COCAINE USE AND PREGNANCY OUTCOME: A META-ANALYSIS.

by Lutiger B., Graham K., Einarson T.R., Koren G.
Department of Pediatrics, Hospital for Sick Children Toronto,

Ontario, Canada., Teratology 1991 Oct;44(4):405-14

Despite a growing number of studies that have investigated the reproductive effects of maternal cocaine use, a homogeneous pattern of fetal effects has not been established and there is little consensus on the adverse effects of the drug. We used meta-analysis to evaluate the reproductive risks of cocaine. We reviewed the 45 scientific papers published in the English language dealing with effects of cocaine used during pregnancy on pregnancy outcome in humans, and identified 20 papers eligible for meta-analysis (cocaine use in pregnancy, pregnancy/fetal outcome studies, human studies, original work, cohort or case control studies, control group present, English language). Our analysis revealed that very few adverse reproductive effects could be shown to be significantly associated with cocaine use by polydrug users when compared to control groups of polydrug users not using cocaine [genitourinary malformations; odds ratio of 6.08 (95% CI 1.18-31.3); gestation age: Cohen's d 0.37 (CI 0.2-0.55)]. When the control groups consisted of no drug users, the polydrug users abusing cocaine had a higher risk for spontaneous abortions [odds ration 10.50 (CI 11.74-64.1)]. Similarly, comparison of users of cocaine alone or no drug users revealed a higher risk for in utero death, in addition to genitourinary tract malformations. Analysis of continuous variables (head circumference, gestational age, birth weight and length) revealed that the effect size was dependent upon the nature of the comparison. Comparison of cocaine users to no drug users consistently yielded a medium effect size (Cohen's d) between 0.50 and 0.58, while comparison of polydrug/cocaine users to polydrug/no cocaine users provided effect sizes small to non existent (0.06-0.37). These discrepancies suggest that a variety of adverse reproductive effects commonly quoted to be associated with maternal use of cocaine may be caused by confounding factors clustering in cocaine users.



COCAINE/POLYDRUG USE IN PREGNANCY: TWO-YEAR FOLLOW-UP

by Chasnoff I.J., Griffith D.R., Freier C., Murray J.
Department of Pediatrics, Northwestern University Medical School, Chicago, IL., Pediatrics 1992 Feb;89(2):284-9 Feb. 1992

The impact of cocaine on pregnancy and neonatal outcome has been well documented over the past few years, but little information regarding long-term outcome of the passively exposed infants has been available. In the present study, the 2-year growth and developmental outcome for three groups of infants is presented: group 1 infants exposed to cocaine and usually marijuana and/or alcohol (n = 106), group 2 infants exposed to marijuana and/or alcohol but no cocaine (n = 45), and group 3 infants exposed to no drugs during pregnancy. All three groups were similar in racial and demographic characteristics and received prenatal care through a comprehensive drug treatment and follow-up program for addicted pregnant women and their infants. The group 1 infants demonstrated significant decreases in birth weight, length, and head circumference, but by a year of age had caught up in mean length and weight compared with control infants. The group 2 infants exhibited only decreased head circumference at birth. Head size in the two drug-exposed groups remained significantly smaller than in control infants through 2 years of age. On the Bayley Scales of Infant Development, mean developmental scores of the two groups of drug-exposed infants did not vary significantly from the control group, although an increased proportion of group 1 and 2 infants scored greater than two standard deviations below the standardized mean score on both the Mental Developmental Index and the Psychomotor Developmental Index compared with the control infants. Cocaine exposure was found to be the single best predictor of head circumference. [note that Dr. Ira Chasnoff was responsible for a very great deal of the original cocaine-baby research in the mid 1980s.]

"The cocaine group was more likely to be white and to use alcohol, marijuana, tobacco and other illicit drugs more heavily than the comparison group."

PREGNANCY OUTCOME FOLLOWING FIRST TRIMESTER EXPOSURE TO COCAINE IN SOCIAL USERS IN TORONTO, CANADA.

Graham K., Dimitrakoudis D., Pellegrini E., Koren G.
Division of Clinical Pharmacology and Toxicology Research Institute, Toronto, Ontario, Canada. Vet Hum Toxicol 1989 Apr;31(2):143-8, 1989 Apr, Vet Hum Toxicol, PG.143-8

Studies of drug-dependent women reveal high rates of adverse fetal effects of cocaine. However, no data are available on the effect of the chemical in social users who discontinue cocaine upon realizing they are pregnant. We report the results of the first phase of a prospective study examining the outcome of pregnancy in women seeking counseling from the Motherisk Program in Toronto. Of 25 women seen in our clinic for 1st trimester cocaine exposure, 92% reported use of 10 g of cocaine and 36% reported marijuana use. Other illicit drug use was rare; cigarette and alcohol use was common. The study group did not experience adverse pregnancy outcome above the rate expected in the general population. There were 23 single births 1 pair of twins, and 1 spontaneous abortion. Birth weight and gestation were within normal limits. Only 1 child had a major malformation, syndactyly. Infant development was within normal limits, as measured by developmental milestones. All children are scheduled for assessment using the Bayley Scales of Infant Development. The results of the BSID will be compared to results from a cannabis-exposed control group and a no-drug control group.

MATERNAL AND NEONATAL EFFECTS OF MODERATE COCAINE USE DURING PREGNANCY.

by Richardson G.A., Day N.L.
Western Psychiatric Institute and Clinic, University of
Pittsburgh PA 15213. Neurotoxicol Teratol 1991 Jul-Aug;13(4):455-60 1991 Jul-Aug

Thirty-four women who reported using cocaine during pregnancy were compared to 600 women who reported no cocaine use during pregnancy and none for the year prior to pregnancy. Subjects were participants in a prospective, longitudinal study of prenatal substance use. The sample consisted of young, predominantly single, low-income women attending a public prenatal clinic. Women were interviewed at the end of their first, second and third trimesters regarding cocaine, alcohol, marijuana, tobacco and other drug use. The majority of the cocaine users were light to moderate users who decreased their use during pregnancy. The cocaine group was more likely to be white and to use alcohol, marijuana, tobacco and other illicit drugs more heavily than the comparison group. The cocaine users had more previous fetal losses but did not differ on other obstetrical complications. Infant growth, morphology and behavior were not affected.

COCAINE IN PREGNANCY: ANALYSIS OF FETAL RISK

by Koren G., Graham K.
Department of Pediatrics & Research Institute, Hospital for Sick Children, Toronto, Ontario, Canada Vet-Hum-Toxicol. 1992 Jun. 34(3). P 263-4

During the last decades there has been a substantial increase in the recreational use of cocaine in young adults and parallelly there has been an increase in its use by pregnant women. We analyzed all published papers on cocaine use in pregnancy and found that for most endpoints studied (eg, prematurity, head circumference) there were many studies showing effects and many showing no effects. Upon meta-analysis, most of the effects could not be shown significant when compared to control groups. In a prospective study in Toronto, babies exposed to cocaine during the first trimester only had Bayley scores at 18-mo of life that were identical to unexposed babies or to those exposed to canabinoids. Motherisk presently counsels women who discontinue cocaine use in the first trimester of pregnancy that there is no increased developmental risk for the baby.

Other references extracted from the Usenet News

COCAINE-ASSOCIATED ABNORMALITIES MAY NOT BE CAUSALLY RELATED.

by Neuspiel D.R.
Am. J. Dis. Child. 1992 Mar. 146(3). P 278-9

THE PROBLEM OF PRENATAL COCAINE EXPOSURE. A RUSH TO JUDGEMENT

by Mayes L.C., Granger R.H., Bornstein M.H., Zuckerman B.
Review Article: 43 refs. Yale Study Center, New Haven, Conn 06510 JAMA. 1992 Jan 15. 267(3). P 406-8

LACK OF EFFECT OF MATERNAL COCAINE ADMINISTRATION ON MYOMETRIAL ELECTROMYOGRAM AND MATERNAL PLASMA OXYTOCIN CONCENTRATIONS IN PREGNANT SHEEP AT 124-145 DAYS' GESTATIONAL AGE.

by Owiny J.R., Myers T., Massmann G.A., Sadowsky D.W., Jenkins S., Nathanielsz P.W.
Laboratory for Pregnancy and Newborn Research, College of Veterinary Medicine, Cornell University, Ithaca, New York. Obstet-Gynecol. 1992 Jan. 79(1). P 81-4

COCAINE IN PREGNANCY: ANALYSIS OF FETAL RISK

by Koren G. Graham K.
Vet. Hum. Toxicol. 1992 Jun. 34(3). P 263-4

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