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#### APPENDIX A

## I. Obstetrical Medication

1. Classification, dosage and routes of administration of obstetric anesthetics and analysmics!

Drugs used for the relief of pain are generally classified according to their major effect, with the understanding that some drugs produce different effects according to dose and route of administration (Bowes, 1970; Davis and Rubin, 1966).

### A. General anesthetics

When given in sufficient dosages, general anesthetics will produce a state of unconsciousness with less of sensation (i.e., anesthesia) that allows any surgical procedure to be carried out, though by themselves they are not pain killers. Anesthesia results from the pronounced functional depression of the CNS. The most commonly used obstetric anesthetics are the inhalation anesthetics, i.e., gases (e.g., nitrous oxide, ethylene, cyclopropone) or volatile liquids (e.g., ether, halothane, methoxyflurane, trichloroethylene). Ghloroform, a potent volatile anesthetic, is hardly ever used in obstetrics because of its dangerous side effects. Volatile liquids can be dropped on a mask held over the patient's face, but more frequently the inhalational anesthetics are administered by means of more or less elaborate breathing apparatus which provides a well controlled mixture of gas (or vapor) and oxygen and absorbs carbon dioxide exhaled by the patient. Inhalation anesthetics generally produce a rapid effect upon administration; upon withdrawal, rapid recovery usually results. Recovery typically occurs within minutes. Methomyflurane has the longest recovery period (30-60 minutes).





General anosthesia can also be produced by high doses of sedatives. The method commonly employed consists of intravenous injection of an ultra-short acting barbiturate (e.g., thiopental in doses from 0.12 gm. up to 1.0 gm.). Intravenous anesthesia has the advantage of rapid, smooth onset with few complications and side effects. On the other hand, barbiturates do not relieve pain, unless administered in doses causing loss of consciousness, so that pain-relieving drugs usually have to be added to provide for post-operative analgesia.

General anesthetics used during the birth process are generally of the inhalation kind. They are nearly always administered at the end of the second stage (i.e., just before expulsion of fetus) though smaller doses of inhalation anesthesia ("whiffs") are commonly used to relieve pains of contractions. Intravenous barbiturate anesthesia is not often used in obstetrics (except for cesarean section) because the recovery is much slower than with inhalation anesthetics.

Other depressants of the CNS, such as alcohol are not used for obstetric purposes. These depressants will, therefore, not be reviewed here.

#### B. Sedatives

Calm, drowsiness, or sleep (i.e., hypnotic effect) can be induced by sedatives. They do not induce loss of consciousness (i.e., general anesthesia) when administered in usual doses, although high doses of some sedatives may be used to produce general anesthesia, e.g., thiopental. Sedatives, like general anesthetics, depress the CNS. The most commonly used sedatives are the barbiturates, usually classified according to time it takes to produce the desired effect and the duration of its effect (ultra-short, short, medium and long

acting). Barbiturates are typically administered orally. Sodium phenobarbital, a long-acting barbiturate, can be injected intra-mulcularly, and is often used pre-operatively in obstetrics for that purpose. (It is also commonly used in the control of convulsions.) The ultra-short acting compounds (e.g., thiopental) are usually administered intravenous. ly for rapid effect. Barbiturates are typically administered in doses varying from 100 mg. to 250 mg. Other sedatives include chloral hydrate, a relatively non-toxic substance (0.25 gm. to 1.0 gm.), ethchlorvynol (Placidyl) (0.1 gm. to 0.5 gm.), and glutethimide (0.25 gm. to 0.5 gm.) (Goodman and Gilman, 1970).

## C. Analgosics and Narcotics

Analgesics (including narcotics) selectively reduce the sensation of pain while producing only minor effects on alertness, as opposed to the action of anesthetics (inhalation anesthetics and barbiturates).

Narcotic analgesics comprise the opium alcaloids (e.g., morphine and codeine) and their synthetic analogues, (meperidine, methadone, levorphanol). When these are given in heavy doses, they can also produce drowsiness and have calming effects similar to barbiturates.

Narcotics act by depressing the functions of the CNS, although the depressing influence is different from general anesthetics. Narcotics have selective rather than general effects. For example, the principal effects of morphine are: (a) suppression of pain; (b) mild drowsiness and euphoria; (c) depression of respiration; (d) nausea and sometimes vomiting; (e) constipation (Goodman and Gilman, 1970). The "withdrawal syndrome" is characterized by irritability, tremor, increased heart rate and blood pressure, lacrimation, sweating, masal discharge,



diarrhea and, occasionally, vomiting. Other narcotics produce similar therapentic effects and have similar withdrawal syndromes with prolonged use.

Narcotics are most commonly employed in early stages of labor to relieve pain, but may also be used in conjunction with anesthetics.

Morphine is usually administered by intramuscular injections of 10 mg.

to 20 mg. The most commonly used obstetric narcotic is meperidine, which is injected intramuscular in doses of 50 mg. to 100 mg.

#### D. Tranquilizors

Tranquilizers are drugs that produce a calming effect, without affecting alertness or inducing sleep. They do not depress CNS function when administered in typical doses. Their main effect consists of reducing the intensity of emotional reactions. Numerous tranquilizers are on the market and they are probably among the most widely prescribed medications in general use. They are divided into two main classes:

(a) "major" tranquilizers (e.g., phenothiazines, rauwolfias, butypherones) have profound effects and are used mainly in psychiatry; (b) "minor" tranquilizers (e.g., benzodiazepines, meprobamate) mainly reduce anxiety and have a very wide field of application.

There are two "major" tranquilizers that are often used in obstetrics. The first is chlorpromazine. It is given in doses of 50 mg. to 100 mg. intramuscularly. It is often used for its potentiating effect on general anesthetics and analysis that allows a smaller dose of the other drug to produce the desired effect. The tranquilizing influence is merely a beneficial side effect. Prometazine, a related compound, is used for the same purpose. The second major tranquilizer used in

obstetrics is reserpine, an alcaloid of the rauwolfia group. It is given in doses of 2 mg. to 4 mg. Like other rauwolfia preparations, it lowers the blood pressure while also producing a tranquilizing effect.

Rauwolfia is scattimes used in late stages of pregnancy though some authors object to such use (Ban, 1969). It appears that some infants are born with effects of this medication (to be discussed below).

The two minor tranquilizers most commonly used in obstetrics are chlordiazepoxide (Librium) in doses of 10 mg. to 25 mg., and diazepam (Valium) in doses of 5 mg. to 10 mg. They are both administered to reduce anxiety and the latter has also a muscle-relaxing effect.

Diazepam is also used to control convulsions. Minor tranquilizers are used in early stages of labor, while chlorpromazine, a major tranquilizer, and related compounds are also used as adjuncts to general anesthesia during expulsion of fetes.

#### E. Local anesthetics

Local anesthetics provide relief from pain by blocking the transmission of impulses through the peripheral nerves (Goodman and Gilman, 1970). Used in such a manner, they do not alter alertness of the patient but can supress CNS function if administered in significant amounts. The commonly used local anesthetics are synthetic derivatives of cocaine (e.g., procaine, lidocaine, mepivacaine). They can be divided into two major classes: the esters<sup>2</sup> and the amides<sup>3</sup>. The former include procaine and are generally characterized by a fairly long latent period (between administration and clinical effect) and a relatively poor ability to penetrate tissues. The amides, on the other hand, act more rapidly and longer and penetrate tissues better. This group, which includes lidocaine, prilocaine and mepivacaine, is widely used to provide obstetrical anesthecia.



In obstetrics, the local anesthetics are employed in three principal ways (Davis and Rubin, 1966):

- 1. <u>Infiltration</u> anesthesia is produced by injecting the drug directly into the tissue (e.g., perincum in preparation for episiotomy). This method is the simplest but not necessarily the safest, as it may require a relatively large quantity of drugs (up to 200 cc of a .05% solution of procaine, or up to 40 ml. of 1% solution of mepivacaine).
- 2. <u>Conduction block</u> is produced by injecting the drug next to a nerve trunk (pudendal or para-cervical block) (up to 10 ml. of 1% procaine or up to 20 ml. of 1% mepivacaine on each side).
- 3. <u>Massive block</u> of spinal nerves leading to the lower part of the body can be produced by one of the following techniques:
- a. in <u>spinal</u> anesthesia the drug (0.5 to 2 cc of 10% procaine or 15 to 30 cc of 1% mepivacaine) is injected into the subarachnoid space, in direct contact with the spinal cord. The result is a transient sensory and motor paralysis of the whole lower half of the body. A variant of this technique is the "saddle block," in which the drug is injected in a manner to affect only that area of the body which would touch a saddle (Davis and Rubin, 1966).
- b. in <u>lumbar epidural</u> anesthesia the drug (in amounts similar to those used in spinal anesthesia) is injected between the dura membrane and the bones of the spine. If the injection is made into the caudal canal (which is an extension of the epidural space) it is called caudal anesthesia.

In spinal and epidural anesthesia, relatively small amounts of the drug pass into the general circulation. On the other hand, these massive nerve blocks produce side effects such as the pronounced fall in the mother's block pressure (a point which will be elaborated later on).



### F. Other drugs

Scopolamine (hyoscine) is used as an adjuvant to narcotics and is reputed to induce ammesia of the painful experience. Succinil choline (Ameetine) is a muscle relaxant used to facilitate surgery and delivery. Little is known about the possible effects of these drugs on the fetus.

The classification of anesthetics, analgesics and sedatives refers to the principal effect, when the drug is used in typical manner. One should keep in mind, however, that all these drugs affect the function of nervous tissue and their effects may overlap. Thus, higher doses of morphine have a sedative effect, tranquilizers may induce sleep and local anesthetics may cause excitation, convulsions or loss of consciousness if introduced into the brain in large amounts.

In this section we have reviewed the principal anesthetics and analgesics commonly used in obstetrics. We turn now to the utilization processes by both the mother and the meanate.

#### 2. Vicissitudes of drugs used in labor

There has been a considerable amount of research into the effects of drugs on the mother and fetus during labor and delivery. One major factor of paramount importance is the time factor, i.e., the interval between administration and delivery, speed of absorption, rate of placental transfer, rate of metabolic breakdown and elimination. The time factor plays a critical role in evaluating the effects of a drug on the mother and the fetus. Contradictions in the data obtained by different observers about drug effects are partially the result of the fact that not all researchers take into account all of these variables. In addition, many of the original inferences were drawn from animal





experiments and it is now recognized that pharmacological effects may differ greatly from man to animal - a point which will be elaborated further on.

When a drug is introduced, by any route, into the mother's body it will:

- (a) enter, to some extent at least, into the smaternal blood circulation:
- (b) be subjected to metabolic transformation by the maternal organism, leading to breakdown and/or elimination;
- (c) pass in variable amounts through the placenta and into the fetus and return from fetal into maternal circulation (before severing the cord) to be metabolized by the mother;
- (d) become metabolized and/or eliminated by the fetus (and later by the newborn).

Some general comments concerning these various stages will be helpful.

(a) Absorption: drugs injected intravenously enter the circulation instantaneously and within seconds are evenly distributed throughout the body. Inhaled drugs are absorbed almost as rapidly. Intramuscular injection or rectal administration requires several minutes while ingested drugs may require an hour or more before peak blood concentration is reached. Peak blood concentration is not synonymous with maximum effect. In order to exert its effect, the drug has to enter the tissues; in the specific case of central nervous system function, passing the blood brain barrier is involved. The blood brain barrier has a different permeability for different drugs (Harper, 1969). Local anesthetics exert their effect at site of the injection but are always sooner or later absorbed into general circulation.

(b) Metabolism: Gases and volatile anesthetics are largely eliminated through the lungs. Synthetic narcotics and short-acting barbiturates (e.g., thiopental) are metabolized in the liver. Long acting barbiturates are eliminated through the urinary system. Of the local anesthetics, esters are metabolized by hydrolysis (i.e., combining with water and splitting into alcohol and organic acid) and thus inactivated. The amide compounds (e.g., lidocaine, mepivacaine) are metabolized and inactivated by a liver enzyme, amidase (Cohen and Olson, 1970).

Contrary to previous opinions, it is now known that many drugs exert significant effects long after having been apparently eliminated by metabolism and after their blood level drops to insignificant amounts (e.g., secebarbital produces mild sedation up to 20 hours, and chlorpromazine a tranquilizing effect up to six months, Goodman and Gilman, 1970). Ashton and Hibben (1967) (in Goodman and Gilman, 1970, pp. 104) found in an animal study after-effects of barbital anesthesia one month later.

(c) Placental transfer: The old notion of the eighteenth century that the placenta serves as a protective barrier between the fetus' independent circulation and his mother (Corner, 1965) was shattered to pieces in 1961, in the popular beliefs, with the tragedy of thalidoside in Europe, (Nehan and Lampert, 1965). A number of babies, whose mothers took this mild sedative in the first weeks of gestation, were born with limb malformations and with other defects. What was thought, early in this century, to be a semi-permeable membrane separating the two circulations, is now known to be an extremely active metabolic unit (Regensan and Ville, 1960; Marx, 1961; Moya and Smith, 1965; Watson and Lowery, 1969; Bowes, 1970; Cohen and Olson, 1970).



It is now believed that any substance found in the maternal blood will cross the placent, to some extent unless it is altered or destroyed during its passa; Most drugs are transfered by simple diffusion, i.e., the molecules prission an area of high concentration to one of low concentration wit. Little if any metabolic energy. The rate depends on: (a) lipid solubility (fat solubility); (b) molecular weight of the drug, (drugs with molecular weight up to 600 readily cross the placenta; (c) degree of ionization (non-ionized, i.e., electrically neutral substances cross more readily). Any change in the pll (alkalinityacidity balance) that increases concentration of dissociated, ionized forms, will slow down transfer of drugs (Hagerman and Ville, 1960; Cohen and Olson, 1970; Burt, 1971). Normally, the pH (the acid-alkali balance) of the fetal blood is slightly higher, i.e., more alkaline, than that of the mother. However, drugs such as local anesthetics may produce acidosis in the fetus, i.e., lower the pH. In that case, an alkaline drug, such as mepivacaine, after having passed through the placental barrier, may become "trapped" in the fetal circulation because the increased acidity leads to increased ionic dissociation of the alkaline drug and, thus, reduces its diffusibility through the placenta back into maternal circulation (Teramo and Rajamaki, 1971). This may be a possible emplanation of why some local anesthetics have been found at higher concentration in the fetal circulation than in the maternal circulation (Teramo and Rajamaki, 1971).

The placenta may also play a role in metabolizing some compounds so that they may reach the fetal circulation faster or be prevented from entering it (Cohen and Olson, 1970). Maternal diseases such as toxemia<sup>4</sup>, diabetes or chronic hypertension (high blood pressure)

which lead to an altered placental vascular bed may also inhibit passage (Cohen and Olson, 1970).

Transfer occurs also by active transport or by special processes such as pinocytosis (engulieent by leucocytes) or through gaps in the placental villi (finger-like projections). The mechanisms of active transfer are still poorly understood (Hagerman and Ville, 1960).

Drug transfer may also occur via the amniotic fluid to the fetus' circulation. This route is also poorly understood but is most interesting in light of the fact that the pH of amniotic fluid at term is 6.9-7.0 while both fetal and maternal blood pH is 7.35-7.4 (Cohen and Olson, 1970). "This differ ace in pH could result in some drugs being concentrated in the amniotic fluid and ingested by the fetus in higher dosage than may be suspected from maternal plasma alone." (Cohen and Olson, 1970).

The type of administration of a drug into the maternal circulation will affect the degree of transfer with more of the drug passing to the fetus after intravenous administration to mother than after oral administration or intramuscular injection, holding dosage level constant.

(d) <u>Metabolism by fetus and neonate</u>: Once the umbilical cord is severed, the neonate is on his own as far as the detoxification and elimination of drugs is concerned. The fetal and neonatal metabolism, however, differs significantly from that of the adult. Both liver function and the excretory function of the urinary apparatus are not yet fully developed (Nelson, Vaugham and McKay, 1969 a, b, c). Compared with older children and adults, the elimination of drugs by the neonate is slower. The neonate's liver is deficient in amidase. This makes the newborn susceptible to the toxic effects of the amide group of





local amosthetics (Cohen and Olson, 1970). Requates have difficulties in conjugating billrubin (the yellow pigmented substance formed by the breakdown of hemoglobin from destroyed red cells). Before being eliminated from the body, bilirubin has to be rendered water soluble by being chemically combined (conjugated) with glucumonic acid. The conjugation is accomplished by an engyme, glucuronil transferase, which is normally present in liver tissues. The liver of the fetus and newborn has a very low level of this enzyme and the process of bilirubin elimination is much slower in the newborn, especially in the premature baby. Excess bilirubin produces joundice and the so called "physiological jaundice" of the neonate is thus due to the relative defficiency in the elimination of bilirubin. About 50 parcent of full term babies and 80 percent of immature infants develop mild jaundice on the third or fourth days of life, when the unconjugated bilirubin has accumulated in the blood stream and is being deposited in the skin (McKilligin, 1970). Any marked increase in the red cell destruction, such as happens in Rh incompatibility, results in severe joundice which may lead to death or to brain damage in the form of kernicterus (yellow coloration of basal ganglia of the brain by bilirebin). Conjugation with glucuronic acid is a detoxifying mechanism used for the elimination of a wide variety of foreign substances including such common drugs as salicilates (aspirin), sulfonamide, chloramphenicol, morphine and others. Thus, bilirubin and many drugs compete for the same detoxifying mechanism in the neonate's liver with the result that joundice may delay elimination of many drugs and many drugs may aggravate joundice. (Kent, 1959; Lucey and Dolan, 1959; Burns, Hodgman and Cass, 1959; Zuelzer, 1961; Done, 1964; Custafson, 1965: Myhan and Lampert, 1965; Adamsons and Joelsson, 1966; Watson and Lowery, 1969; Helson, et al., a,b, 1969; Burt, 1971).



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In order to stimulate the production of the drug-metabolizing enzyme, glucuronil transferase, physicians sometimes advocate the administration of barbiturates (Foutz, 1965; Young and Yu, 1971), such as phenobarbitone, or of benaypirene. This, however, does not solve the whole problem because the meanate's glomerular filtration (passage of the fluids from the blood into the kidney glomeruli and formation of fluid which eventually becomes urine) is low (Nelson, et al., 1969 b). Thus some conjugated bilirubin and/or drug continues to circulate in the neonate's body.

The elimination of drugs may be further slowed down if the metabolic processes are deranged, e.g., by acidosis or lowered body temperature. Since a number of drugs may produce acidosis (e.g., local anesthetics) or interfere with feeding (i.e., reduce caloric intake) and hence interfere with heat regulation, a vicious circle may start. The fall in temperature is even more pronounced in the immature and malmourished infant (Adamsons and Joelsson, 1966).

From the point of administration of the drug to its elimination by the mother and/or meonate is a long and complex process. It is not yet a fully understood process, but what is already known suggests that the introduction of analgesics and anesthetics into the mother's body during labor and delivery starts a chain of effects that invariably add to the demands of the birth process on the system functions in the meanate.

### I. Effects on mather and newborn

There have been a number of studies on the effect of obstetrical drugs. The can be divided into two groups; the effect on the mother and the effect on the infants.

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## 1. Effects on maternal physiology and labor

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When considering relations between a drug and fetus! metabolism, much more than a simple pharmacological effect of the drug itself may be involved. It is true that in many instances the drug crosses the placenta unchanged and affects the fetus in a fashion similar to that in which it affects adults. Most of the volatile anesthetics, the barbiturates and many narcotic analgesics probably affect the fetus in this manner (as will be described below). But a drug may influence the fetus also by altering the maternal physiology in such a way that the intrauterine environment is changed. It has recently become apparent that spinal anesthesia may have far-reaching consequences even in the cases where drugs themselves do not cross the placenta in significant quantities. At the time of casarean section, a patient who lies in a supine position and then is given a spinal anesthesia, may experience an alarming hypotension (Ucland, Gills, and Hansen, 1968) which can be reflected in the reduction of fetal oxygenation and increased acidosis (Stenger, Andersen, de Pauda, Eitzman, Gessner, Preptousky, 1964). Anything that alters placental transfer of respiratory gases (oxygen, carbon diomide) electrolytes, water or metabolic end products (urea) will jeopardize the fetus to a certain extent. Consequently, a drug must be considered not only for its direct effect upon the fetus but also for its indirect and no less important effect on maternal physiology.

Friedman and Sachlleben (1961) have warned against dysfunctional labor due to a prolonged latent stage (predilatation stage of the contractions). Both local and general anesthesia may have adverse effects on the fetus since they may unnecessarily prolong the latent



stage (above 20 hours) to the point of dynfunctional labor (contractions which do not produce dilatation and expulsion of the fetus). Dynfunctional labor may lead to asphysia (suffocation). Lucey, Hibbard, Behrana, Esquivel de Gallando and Windle (1964) have found a significant correlation between asphysia and kernicterus in Phesus monkeys, and they have concluded that the more ismature the newborn the greater the dangers of birth asphysia, intrauterine insults and drug effects.

## 2. Direct effects on newborn

The newborn's transition from intrauterine to extrauterine life imposes upon him the need to activate a number of functions that have been dormant or incompletely activated (Snyder, 1949). Some of them, such as respiratory activity and maintenance of body temperature, must be established immediately at some minimal level of acceptable functioning.

The birth process itself with the sudden, often catastrophie, alteration in physiology may be a hazardous experience for the fetus. James (1960) at Columbia University studied a large number of babies immediately after birth and found that all the infants were subjected to varying degrees of oxygen deprivation and carbon dioxide retention during the course of labor and delivery. Under normal circumstances most infants tolerate this brief "asphyxia" without difficulties and within a short time show little evidence of the biochemical storm they have recently survived. Failure of the oxygen supply during labor, however, results in depression or absence of fetal respiratory movement at birth, 5 as well as in vascular injuries giving rise to edema and hemorrhages of the lungs and other organs. These, in turn, oggravate the lack of oxygen thus creating a vicious cycle (James, 1960).



In premature infants, oxygen deprivation is closely linked with perinatal mortality. Thus, the fetal respiratory system is the site of greatest voluerability to injury in labor and delivery and that is why for years the majority of the research has been concerned with the relation of obstetric medications and meanatel depression (Snyder, 1949). Even in 1933, Shute and Davis observed that morphine could increase the chances of asphyxia in utero as indicated by change of rhythm of fetal heart. Asphyxiated infants were, in turn, more susceptible to morphine and showed severe symptoms of narcosis. Snyder (1949) summed it up: "All drugs commonly given for the relief of pain tend to alter the functioning of respiration thus striking the fetus at the point which has been found to be of maximum susceptibility to injury during labor." Many observers disagree with the statement and the research on whether narcotics (e.g., meperidine) cause depression in the newborn, ranges from studies that claim zero percent depression to studies that attribute 32% of their newborn depression to mercridine (Shnider and Moya, 1964). . Garcia, Waltham and Lubin (1953) even recommended the administration of meperidine in quantities of up to 100 mg., but they also reported that some of the babies in their study had to be resuscitated by artificial respiration lasting up to 90 seconds before onset of respiration. However, they did not attribute such depression to meperidine. Others, such as Zaru, Esposito and Zaru (1967), have advocated continuous infusion of meperidine (average per hour 40.3 mg.) since "obstetric and subjective evaluation of pain relief was excellent and newborn depression was not significant." In contrast, Flowers, Rudolph and Desmond (1969, who used diazepam (Valium) which is classified as a

"minor" tranquilizer and a mild analgesic, found that a significant percentage of neonates suffered moderate depression and some showed severe depression in comparison with a control group that did not have any drugs. Flowers, et al. attributed the depression to a hypotonic effect of discepam and not to any direct offect of the respiratory center in the CNS. This drug has lately been used in the management of neonatal narcotic withdrawal syndrome (Nathenson, Golden and Litt, 1971), since it produces temporary hypoactivity and hypotonicity in meonates. The concentration of barbiturates, e.g., amylobarbitone, in the fetal liver is already relatively high 🍹 to 2 hours after injection and decreases very slowly. This accumulation might indicate an exhaustion of the detoxicating capacity of fetal liver (Pleman and Persson, 1957). Floman and Persson (1957) also studied the concentration of barbiturates in fetal brains. They found a much higher amount of barbiturates concentration in the region of the fourth ventricle as compared to the cortem. This is significant since the medullar respiratory center lies in the vicinity of the fourth ventricle.

Despite these findings, Bran and Montalvo in 1971, advocate the use of barbiturates in labor, claiming (on the basis of animal experiments) that barbiturates protect the neonates against the effects of prolonged anomia (oxygen deprivation). Epstein and Coacley (1967) reported that local anesthetics (lidocaine and prilocaine) had little depressing effect on the neonate. However, Levy (1953) and Morisima, Daniel, Finster, Popper and James (1966) found that a relatively high percentage of neonates were depressed even with local anesthetics such as mapivacaine. These drugs, which were not supposed to reach the fetus,



did pass through the so called placental barrier into the fetal blood stream in significant amounts.

Drugs may affect the neonate's respiration in other ways too. For example, reserpine is a relatively mild tranquilizer; for this reason it has been employed to ease the course of labor. The adverse effects in the adult do not appear to be disturbing. Stuffiness of the nose is the major frequent complaint. A stuffy nose in the newborn may, on the other hand, produce mild to severe respiratory difficulty because of the relative inability of the infant to breathe through the mouth (Whan and Lampert, 1965).

The confusing and contradictory data on depression of neonates produced by different drugs may be due to two reasons. Firstly, many of the basic experiments have been conducted on animals. Animals differ in their reaction to drugs and are certainly different from humans (Done, 1964). For example, thalidomide did not produce any teratogenic effect (maldevelopment) in rats and in monkeys it produced only sterility (Nyhan and Lampert, 1965). Secondly, the importance of the time interval between administration and delivery has often been overlooked, even though there has been important evidence about this factor since 1933. That year Shute and Davis pointed out that morphine has the maximum effect on the neonate when administered to the mother in labor anywhere between one and six hours before delivery. This was true even if mothers had received only 50 mg. of meperidine. Shnider and Moya (1964) sutdied the effects of meperidine on newborn infants and found that there was no statistically significant effect if the drugs were administered within one hour before birth (confirming Shute and Davis' conclusions). However, there was a significant increase in

the percentage of depressed babies if the drug was administered more than one hour before delivery. This was true even if mothers had received only 50 mg. of meperidine. Peak effect of drugs occurred if the drug had been administered somewhere between 3/2-4 hours prior to delivery. These conclusions are quoted by many writers. Shuider and Moya and other investigators have based their conclusions on the Apper 7 Score taken at 1 and 5 minutes immediately after birth. Shuider and Moya's results could be explained by suggesting that if the drug is administered less than one hour before birth, the newborn will receive a significantly smaller amount of drugs. However, as mentioned before, the drugs that pass through the placenta do so within seconds after the injection or inhalation and thus the explanation can be questioned. A more likely possibility is that the observations of Shmider and Moya and others can be explained by the fact that the babies in their studies were examined for depression in the first minutes after delivery and none of the studies concerned mentions the search for drug effects after two, three, or more hours after delivery. Thus, one may suspect that babies whose mothers' were given medications during the last hour preceding delivery are not necessarily free from effects of the drug but that the peak effect has yet to manifest itself.

It is the pediatrician who sees the newborn two, three or more hours after delivery. Brazelton (1970) noted: "...(Some) neonates had excellent Appar Scores in the delivery room and remained clinically responsive for half an hour - long enough to be sent to the nursery downstairs. After this initial period of responsiveness, (which I now postulate is largely due to the meanate's ability to mobilize his resources to respond to the stimulation of labor, delivery and the



onslaught of new environmental stimuli), these bubies shifted rapidly into a frightening state of relative unresponsiveness and they became unresponsive to any but very disturbing stimuli, with little spontaneous motor activity; they also had very slow heart and respiratory rates. Diffuse acrocymosis (bluish extremeties) demonstrated their poor circulatory response to the hypoxia that was present, and their ability to clear mucus from their airways became impaired. This depressed behavior lasted for a period of a few hours to a day and then tapered off not-so-gradually; subclinical behavior manifestations could be demonstrated for as long as a week in many infants." (Brazelton and Robey, 1965).

Drug effects are not limited to the functions measurable by the Apgar Scale, which is clinically useful but a rather crude estimate of infantile physiology. There have been a few attempts to investigate other aspects of infant's behavior and functioning using EEG, sucking behavior, sleep and smiling, attention and mother-child interactions. In some of these areas there is only the briefest of literature; in others, it is a bit more extensive; in none of them is there a definitive literature.

#### Neurologic examination and EEG

Borgstedt and Rosen (1968), in a controlled study of 52 infants, found that "behavioral impairment" (as measured by infant's alertness and reactivity) as well as EEG alterations were highly correlated with obstetric medication (meperidine, prometazine, phenobarbital). The behavioral changes disappeared in most cases within three days, but EEG changes persisted in ten infants.

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### Sucking

Both Brazelton (1961 II) and Kron (1966) independently studied sucking behavior. In Brazelton's study, two groups of meanates were evaluated. One had relatively little premedication, i.e., barbiturates not exceeding 60 mg. with or without anesthetic, general or local; and the other group, 150 mg. or more with general or local anesthesia. The less medicated group started to suck well on the second day. The neonates in the heavy premedication group showed a lag of 48 hours duration in their specific ability to adapt to breast feeding. Weight gain was also delayed 24 hours in the heavily medicated group. Kron's (1966) results confirmed these findings. His control group had no medications and he used a more refined measure of sucking. The bottle was attached to instruments which measured the rate of feeding, pressure of suction and amounts. By studying only bottle fed babies, the possibly confounding factor of drug effects on the nursing mother was excluded.

The implications of these studies are related to the fact that body temperature control may be affected by inadequate caloric intake.

## REM and Smiling

Emde and Koening (1969 a, b) found that neonatal smiling occurred during states of REM sleep<sup>S</sup> and drowsy REM and had a significant tendency to occur in bursts. Smiling was also found to have a characteristic distribution within each REM period and to be evenly distributed across successive REM periods. Amount of smiling was found to be influenced by depressant medications given to the mother within 8 hours before delivery. Infants of these mothers smiled significantly less both in number of smiles and smiles weighed for intensity. Nedications did not seem to affect the length of REM states.



#### Attention

Stechler (1964) found that visual attentiveness in 2 to 4 day old infants, was affected if the mother had received analgesics and hypnotic drugs during labor. There was negative correlation between the dosage of the depressing drugs and neonates' attention to visual stimuli. In a study that is not directly related to our discussion, Lewis, Bartels, Campbell and Coldberg (1967) used the Apgar Scale as a measure of condition at birth against which they compared the visual attentive behavior of infants at 3, 9 and 13 months. data indicated that infants who rated between 7 to 9 on the Apgar Scale at birth were significantly less attentive than infants who rated 10. This difference, in general, held over the first year of life and according to Lewis et al., indicate that individual differences in infant attention within the first year of life are a function, in part, of birth condition. Lewis, et al. also found that habituation at the age of three months in high Apgar score infants was much more rapid than in the low score infants. There was no difference in habituation rate at 9 and 13 months. Lewis, et al., however, do not relate their observations to maternal medication of their subjects, but instead discussed the birth condition as a global concept. Conway and Brackbill (1970) found that neonates who have been subjected to greater amounts of obstetrical medication (analgesics and anesthetics) lagged significantly in their ability to inhibit responding to an auditory stimulus.

These findings may have important implications concerning the welfare of the infant since "habituation is the efficient response to stimulation that is no longer providing the organism with useful



information" (Lewis, et al.). Reconates just cannot get up and walk away from the stimulus which by them may become aversive for them. Conway and Brackbill (1970), who studied the infants on their second and fifth days and at one month, also found that "the medicated meanates performed significantly poorer on standard behavioral tests than infants whose mothers have not been medicated during labor." The differences persisted even at the age of one month -- as measured by the Bayley Motor Scale (1969), which at the one month age level consists largely of postural adjustment items. No significant differences were noticed for the Bayley Mental Scale, in which the age appropriate items concentrate more heavily on testing visual regard, that is, eye coordination and following in horizontal, vertical, and circular direction. Visual differences were also found at 5 days of age, but no differences were found on the second day, probably because of the swelling of the eyelids and consequent visual impairment caused by the silver nitrate given to all infants shortly after delivery. Significant differences were found at 2 and 5 days in performance on the Graham Muscle Tension Subscale (Graham, 1956). The babies with history of obstetrical medication performed less well. Conway and Brackbill followed some babies till the age of 5 months. At this age there were no significant differences on the Bayley Scale nor in habituation scores although the latter showed a tendency toward quicker habituation with less medication (Conway, 1972).



#### Pootnotes

 The reader will find Gordman & Gilben (1970) complete reference on drug transmint and Snyder (1949) good reference on obstatric anesthesia and analysis.

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- 2. An eater is an enganic egapound formed by combining an alcohol with an acid (Hamper, 1969, p. 543).
- 3. Amides are compounds containing the group =00(NH2) or its substitutes (Harper, 1969, p. 545).
- 4. Toxomia is a toxic state associated with pregnancy and its main symptoms are: clevated blood pressure, excessive veniting, change in kidney function.
- 5. The fictus has respirately nevements already in utero and they increase when term approaches.
- 6. "Rechard degression" means a reduction or slowing down of a number of physiclogical functions: respiration, heart rate, mobility, etc.
- 7. The Appar Score is based upon the combined rating of five indicators: heart rate, respiratory effort, nucele tone, reflex irratibility and color as judged at 1 minute and 5 minute intervals after delivery.

  Each is rated on a scale of 0 to 2, with zero indicating no function; 1, function present but poor; and 2, function perfect. Thus, an infant in perfect condition would require a score of 10. This Scale is now used by most obstatricians and rescarchers in order to determine intensity of neonatal depression (Appar, V., 1953).



8. RET or Rapid Eye Movement sleep is the phase of sleep usually associated with dreaming and also called "active sleep." The time percentage of active sleep (compared to total sleep time) decreases progressively from 80% in premature newborns to 18% in adults. Sedatives decrease REM in adults (Bartaen, 1966).

### APPENDIX B

#### APPENDIX B

#### MANUAL FOR SCORING THE BRAZELTON SCALE

#### Recommended Scale Order (See discussion above)

- 1. Observe infant for 2 minutes note state
- 2. Flashlight (3-10x) through closed lids
- 3. Rattle (3-10x)
- 4. Bell (3-10x)
- -5. Uncover infant
- 6. Light pinprich (4x)
- 7. Ankle clonus
- 8. Plantar grasp
- 9. Babinskí
- 10. Undress infant
- 11. Palmar grasp
- 12. Passive movements and general tone
- 13. Orientation inanimate: visual, auditory
- 14. Pull to sit
- 15. Standing
- 16. Walking
- 17. Placing
- 18. Incurvation
- 19. Body tone across hand
- 20. Crawling prone responses
- 21. Pick up and hold
- 22. Glabella reflex
- 23. Spin tonic deviation and hystagmus
- 24. Orientation animate: visual, auditory, visual and auditory
- 25. Cloth on face
- 26. TNR
- 27. Moro

#### States

"State of consciousness" or "state" is one of the most important variables in any observation period. Reactions to stimuli must be interpreted within the context of the presenting state of consciousness. These reactions vary markedly from state to state in each infant. State depends on physiological variables such as hunger, nutrition, degree of hydration, time within the wake-sleep cycle of the infant, etc. The patterns of states as well as the movement from one state to another appear to be important





characteristics of infants in the meanatal period, and this kind of evaluation may be the best predictor of the infant's receptivity and ability to respond to stimuli in a cognitive sense. Our criteria for determining states are based on our experiences and on those of others, and are comparable to the descriptions of Prechtl, et al. (15).

#### Sleep States

- (1) Deep sleep with no spontaneous activity except startles or startle equivalents at quite regular intervals; external stimuli produce startles with some delay; suppression of startles is rapid, and state changes are less likely.
- (2) Light sleep with eyes closed, low activity level with random movements and startles or startle equivalents; responsive to internal and external stimuli with startle equivalents, often with a resulting change of state.

#### Awake States

- (3) Eyes may be open or closed, eyelids fluttering, drowsy, or semi-dexing; activity level variable with interspersed mild startles from time to time; reactive to sensory stimuli, but delay in response often seen; state change after stimulation frequently noted.
- (4) Alert, bright look; seems to focus attention on source of stimulation such as an object to be sucked, visual or auditory stimulus; impinging stimuli may break through, but with some delay. Motor activity is at a minimum.
- (5) Eyes open, considerable motor activity with thrusting movements of extremities, even a few spontaneous startles; reactive to external stimulation with increase in startles or motor activity, but discrete reactions difficult to distinguish because of general high activity level. Intermittent fussing does not result in a change of state.
- (6) Crying. Characterized by intense crying which is difficult to break through with stimulation.

We have suggested in parentheses appropriate states in which the assessment can be made for each state. Since state behavior is an integral part of any observation of the newborn, it is vital that this reflect the starting point



from which all the rest of the observations are made. The reactions are state-related, and an infant's use of states as a framework for his reactions to the observer may be most important as part of the observation.

#### Initial State

In the two minutes before stimulation is begun, an assessment of the infant is made by observing the infant's spontaneous behavior, respirations (as observed by the movement of the gown or covering sheet), eye movements, startles, and responses to concurrent spontaneous events in the environment. States are scored according to the criteria given above.

#### Predeminant States

At the end of the observation period, E should record the two or, at most, three states within which the infant performed. Since the most important influence on his scores will be his available states, it is important to have an idea of the range, as well as the kinds of states used by the infant in this period, their importance to him in controlling himself, and the amount of time spent in them.

#### IX. Scale Items and Manual Description

#### 1. Response Decrement to Light (2,3)

One of the most impressive mechanisms in the mechanism is his capacity to decrease responses to repeated, disturbing stimuli. This should measure the decrement which occurs in a quiet state (2,3) after the infant has responded with an aversive reaction to the flash-light shined briefly into his eyes (closed or open). Since some babies alert as the light is used, there is no esservable aversive reaction. When this happens, wait until he is alert, and after he begins to react with an aversive reaction (tight blinking, general motor activity, and change in respiration) habituation is measured by a real decrement in the extent of the above.

Up to 10 stimuli can be used. Criterion for shutdown equals two trials past. Score the most observed decrement. Stimuli presented

every five seconds after the end of each provious response. This implies the observer's ability to judge the end of each reaction. This test should be done with a standard 8" flachlight with two modium sized batternies in good working condition. Flashes must be discrete and ambient noise level should be accounted for and ruled out as much as possible. Of course, a baby in a semi-darkened quiet room will respond differently than one in a brightly lit noisy mursery, and the ideal of the quiet, darkened room carmet always be achieved. Reactions which are graded in terms of the neonate's ability to centrol them over time are: a) all or none startle of entire body, b) delayed and graded localized startle, c) respiratory changer, d) blinks of cyclids. Delaying and finally simitting out any reactions are degrees of the same kind of habituation. Evaluate him at the end of 10 flashes for scoring unless he has successfully reached criterion before that. If baby is too sleepy to show a response, he can be roused slightly by shaking the bed or uncovering him. If there's never any response, score him MA.

- 1 No diminution in high response over the 10 stimuli.
- 2 Delayed startles and rest of responses are still prosent, i.e., body movement, eye blinks, respiratory changes contimum over 10 trials.
- 3 Startles no longer present but rest are still present, including body movement in 10 trials.
- 4 No startles, body movement delayed, respiratory and blinks same in 10 trials.
- 5 Shutdown of body movements, some diminution in blinks and respiratory changes in 9-10 stimuli.
- 6 ... in 7-8 ctimuli.
- 7 ... in 5-6 stimuli.
- 8 ... in 3-4 stiruli.
- 9 ... in 1-2 stimuli.
- 2. Response Decrement to Rattle See below.

#### 3. Response Pecrement to Fell (2,3)

These are a measure of the meanate's ability to shut out a disturbing auditory stimulus. Hence (as in habituation to light) the stimulus must be able to break through his ambient state and create a startle response. The bell may be more successful in producing a startle response, especially in a noisy nursery. Often the rattle may bring him out of his generally shut-down state, and the test should then be completed with the ball. A bell is that used in a standard Gesell test. He is scored (as above) for an aversive reaction (general startle, tight blinking and respiratory changes). As he habituates, he tends to delay these reactions and finally shuts them out. Often the chut-out is a temporary one, but this reflects his capacity to do so. If the baby is too sleepy to show a response, he can be roused slightly by challing the bed or uncovering him. If there's never any response, score him 114.

Staralli are brief, discrete and presented five seconds after the



end of the previous response while the baby is in state 2 or 3. Present the stimulus until you have had no response for three consecutive times or until 10 stimuli have been presented. After the rattle, repeat the procedure with the bell.

- 1 No diminution in high response over the 10 stanuli.
- 2 Delayed startles and rest of responses are still present, i.e., body movement, eye blinks, respiratory a changes continue ever 10 trials.
- 3 Startles no longer present but rest are still present, including body movement in 10 trials.
- 4 No startles, body movement delayed, respiratory and blinks same in 10 trials.
- 5 Shutdown of body movements, some diminution in blinks and respiratory changes in 9-10 stimuli.
- 6 ... in 7-8 stimuli.
- $7 \dots$  in 5-6 stimuli.
- $8 \dots$  in 3-4 stimuli.
- $9 \dots$  in 1-2 stimuli.

#### 4. Response Decrement to Pinprick (1,2,3)

As a test of response decrement to tactile stimulation the diaper pin may be used to prick the heel of the infant's feet when he is quiet. This may be repeated several times. The examiner watches for how totally and how rapidly the whole body responds to this pinprick. In an immature or CHS-damaged infant, the opposite foot withdraws and the whole body responds as quickly as the stimulated foot (a demonstration of the all-or-none aspect of an immature organism). The degree, rapidity, and repetition of this "spread" of stimulus to the rest of the body is measured here. The other aspect is the infant's capacity to shut down this spread of a generalized response. When he continues to respond in an obligatory, repetitive way, he rates a low score. As he demonstrates a suppression of responses to the stimulus and changes his state to a more alert, receptive one, he deserves a high score. Many infants demonstrate some but not all of this behavior, and it may be evidence of excellent CNS function. Middle scores are saved for infants who demonstrate some habituation but not an accompanying state change of alertness.

The foot should be pricked at least four times. If no response decrement occurs, the stimulation should be stopped. If decrement occurs, a fifth stimulus and more can be applied to test the extent of the decrement. (For the squeamish, an appropriate stimulus is a pin pushed through a cork to extend 1/16th of an inch beyond the cork.)

1 - Response generalized to whole body. Both feet withdraw together. No decrement in response.



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- 2 Response limited to stimulated foot. No decrement of response.
- 3 Variable response to stimulus. Response decrement but return of response.
- 4 Response decrement after five trials. Localized to stimulated lag. No change to alert state.
- 5 Response decrement after five trials. Localized to stimulated foot. No change to alert state.
- 6 Response limited to stimulated foot after 3-4 trials. No change to alert state.
- 7 Response limited to stimulated foot after 1-2 trials.
  .No change to alert state.
- 8 Response localized and minimal. Change to alert state (4).
- 9 Complete response decrement. Change to alert state (4).

#### 5. Orientation Response - Inanimate Visual (4 only)

Since most neonates will demonstrate some ability to fix on a visual object (a contrasting bright or shiny object, e.g., a bell, red ball, white mask) and follow it horizontally for brief excursions, this is a measure of that ability. It is highly state-related, and may not be demonstrated in any one exam, but, under optimal conditions (a quiet, semi-dark room), it is repeatable; following with the eyes is also accompanied by head-turning to follow. Vertical following seems of an even higher order, and many babies will stretch their necks to follow up and down. This is a summary score.

The infant may respond with (1) alerting (decrease in random activity, focus on examiner's face when it is in his line of vision, slow regular respirations, and follows face when it moves in arcs) and (2) brightening (change in facial expression, widening of eyes and brighter look, jagged respirations, with an associated decrease in random activity).

When the infant will not attend or fellow in the bassinet, he may be held on the E's lap, slightly propped up. This facilitates his doll's eye reflex; his eyes open, and he attends to the object. Obviously, the act of holding him restrains interfering movement and helps alert him. But he may also be distracted by the examiner's face. Held at the E's shoulder, his following responses can be determined by another examiner.

- 1 Does not focus on or follow stimulus.
- 2 Stills with stimulus but no focus.
- 3 Stills, focuses on stimulus when presented, little spontaneous interest, no following.
- 4 Stills, focuses on stimulus, brief following.
- 5 Focuses and follows with eyes horizontally and/or vertically for at least a 30° arc. Jerky movement.



loses stimulus but finds it again. No following with head, some spontaneous interest.

6 - Follows for 30° ares, not with head. Eye movements are smooth.

- 7 Fellows with eyes and head at least 60° horizontally, briefly vertically, partially continuous movement, loses stimulus occasionally, head turns to follow.
- 8 Follows with eyes and head  $60^{\circ}$  horizontally and  $30^{\circ}$ vertically.
- 9 Focuses on stimulus and follows with smooth, continuous head movement horizontally, vertically, and in a circle. Follows for at least a 120° arc.

# 6. Crientation Response - Inanimate Auditory (4,5 states)

This is a measure of his response to the rattle or a soft bell (non-social) as a stimulus when he is in an alert state. The auditory stimuli should be presented to one side and out of sight (at least 6" away and no more than 12") so that one can observe the infant's eyes and head as they restond to the lateralized stimulus. This scores his best performance in one of the evake states to the stimulus. Latency altering degree of eve shift and head turning to the stimulus are scored. Brightening of face and eyes can be seen, and they are evidences of his attention to the stimulus.

- 1 No reaction.
- 2 Respiratory change or blink only.
- 3 General quieting as well as blink and respiratory changes.
- 4 Stills, brightens, no attempt to locate source.
- 5 Shifting of eyes to sound, as well as stills and brightens.
- 6 Alerting and shifting of eyes and head turn to source.
- 7 Alerting, head turns to stimulus, and search with eyes.
- 8 Alerting prolonged, head and eyes turn to stimulus repeatedly.
- 9 Turning and alerting to stimulus presented on both sides on every presentation of stimulus.

# 7. Orientation - Animate Visual

The next three items score the attention which is called up by the examiner's social cues--voice, face, cuddling, holding, rocking, etc. The infant may respond with electing, brightening, and settling into the arms. He may turn his head to seek the voice or face. Having caught the examiner, he may rivet his attention, and "lock" on for long periods. No interest is unusual. How he is held may strongly influence this, and the E should attempt to



reproduce two maneuvers commonly used by mothers: (1) hold the infant in a cuddled position in the arms up against the chest, and (2) upright on the shoulder in a bubbling position.

For the "visual only" item the examiner places his face in the B's line of vision then moves it slowly in lateral and vertical arcs until the B stops following.

- 1 Does not focus on or follow stimulus.
- 2 Stills with stimulus but no focus.
- 3 Stills, focuses on stimulus when presented, little spontaneous interest, no following.
- 4 Stills, focuses on stimulus, brief following.
- 5 Focuses and follows with eyes horizontally and/or vertically for at least a 30° arc. Jerky movement, loses stimulus but finds it again. No following with head, some spontaneous interest.
- 6 Follows for 30° arcs, not with head. Eye movements are smooth.
- 7 Follows with eyes and head at least 60° herizontally, briefly vertically, partially continuous movement, loses stimulus occasionally, head turns to follow.
- 8 Follows with eyes and head 60° horizontally and 30° vertically.
- 9 Focuses on stimulus and follows with smooth, continuous head movement horizontally, vertically, and in a circle. Follows for at least a 120° are.

#### 8. Orientation - Animate Auditory (4,5)

The examiner removes his face from infant's line of sight and talks to him from one side (6 to 12 inches from ear).

- 1 No reaction.
- 2 Respiratory change or blink only.
- 3 General quieting as well as blink and respiratory changes.
- 4 Stills, brightens, no attempt to locate source.
- 5 Shifting of eyes to sound, as well as stills and brightens.
- 6 Alerting and shifting of eyes and head turn to source.
- 7 Alerting, head turns to stimulus, and search with eyes.
- 8 Alerting prolonged, head and eyes turn to stimulus repeatedly.
- 9 Turning and alerting to stimulus presented on both sides on every presentation of stimulus.

#### 9. Orientation Animate - Visual and Auditory (4 only)

The same criteria for scoring are used as in Items 5 and 7. The same conditions pertain except that the examiner's voice is used to reinforce face, both on the bed and when infant is held. Voice is continuous while face is moving.

- 1 Does not focus on or follow stimulus.
- 2 Stills with stimulus but no focus.
- 3 Stills, focuses on stimulus when presented, little spontaneous interest, no following.
- 4 Stills, focuses on stimulus, brief following.
- 5 Focuses and follows with eyes horizontally and/or vertically for at least a 30° arc. Jerky movement, loses stimulus but finds it again. No following with head, some spontaneous interest.
- 6 Follows for 30° arcs, not with head. Eye movements are smooth.
- 7 Follows with eyes and head at least 60° horizontally, briefly vertically, partially continuous movement, loses stimulus occasionally, head turns to follow.
- 8 Follows with eyes and head 60° horizontally and 30° vertically.
- 9 Focuses on stimulus and follows with smooth, continuous head movement horizontally, vertically, and in a circle. Follows for at least a 120° arc.

#### 10. Alertness (4 only)

This is an assessment of the frequency of the best periods of performance in 4. Often this is elicited while the E holds the infant. Since newborns are as variable as they are, and are alert for such a short period, one must assume that any period of alertness in a 30 minute exam may be taken as an index of the infant's "capacity for responsiveness." In a less randomly selected time sample than this, or when one can wait for a spontaneous period of alertness, this measure might be a better index of his availability, but I have found that most infants show small periods of alert behavior during an exam. These should be assessed. Alerting is defined as brightening and widening of eyes, while orienting is used for the response of turning toward the direction of stimulation.

- 1 Inattentive--rarely or never responsive to direct stimulation.
- 2 When alert restansivity brief and generally quite delayed--alerting and orientation very brief and general.
- 3 When alert responsivity brief and somewhat layed-quality of alerthess variable.



- 4 When alert, responsivity somewhat brief but not generally delayed though variable.
- 5 When elert, responsivity of moderate duration and response generally not delayed and less variable.
- 6 When alert, responsivity moderately sustained and not delayed. May use stimulation to come to alert state.
- 7 When alert, episodes are of generally sestained duration, etc.
- 8 Always has sustained periods of alertness in best periods. Alerting and orientation frequent and reliable. Stimulation brings infant to alert state and quiets infant.
- 9 Always alert in best periods. Stimulation always elicits alerting, orienting. Infant reliably uses stimulation to quiet self or maintain quiet state.

#### 11. General Tonus - Predominant Tone (4,5)

This scores the tone of the baby in his most characteristic states of responsiveness. Since this must be a summary assessment, it should include the overall use of tone as he responds to being handled. This should be assessed in state 4--unless there is no opportunity to produce such an assessment. This should not be assessed in 6.

Tone is assessed in such maneuvers as spontaneous activity, pull to sit, holding him over hand herizontally, prone placement, etc., and should be an overall assessment of his body tone as he reacts to all of these.

- 1 Flaccid, limp like a ragdoll, no resistance when limbs are moved, complete head lag in pull to sit.
- 2 Little response felt as he is moved, but less than about 25% of the time.
- 3 Flaccid, limp most of the time, but is responsive about 25% of the time with some tone.
- 4 Some tone half the time, responds to being handled with some tone less than half the time.
- 5 Tone when handled, lies in fairly flaceid state in between handling.
- 6 Variable tone in resting, responsive with good tone as he is handled approximately 75% of the time.
- 7 Is on the hypertonic side approximately 50% of the time.
- -8 When handled he is responsive with hypertonicity about 75% of the time.
  - 9 Hypertonic at rest (in flexion) and hypertonic all the time (abnormal).

Supplementary Score - After most of the shaped summary scores, there will be an apportunity to score a second kind of observation.



This need not be utilized. When it is used, it will mean that the first score represents the score for the major part of the observation, since using a summary score for two very divergent types of behavior negates the importance of each. This second score gives an opportunity to assess body tone of a secondary kind and, also, some idea of the range of tone which the baby may present. Hence, this can be used to denote a minority value, which may or may not have significance for the long run. For example, this score could predict future behavior, or it may present evidence to contradict complete reliance on the susmary score.

#### 12. Motor Muturity (4,5)

This is a measure of motor responses—spontaneous and elicited—assessed throughout the exam in the alert states. The arm movements become the easiest to score. The assessment is of (1) smoothness versus jerkiness which reflects the balanced flexor and extensors versus the unbalanced cogwheel movement of the premature or CNS irritation with flexors and extensors competing, and (2) freedom of ares of movement (90°)(arms on bed) versus restricted arcs (45° etc.)(arms and legs in flexion). The premature has unlimited freedom of movement (floppy) in lateral, sagittal, and cephalad areas, but the movements are jerky and cog-like, evershooting their marks. The very mature infant has both freedom of movement in all directions associated with a smooth, balanced performance (not floppy). The average newborn is somewhat limited in arcs of movement—especially those above the head, and somewhat in the lateral plane.

- 1 Cogwheel-like jerkiness, overshooting of legs and arms
  in all directions.
- 2 Jerky movements and/or mild eversiooting.
- 3 Jerky movements, no overshooting.
- 4 Only occasional jerky movements predominating arcs to 45°.
- 5 Smooth movements predominate, arcs predominately 60° half the time.
- 6 Smooth movements, arcs predominately 60°.
- 7 Smooth movements and arcs of 90° less than half of the time.
- 8 Smooth movements and unrestricted arms laterally  $90^{\circ}$  most of the time.
- 9 Smoothness, unrestricted (90°) all of the time.

#### 13. Pull-to-sit (3,5)

The examiner places a forefinger in each of the infant's palms. With the arms extended, the infant's automatic grasp is used to pull him to sit. The shoulder girdle muscles should respond with



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tone, and muncular attempts to participate as he is pulled into a sitting position. Usually he will also attempt to right his head into a resition which is in the midline of his trunk and parallel to his body. Since his head is heavy and out of proportion to the rest of his body mass, this is not usually possible and his half is falls backward as he comes up. In a seated position, he off apts to right his head, and it may fall forward. Several attempts to right his head, and if pay fall forward. Several attempts to right it can be felt six the shoulder measier at the enaminer unlittain, his grapp on the infant a name. A fly infants make no attempt at all.

Some infants resist flexion and head righting by arching back-ward. This must be evereone before he can be scored. The average infant makes one or two attempts to maintain his head in an upright position after he is sented, and can participate as he is brought to alt. This should be scored when he is awake enough to participate (3,5), and is scored on his best performance.

- 1 Head flops completely in pull to sit, no attempts to right it in sitting.
- 2 Futile attempts to right head but some shoelder tone increase is felt.
- 3 Slight increase in shoulder tone, senting brings head up once but not maintained, no further efforts.
- 4 Shoulder and sen tone increase, seeping brings head up, not institutined but there are further efforts to right it.
- 5 Head and shoulder tone increase as pulled to sit, brings head up care to midline by self as well, maintains it for 1-2 seconds.
- 6 Head brought up twice after seated, shoulder tone increase as comes to sit, and maintained for more than 2 seconds.
- 7 Shoulder tone increase but head not maintained until seated, then can keep it in position 10 seconds.
- 8 Excellent shoulder tone, head up while brought up but cannot maintain without falling, repeatedly rights it.
- 9 Head up during lift and maintained for one minute after scated, shoulder girdle and whole body tone increases as pulled to sit.

#### 14. Cuddliness (4,5)

This is a measure of the infant's response to being held. There are several components which are scored in numbers of his responses to being held in a cuddled position maximat the examiner's chest, and up on his shoulder. The responses are a measure of his negative, or positive responses, as well as none at all.

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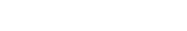
- Actually resists being held, continuously pushing away, throshing or stiffening.
- 2 Resists being held most but not all of the time.
- 3 Doesn't resist but doesn't participate either, lies passively in arms and against shoulder (like a sack of ment).
- 4 Eventually molds into arms, but after a lot of nestling and cuddling by examiner.
- 5 Usually rolds and relaxes when first held, i.e., nestles head in crook of neck and of elbow of examiner. Turns toward body when held herizontally, on shoulder he seems to lean forward.
- 6 Always molds initially with above activity.
- 7 Always molds initially with nestling, and turning toward body, and leaning forward.
- 8 In addition to molding and relaxing, he nestles and turns head, leans forward on shoulder, fits feet into cavity of other arm, all of body participates.
- 9 All of the above, and taby grasps hold of the examiner to cling.

#### 15. <u>Defensive Movements</u> (4)

A small cloth is placed with examiner's fingers asserting light pressure over the upper part of the face which would partially occlude the nose, and is kept in place for one minute, or until the infant responds with a series of responses:

(1) general quieting (b) mouthing (c) head turning and rooting from side to side (d) head turning largeral as well as mathematical training larger as well as a second contraction of the second contraction of the

- (d) head turning lateral as well as nech stretching up and down (e) general undirected increase in activity (f) directed swipes in general area of cloth (g) directed swipes in specific area of cloth which removes the cloth. Infant's hands should not be under cloth.
  - 1 No respense.
  - 2 General quieting.
  - 3 Nonspecific activity increase with long latency.
  - 4 Same with short latency.
  - 5 Rooting and lateral head turning.
  - 6 Neck stretching.
  - 7 Nondirected swipes of arms.
  - 8 Directed swipes of arms.
  - 9 Successful removal of cloth with swipes.



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- 1 Not connolable.
- 2 lacifier in addition to dressing, holds are reching.
- 3 Dressing, holding in arms and recking.
- 4 Holding and rocking.
- 5 Picking up and holding.
- 6 Hand on belly and restraining both arms.
- 7 Hand on belly steadily.
- 8 Examiner's voice and face alone.
- 9 Examiner's face alone.

#### 17. Peak of Excitement (6)

This is a measure of how much motor and crying activity the infant gives off to the observer at his peaks of excitement, and responsiveness pulls him toward the mean. The kind of intense reactions which some infants demonstrate when they reach their peak of excitement shows an unavailability to the outside world, and must be scored high. Others are hardly able to be jogged to respond at all, and their peak is very low. An average and optimal response would fall in the moderate, reachable range, in which the infant could be brought to respond to stimuli in spite of a high degree of upset or excitement, but then return to more moderate states.

- 1 Low level of arousal to all stimuli. Never above state 2, does not awaken fully.
- 2 Some arousal to stimulation--can be awakened to state 3.
- 3 Infant reaches state 4 briefly, but predominantly is in lower states.
- 4 Infant is in state 5 after orimulation.
- 5 Infant reaches state to after stimulation once or twice, but predominantly is in state 5 or lower.



- 6 Infant reaches state 6 after stimulation, but returns to lower states spontaneously,
- 7 Infant reaches state 6 in response to stimuli, but with consoling is easily brought back to lower states.
- 8 Infant screams (state 6) in response to stimulation, although some quieting can occur with consoling, with difficulty.
- Infant achieves insulated crying state. Unable to be quieted or soothed.

#### 18. Rapidity of Euildup (from 1,2 to 6)

This is a measure of use of states from quiet to agitated state. It measures the timing and the number of stimuli which are used before he changes from his initially quiet state to a more agitated one. Since this implies that we start with an initially quiet baby, it measures the period of "control" which he can maintain in the face of increasingly aversive stimuli as well as the additive effect of these stimuli in changing his initially quiet state. The first preference is when one can observe the infant as he changes from a sleep state or a quiet awake one (5) to an agitated crying state (6).

- 1 No upset at all.
- 2 Not until TNR, Moro, prone placemer and defensive reactions.
- 3 Not until TNR, Moro, prone placement or defensive reactions.
- 4 Not until bulled to sit.
- 5 Not until undressed.
- 6 Not until pinprick.
- 7 Not until uncovering him.
- 8 At first auditory and light stimuli.
- 9 Never was quiet enough to score this.

#### 19. <u>Irritability</u> (3,4,5)

This measures the number of times he gets upset as well as the kind of stimuli which make him cry. Since the presentation of the stimuli is fairly set but some may bring about crying, others even more aversive may not, we have tried to make the scores flexible by counts of number of aversive stimuli.

#### Aversive Stimuli

uncoverpinprickundressTNRpull to sitMoropronedefensive reaction

- 1 Ro irritable crying to any of the above.
- 2 Irritable crying to one of the stimuli.
- 3 Irritable crying to two of the stimuli.
- 4 Irritable crying to three of the stimuli.
- 5 Irritable crying to four of the stimuli.
- 6 Irritable crying to five of the stimuli.
- 7 Irritable crying to six of the stimuli.
- 8 Irritable crying to seven of the stimuli.
- 9 To all of them.

#### 20. Activity (alert states)

This is a summary of the activity seen during the entire observation especially during the alert states. The activity consists of two kinds - (1) spontaneous, and (2) in response to the stimulation of handling and the stimuli used by the observer. A further dimension is reflected in the inaccessibility of the activity in a hyperactive child--vin. the activity is not interfered with by the observer's maneuvers. Amount of activity is graded: much = 75% or more of the time, moderate refers to 50% of the time, slight = 25% of the time. After stimulation which triggers activity, the amount of activity which persists can be assessed; much, builds up first, perpetuates itself for a period after activity is initiated; average, no buildup, and at least 3 cycles of activity which is decreasing all the time; little, 2.or 3 cycles of activity which die out quickly.

	SPONTANEOUS	ELICITED
1	none	none
2	none	brief
3	slight	1.ittle
4	moderate	little
5	. moderate	moderate
G	moderate	much .
7	much	much
8	continuous	consolable
9	continuous	unconsolable

There may be a more marked difference between spontaneous and elicited than this scale reflects. Then, he should be scored midway between them, and the examiner should be alert to the fact that this reflects a kind of discoordination, such as is seen in metabolic imbalance or CSS irritation.





#### 21. Tresuloumess (all states)

Since this may be a measure of CNS irritation or depression, and may occur for metabolic reasons, or since it may be a sign of immaturity, it becomes one more way of assessing all of these. Tremulousness is demonstrated at the end of a startle, and as a baby comes from sleeping to awake states. There is some tremor of the chin and extremities which can be expected in the meanate's first week. As the infant is dehydrated normally in the second and third day, metabolic imbalances cause tremulousness. In light sleep or as he startles in deep sleep, treads of the extremities are noted. As he becomes alort and active, the tremulousness should be overcome with smooth, voluntary behavior of the limbs. Aversive stimuli set off a startle which is followed by a return of tremulousness of the chin and extremities. Mildly aversive stimuli should not cause observable tremors in their reactions (see introduction for lists of aversive stimuli). Quivering and tremors are synonymous.

- 1 No tremors or tremulousness noted.
- 2 Chin quivering only during sleep.
- 3 Chin quivering and brief tremors of extremities only during sleep.
- 4 Chin and extremities quiver in response to one aversive stimulus.
- 5 Quivering with first presentation of aversive stimulus and/or with crying.
- 6 Quivering with some aversive stimuli and/or with state changes.
- 7 Quivering with most aversive stimuli, some mildly aversive stimuli and/or with state change.
- 8 Tremors with some state changes and/or with all aversive and mildly aversive stimuli.
- 9 Tremulousness with all stimuli and also with all self-initiated activity.

#### 22. Amount of Startle during Exam (3-6)

Both spontaneous startles and those which have been elicited in the course of stimulation are included in this. Some infants never startle during an exam, except when a Moro is elicited. Abnormally sensitive infants overreact to any disturbing stimulus with a startle, and have observable startles for no observable reason—hence they must be considered "spontaneous" or due to internal stimuli.

- 1 No startles noted.
- 2 Startle as a response to the Examiner's attempts to set off a Moro reflex--only.
- 3 Startles to two aversive stimuli (including Moro).



- 4 One spontaneous startle and at least one aversive stimulus boside a Moro.
- 5 Startles to (3) aversive stimuli at the first presentation.
- 6 One spontaneous startle and/or startle responses to aversive stimuli.
- 7 Several spontaneous startles and/or startling to all aversive stimuli.
- 8 Startles to all stimuli which Examiner presents (aversive and mildly aversive).
- 9 Startles to self-initiated stimul; and/or to all of Examiner's presented stimuli.

## 23. Lability of Skin Color (as infant moves from 1 to 5)

This measures the changes of color and vascularity which take place in a period of ewam, e.g., the acrocyanosis of peripheral mild cyanosis when the extremity is left uncovered, the change from pink to pale or purple when the baby is undressed-monthing and a web-like appearance may occur in an effort to maintain body heat. A normal newborn is likely to demonstrate mild color changes several times in an exam during which he has been undressed, disturbed, and upset. This should be assessed in particular as the infant comes from a sleep state 1 to 5. The length of time after undressing before he begins to change color is a good way to determine this. Additionally, the frequency-degree of change should be scored. No change in color may be the result of depressed or overstressed autonomic and vascular system, as seen in dopey, pale, or cyanotic infants. Marked changes which vary from minute to minute would be seen in prematures or babies who were not yet adjusted to extrauterine temperature changes, or in infants whose central and autenomic nervous systems were unable to master the changes during an exam.

Acrocyanosis should be indicated when there is more than mild, localized cyanosis of the extremities or around the mouth, and especially when the infant is not in enough stress to account for such mild changes.

Paling should be checked when paleness is unusual or excessive.

Reddening might be the result of unusual vascular changes, dehydration, or skin irritation.

Any other skin abnormality should be recorded as it might reflect metabolic or hematologic variations, which could influence the behavioral outcome of the energy.

- 1 Pale, eyanotic and doors not change during exam.
- 2 Good color which does not change during entire exam.



- 3 Healthy skin color, no change except change to blue around mouth, or extremities when uncovered or red when crying, recovery is rapid.
- 4 Acrocyanosis around mouth and extremities when undressed, slight change in chest or abdomen but rapid recovery.
- 5 Bealthy color but changes color all over when uncovered or crying; face, lips, extremities may pale or redden, mottling may appear on face, chest, limbs; original color returns quickly.
- 6 Change in color during exam, but color returns with crying or covering.
- 7 Healthy color at outset, changes color to very red or blue when uncovered or crying; recovers slowly if covered or soothed.
- 8 Good color which rapidly changes with uncovering; recovery is slow but does finally recover, when dressed.
- 9 Marked, rapid changes to very red or blue, no recovery to good color during rest of exem.

#### 24. Lability of States (all states)

This measures the infant's state performance over the exam period. Frequency of state changes over a recognizable, wide swing are counted. (Sleep to awake, crying to alert, sleep to crying, crying to sleep.) Counting should include changes upward and downward over the exam period of 30 minutes. In the event an exam does not take 30 minutes, provide it to half an hour by using the formula,

Score = state change, X 30, divided by the length of exam in minutes.

The score corresponds to the frequency of swings:

- 1 = 1-2 swings as prorated
- 2 = 3-5
- 3 = 6 8
- 4 = 9-10
- 5 = 11-13
- 6 = 14-15
- 7 = 16-18
- 8. = 19-22
- 9 23 on up.



#### 25. <u>Self Quieting Activity</u> (6,5 to 4,3,2,1)

This is a measure of activity which the baby initiates in a fussing state in an observable effort to quiet himself. The number of activities which can be observed is counted. Their success is measured by an observable state change which persists for at least 5 seconds. Most United States babbes cry or fuss vigorously at some time during the exam (state 6). For these who never do cry, the supplementary score can be used, measuring the same number of efforts. If none, BA can be used. The activities which can be counted are: (1) hand to mouth efforts (2) sucking on fist or tongue (3) using visual or auditory stimulus from the environment to quiet himself (more than a simple response is necessary to determine this).

- 1 Cannot quiet self, makes no attempt, and intervention is always necessary.
- 2 Brief attempts to achieve hand to mouth as if to quiet self, but no success.
- 3 Attempts to bring hand to mouth, and/ or quiets briefly.
- 4 Brings hand to mouth, attempts to suck on fist but without success, quiets for a short time perceptibly.
- 5 Makes at least two attempts to suck on hand or fist and/or has two successful brief quieting periods.
- 6 Two attempts to quiet self result in observable successful quieting for periods.
- 7 Repeats hand to mouth, sucking and/or uses visual or auditory stimuli to quiet self for three successes, but all are brief.
- 8 Uses maneuvers to quiet self three times for short sustained periods.
- 9 Consistently quiets self for sustained periods.

#### 26. Hand to mouth facility (all states)

This is measured in all states. A hand to mouth reflex is inborn, and seems to be a response to stroking the cheek or the palm of the infant's hand. It can be triggered off by mucous and gagging in the neonate, by discomfort, by placing him in prone. It is seen spontaneously as the neonate attempts to control himself or comfort himself when upset. This is a measure of his ability to bring his hands to his mouth in supine as well as his success in insertion. Some infants bring their hands to their mouths repeatedly, insert a part of the fist or fingers, and suck actively on the inserted part.

- 1 No attempt to bring hands to mouth.
- 2 Brief swipes at mouth area, no real contact.
- 3 Hand brought to mouth and contact, but no insertion, once only.

263

- 4 Hand brought next to mouth area twice, no insertion?
- 5 Hand brought next to mouth area at least 3 pimes, but no real insertion, abereive attempts to suck on fist.
- 6 One insertion which is brief, unable to be maintained.
- 7 Several actual insertions which are brief, not maintained, abortive sucking attempts, more than three times next to mouth.
- 8 Several brief insertions in rapid succession in an attempt to prolong period, sucking at this time.
- 9 Fist and/ar fingers actually inserted and sucking on them for 15 seconds or more for several brief insertions.

#### 27. <u>Smiles</u> (all states)

Smiles are seen in the neonate. They surely can be of reflexive grimacing in nature, and they also occur "appropriately"—or in response to soft auditory and/or visual cues. Occasionally, when the baby is handled and restrained in a cuddling position, a smile comes deross his face as he relaxes. I have seen close replicas of "social smiles" in the newborn period—when an examiner leans over his crib and talks softly to him. They are difficult to be sure of, may consist primarily of a softening and brightening of the infant's face with a reflex grimace thrown in, and they may certainly be difficult to reproduce. Hence, one hesitates to call these social "smiles," but they surely are the facial precursors of such smiling behavior. A mother reinforces them as such.



#### Elicited Reflexes

These are described in Prechtl and Beintema's monograph (11) and need not be described here. Their procedure is followed for eliciting the 16 reflexes listed. Since this is not designed to be a neurological assessment, these will serve as baseline data for a more formal neurological where it is indicated. This manual scorest

X = omitted.

0 = reflex not able to be elicited despite several

L = hypoactive response.

M = normal response as determined by Prechtl's manual (11).

H = hyperactive response.

 $\Lambda$  = asymmetrical response, either in terms of lateralization or segments of body (arms vs. legs, etc.). Since this may be of importance in assessing neurological damage, real, repeated asymmetry should be carefully assessed and noted, to be followed by a formal neurological assessment.

Examples of our use of these reflexes are:

Crawling includes all of the prone responses; head-lifting and head-turning, crawling, hand-to-mouth in prone.

Tonic deviation of head and eve is an 8th nerve response to being rotated in front of the examiner. He is held under both arms; then, examiner and infant rotate slowly in a circle. Eyes and head go ahead of examiner, then nystammus of the eyes begins to occur, both in response to an 8th nerve compensatory reaction and as the eyes catch the passing light while they rotate.

### Passive Movements of Arms and Lers

As defined in Andre Thomas, Chesni and D'Argassies, The Neurological Exam of the Infant (10), this becomes a measure of consistency and extensibility of muscle tone, in reaction to passive stretching of the limbs as well as the amount and degree of recoil of the limb after extension. As a surmary of these in all the limbs and the trunk, it represents the muscle tone of the body plus its reaction to stimulation. A big, floppy baby may have no resistance to stretching of his limbs. A very tense, jittery infant will be very resistant to being moved, and limbs will snap back into flexion after being stretched. Infants normally show some resistance to having their extremities stretched, and a little snapback is





normal. The degree to which limbs must be entended (up to full extension) in order to meet resistance, as well as the abount of snapback (which accounts the overreaction of flower muscles) is scored. Legs are usually more resistant to extension than arms, and very lew infants do not attempt to maintain tone of their legs against stretching. Inequality of the two sides is a very important part of this assessment. (See Prochil (11).)

#### Descriptive Paragraph (optional)

#### Descriptive Scores (optional)

This is a summary of all the subjective impressions which have been amassed in the period. They include the style with which the infant reacts, the examiner's major impressions about the infant, his feelings about the appearance and behavior of the infant, his predictions about the kind of responses these will call up in his mother, as well as predictions about their altimace outcome as the child grows. This will be the paragraph which will help the examiner to remember the child later, and may be an important way of categorizing infants, or understanding the scores in the different categories, and of understanding meaningful constellations of these categories. This is not expected to be subject to interscorer reliability.

The subjective reaction of the E is subnumed under "attractive" in an attempt to objectify this.

Interfering variables such as light, noise, too many observers, etc. should be scored and listed.

Need for stimulation scores the result of the infant's observable responses. Some infants seem to need stimulation from outside himself in order to function smoothly and well. These infants would score high on this measure. Others seem to pay little attention to outside stimulation, respond automatically. They deserve a low score.

The kind of activity which the infant uses characteristically to quiet himself has been of some interest to many observers. This can be checked and/or scored on a 3 point scale.

Comments: Write a descriptive paragraph about the baby which includes the particular characteristics which are of interest in your study. This paragraph serves as a reminder of the unique characteristics of the baby which are not recordable elsewhere.



#### APPENDIX C



#### APTFIB9X C

# BORRYLORAL AND HEMOLOGICAL ASOMORDER SCALE Revised Relation: Aug. 1971 (Y. Barry Bendelson)

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APPENDIX D

# THE UNIVERSITY OF KANGAS LAWRENCE, KANSAS 66044

#### Department of Human Development



#### APPENDIX D

te Infant Research Program is part of the Kansas Center for Research in Early Childhood ducation at the University of Kansas. We are ultimately interested in understanding what the best experiences for individual children so that each child can be helped to enjoy stimal development. As part of this effort we are engaged in working on the development is a behavioral scale for newborn infants.

iministering the scale involves taking the infant in his own basinette to a quiet room where is examined by experienced personnel. Hospital procedures of scrubbing and gowning a followed prior to each infant examination. The examination procedures have been reawed and approved by your doctor. A description of those procedures is provided for our information.

e are now testing a number of the babies born in this hospital. If you are willing to have ur baby examined in the hospital, please sign at the bottom. Your cooperation in this after will be greatly appreciated. We are hopeful that our research and the work of hers around the country will lead us to a better understanding of how children grow and arn. We shall then be able to help all children reach their full potential. The willingness parents to have their babies participate in a program such as this will bring us nearer that goal.

Thank you very much,

They are hopen down

Frances Degen Morowitz, Ph.D. Professor in Human Development and Psychology

#### Stormont-Vail Hospital

1000

have read the above letter and the description of the examination procedures contained on a reverse side, and I consent to the examination of my baby by authorized persons from a University of Kansas Infant Research Program.

enderstand that while the hospital is cooperating with the Department of Human Development, diversity of Kansas, by allowing the use of hospital facilities, the examination is not done shospital employees, nor is the hospital responsible therefor.

further understand that certain information concerning my child will be obtained from the spital records, and I authorize Stermont-Vail Hospital to release the requested information medical record and my baby's medical record.

* * * * * * * * * * * * * * * * * * * *	•		
iness:		271	Signature
DIC.		126	

## APPENDIX E



The numbers from one to twenty-seven in the following figures represent the following Brazelton Scale Items:

- 1 Response decrement to light
- 2 Response decrement to rattle
- 3 Response decrement to bell
- 4 Response decrement to pinprick
- 5 Orientation insulpate visual
- 6 Orientation inanimate auditory
- 7 Origination animate visual
- 8 Orientation animate auditory
- 9 Orientation animate visual and auditory
- 10 Alextness
- 11 General Tonus
- 12 Motor Maturity
- 13 Pull to sit
- 14 Cuddliness
- 15 Defensive movement
- 16 Consolability
- 17 Peak of excitoment
- 18 Rapidity of build up
- 19 Irritability
- 20 Activity
- 21 Tremulousness
- 22 Startle
- 23 Lability of skin color
- 24 Lability of state
- 25 Self quieting activity
- 26 Hand-mouth facility
- 27 Smiling .

APPENDIX E TABLE 1

regar r

BRAZELTON ITEMS CORRELATED WITH DAYS 2, 3, 4, 5, 7, 10 AND 28

DAY ONE

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DAY ONE

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2	7.05	2	2.23
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4	5.07		2.24
<u>/</u> 5	4.07	4 5 6	2.69
6	4.59	6	2.07
7	5.23	7	2.50
8	5.52	7 8 .	1.69
9	5.30	9	3.32
10	4.71	10	3.04
11	4.59	11	1.22
12	3,98	1.2	1.28
13	4.13	1.3	1.81
14	5.20	14	1.47
15	4.50	15	2.46
16	7.07	16	2.59
17	5.80	17	1.36
18	4.48	18	1.81
19	3.50	19	1.73
20	4.02	20	1.34
21	3.30	21	2.36
22	2.95	22	1.61
2.3	5.20	23	1.84
24	4.32	24	2.22
25	5.61	25	3.19
26	4.43	26	2.64
27	0.57	_27	0.85



APPENDIX E TABLE 2

DAY TWO

BRAZELTON'IBGIS CORRELATED WITH DAYS 1, 3, 4, 5, 7, 10 AND 28

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20	.50***	.40**
19	.36*	. 54***
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8 9	5.34 5.39	8 9	1.43 2.16
10	4.23	10	2.12
11	4.84	11	0.91
12	3.68	12	1.12
13	4.02	13	1.65
14	4.66	14	1.40
15	5.05	15	2.33
16	6,41	16	2.43
17	5.95	17	1.70
18	5.30	18	1.58
19	4.61	19	1.71
20 21	4.27 4.09	20 21	.42 2.31
22	3.32	22	1.58
23	4.91	23	1.90
24	5.16	24	2.11
25	4.36	25	2.81
26	4.25	26	2.57
2.7	0.50	2.7	0.84

APPENDIX E TABLE 3 DAY THREE

BRAZELTON ITEMS CORRELATED WITH DAYS 1, 2, 4, 5, 7, 10 AND 28

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7	5.34	6 7	2.51
8	5.39	8	1.84
8 9	5.64	9	2.49
10	4.57	1.0	2.42
11	4.32	11	1.17
12	3.77	12	1.58
13	4.73	1.3	1.96
14	5.00	14,	1.61
15	5.05	15	18
16	3,57	16	2.73
17	6.36	17	1.56
18	4.50	18	1.52
19	4.27	1.9	1.77
20	4.52	20	1.68
21	4.02	2]	2.18
22	3.27	22	1.58
23	4.50	23	1.95
24	4.52	24	1.76
25	4.84	25	2.52
26	4.89	26	2.09
_27	0.43	_27	0.82

TABLE 4

DAY FOUR

BRAZELTON ITEMS CORPELATED WITH DAYS 1, 2, 3, 5, 7, 10 AND 28

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DAY FOUR (continued)

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16	5.75	16	2.40	
17	6.05	17	1.63	
18	4.57	1.8	1.58	
19	4.25	19	1.75	
20	4.98	20	1.37	
21	3.50	21	2.15	
22	3.22	22	1.67	
23	4.98	23	1.61	
24	4.77	24	2.05	
25	5.32	25	2.58	
26	5.00	26	2.60	
27	0.93	27	1.68	

APPERIOTS R TABLE 5

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	4.86	5	2.55
5 6 7 8 9	4.16	6	2.24
7	5. "	7	2.34
8	5.	8	1.85
	5.	9	2.39
10	•	10	1.88
11	4.75	1.1	1.17
12	4,34	12	1.67
13	3.93	1.3	1.97
14	÷, •, €	14	1.62
15	5 56	15	2.67
16	.75	16	2.53
17	6.05	17	1.85
18	4.34	13	2.05
19	3.80	19	1.96
20	4.84	20	1.46
21	2.84	21	2.03
22	2.58	22	1.51
23	4.50	23	. 1.98
24	4.68	24	2.27
25	4.86	25	2.88
26	4.57	26	2.59
27	0.70	27	1.23

TABLE 6 TABLE 6

DAY SEVEN

BRAZELTON ITEMS CORRELATED WITH DAYS 1, 2, 3, 4, 5, 10 AND 28

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DAY SEVEN (continued)

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20		.41*** .42*** .37* .43** .41**	.43	. 38**	
19	.31*	.32*	.38*		
18	.35*	. 34*	**07.	.70****	-
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DAY SEVEN
EDARS AND STABLARD DEVIATIONS

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2	7.59		2.37
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5	5.02	5	2.20
5 6 . 7	5.00	6	1.78
	5.84	7	2.07
: 8	5.82	8	1.53
9	5.95	9	2,21
10	5.32	1.0	2.22
11	4.82	11	1.15
12	4.32	12	1.34
13	4.84	13	1.89
14	4.90	14	1.70
15	5.57	15	2.42
16	5.73	16	2.53
17	5.84	17	1.57
18	3.77	18	1.93
19	3.39	19	1.66
20	4.70	20	1.42
21	3.07	21	2.08
22	2.64	22	1.24
23	4.49	23	1.74
24	4.32	24	. 2.07
25	5.70	25	2.89
26	3.86	26	2.30
_27	1.09	_27	1.80

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BRAZELTON ITEMS CORRELATED WITH DAYS 1, 2, 3, 4, 5, 7 AND 28

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DAY TEN

MEANS AND STILLDARD DEVIATIONS

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1 2	8.04	1 2 3 4	2.24
3	7.93	<u>~</u>	2.43
4	6.09		2.44
5	5.25	4	2.44
6	5.07	5 6	1.55
7	6.14	7	2.14
8	5.57	8	1.50
9	6.23	9	1.90
10	5.57	1.0	2.41
11	4.80	11	1.11
12	4.09	12	1.51
13	4.55	13	1.74
14	4.77	14	1.50
15	6.34	15	2.40
16	6.43	16	2.97
17	5.60	17	1.94
18	4.16	18	2.37
19	3.30	19	2.14
20	4.57	20	1.26
21	2.89	21	2.01
22	2.50	22	1.15
23	4.43	23	1.69
24	4.09	24	2.36
25	5.57	25	3.1.9
26	3.60	26	2.23
27	1.00	27	1.56



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# MEANS AND STANDARD DEVIATIONS

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	5.61	4	2.96
5 6 7	6.34	5	2.28
6	5.61	б	1.94
7	7.27	5 6 7 8	1.82
8 9	6.25	8	2.15
	7.20	9	1.95
10	6.43	10	2.13
11	5.40	11	1.30
12	5.78	12	1,76
13	5.59	13	2.37
1.4	4.73	14	1.95
15	6.59	15	2.24
16	5.55	16	3.30
17	5.93	17	2.24
18	4.43	18	2.49
19	3.00	19	2.06
20	5.25	20	1.53
21	2.55	21	1.86
22	2.18	22	1.03
23	4.57	23	1.56
24	4.55	24	2.67
25	4.77	25	3.45
26	2.82	26	2.55
_27	1.23	_27	J 40



APPENDIX E TABLE 9

SCALE RELIABILITY BY SUBJECT AND BY USING  $\frac{A}{A+D}$  FORTULA TWO SCORES ADJACENT

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	63	14	29	7.5	7.8			11	61	74	<b>3</b>	30	69
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ige 9 (c	7-10	79	7.1	4	65	29	58	99	6	-1 0 I		m 93	7.9	7.9	7.9	. 6.	<u>.</u> 5	52	င်ဆ	88	7.1	7.4	61	7.5
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•	2-3	61	69	77	86		59	72	in 10	~	J :	 30	(1)	7.2	83	83	71	67	817	53	63	91	6.4	99
	1-2	67	81	7.3	16	63	81	97	75	7.8	• 1	2 ;	66	7.3	88	92	78	7.5	9/	69	57	92	50	7.7
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TABLE 1

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TABLE 2

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TABLE 3

DAY THREE

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Der, mev.	15	747						817		
Censel	16	-	89.						× / -	
Peak excitement	17		82						2	17.
Rapid bldup	18		62						-   -	11/1
11:11:	1.9		35							133
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Incard,	2.1				0%.					C: j
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ing. sith color	23		_				111	-		
Lab. state	24		72							74
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TABLE 4
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TABLE 5

DAY FIVE

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APPENDIK F

TABLE 6 DAY SEVEN

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	II						-						42					.73	.86	67	78				53	08			
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•	ITEMS		ç:	3	7;	5	ی،		(င		6	1.0	11	12	1.3	14	1.5	16	17	18	19	26	7.7	22		2.4	:22	26	17
	STENS	Hobit, light		Habir, bell	Pinnrick	Ortent, inan, vis.	Ortone, inn. and.	(" gnt, "" vis.	Crient, sn. and.	Orient, an. vis.	end and.	Aisteness	Gen, Ten,	Notor, mat.	Pull sic	0.121.0		Censel -	Penk excitement	Regid bleep	11.11	1200	Trem!	0.12.12.20	in the color	leb. state	Self-quiet	Hand-mouth	year ics

TABLE 7 DAY TEN

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Kils	Habit, light	Hebit, rattle	Eavit, bell	Pinorick	Orient, igan, vis.	Orient, ivan, and.		The Control of the Co	Ξ,	and ond.	Al- riness	Car. Ten.	Motor, mat.	Pull sit	Critale	ven 7	[031.03	Pysk eneitement	Replie 51dup	Trit	veriv.	Trend	Servele	ich, skin color	1. 1	7 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -		Smiles	340 4 (3

TABLE 8

DAY TWENTY EIGHT

# APPENDIX G



#### TABLE 1

#### DRUG CODE

- 1. Local and Regional Anesthetics (Classified according to route of administration):
  - 1.0 unknown or others (i.e., not listed)
  - 1.1 perincal (local)
  - 1.2 pudendal or paracervical block
  - 1.3 spinal, saddle block, caudal, epidural) regional

#### Tranquilizers

- 2.0 unknown and not listed
- 2.1 Chlorpromazine (Thorazine), Base dose: 50 mg
- 2.2 Diazepam (Valium), Base dose: 5 mg2.3 Chlordiazepoxide (Librium), Base dose: 10 mg
- 2.4 Hydroxizine (Atarax), Base dose: 25 mg
- 2.5 Promethazine (Phenergan), Base dose: 25 mg

## 3. Narcotic Analgesics

- 3.0 not listed or unknown
- 3.1 Meperidine (Demercl), Base dose: 50 mg
- 3.2 Alphaprodine (Nisentil), Base dose: 30 mg
- 3.3 Fentanyl citrate, Base dose: 0.1 mg (given only in combination with Droperidol (Innovar), Base dose: 5 mg
- 3.4 Morphine, Base dose: 10 mg

## 4. Barbiturates -

- 4.0 other or unknown
- 4.1 Thiopental (Na Penthotal), I.V. (dose not usually recorded)
- 4.2 Secobarbital (Seconal), P.O., Base does: gr. 1/2 (or rectal)

### 5. <u>Inhalation General Anesthetics</u>

- 5.0 other and unknown
- 5.1 Nitrous oxide
- 5.2 Cyclopropane
- 5.3 Methoxyflurane (penthrane)
- 5.4 Fluothane
- 6. Scopolamine (hyoscine), Base dose: 1/2 amp.
- 7. Muscle Relaxant Succinil choline(Anectine)

# Intercorrelation Between Drug Grouped According to Type (Using Pearson r.)

# Significent Correlations

	21	> 2	3	<u> </u>	≦. 5	<del>5</del> 6	7	€ All
٤ ١								
₹ 2	. 23							
₹ 3	18	10						
₹ 4	20	10	.321					
₹ 5	56 <sup>.3</sup>	··22	37	.27				
6	54 <sup>113</sup>	" <b>-</b> .50	.33	.31	.53	*		
7	- J <sub>1</sub> O.3	04	01	.17	.33	05_	ļ	
€ A11	29	.04	.71	··· 08. ··	.60°	.47	.18	

 $-\xi 1 = all local anesthesia$ 

£2 = all tranquilizers

£3 = all narcotics

£4 = all barbiturates

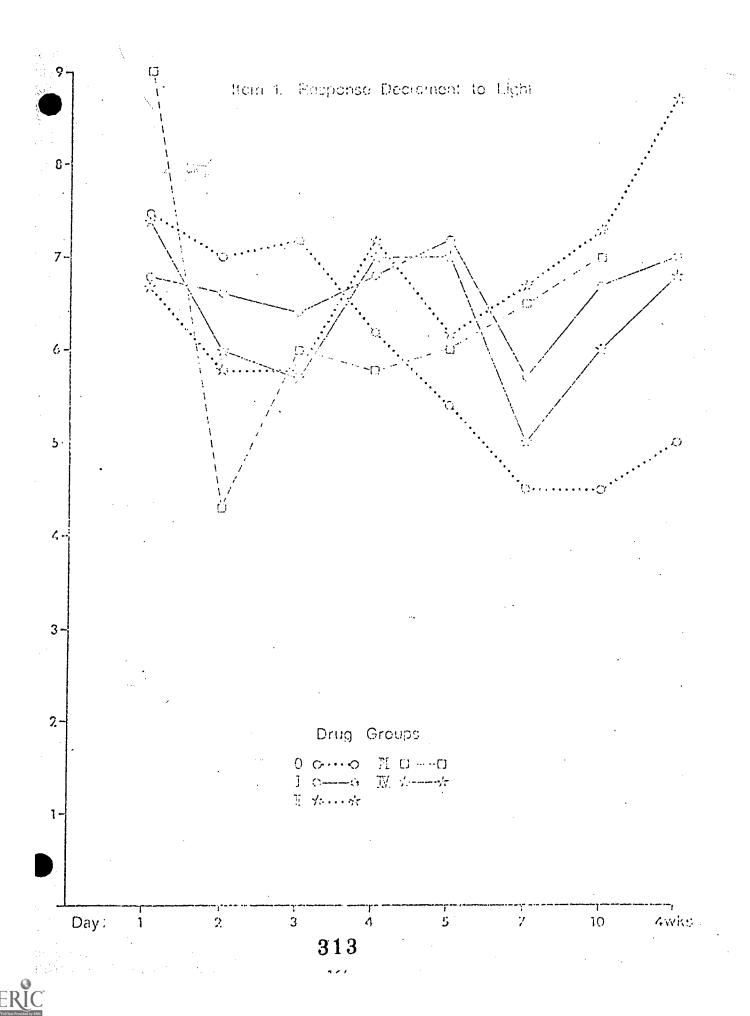
 $\xi$  5 = all general anesthetics

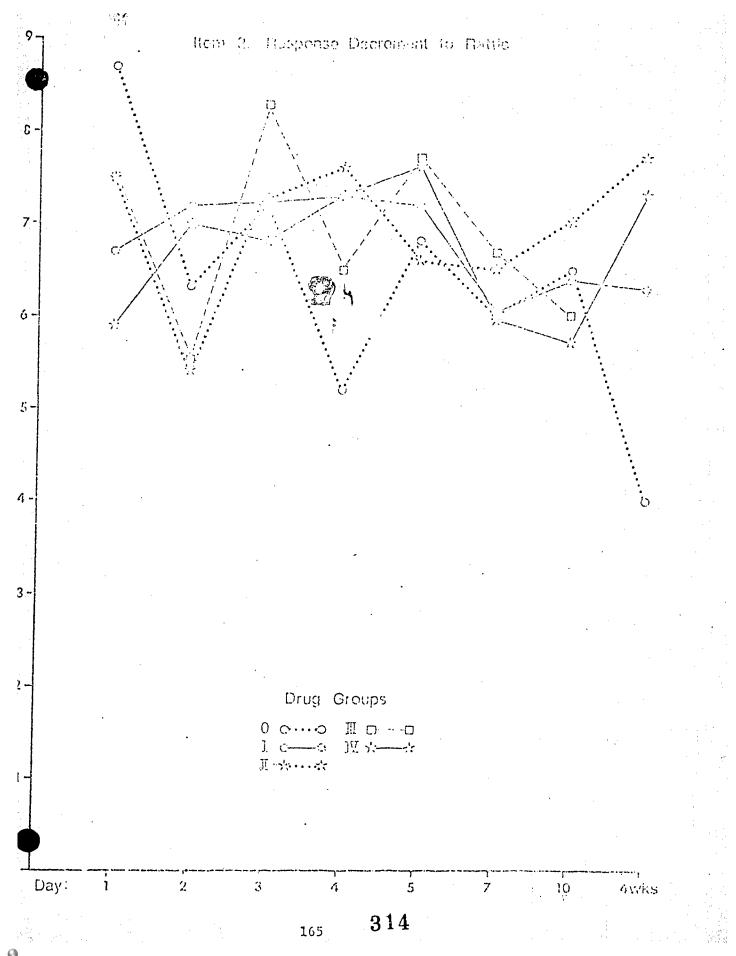
. 6 = Scopolamine

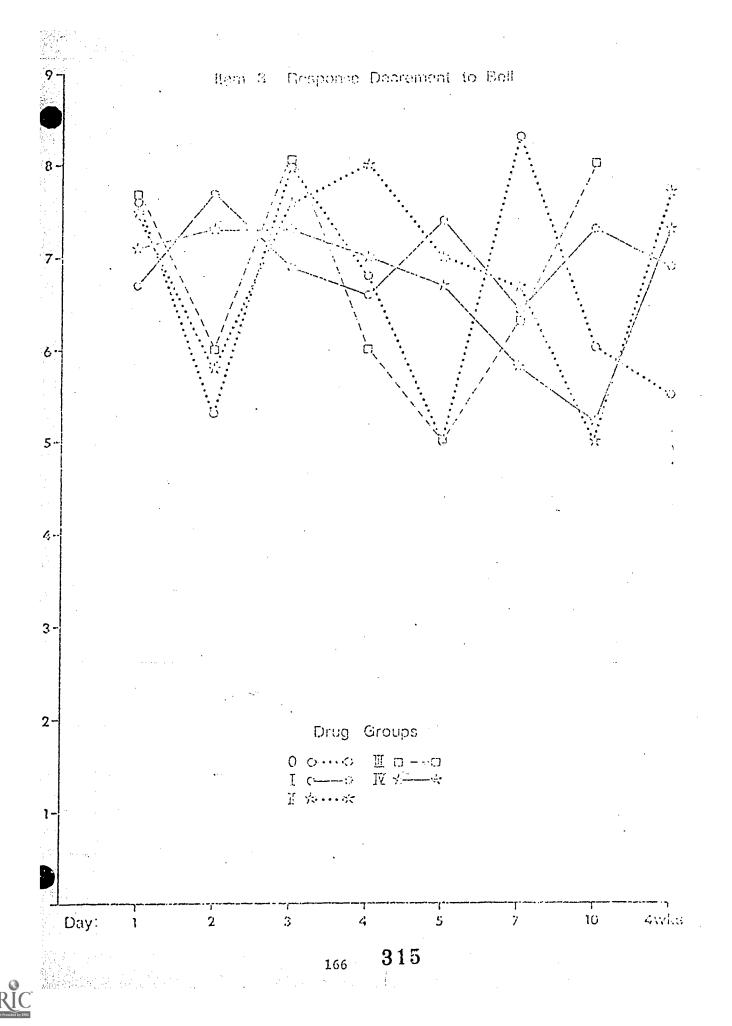
7 = muscle relaxant

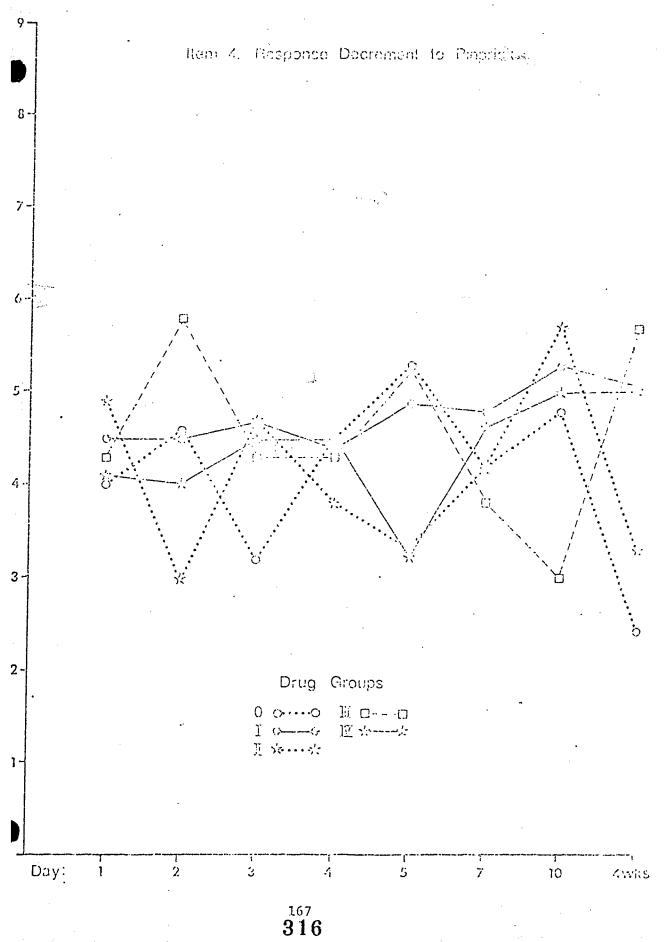


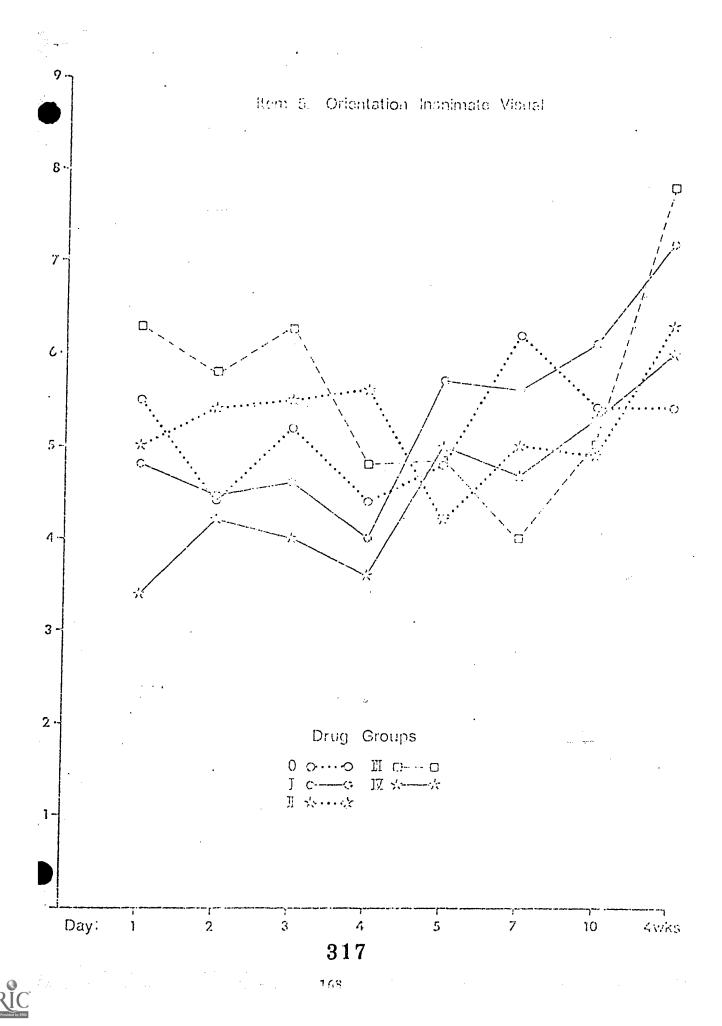
APPENDIX H

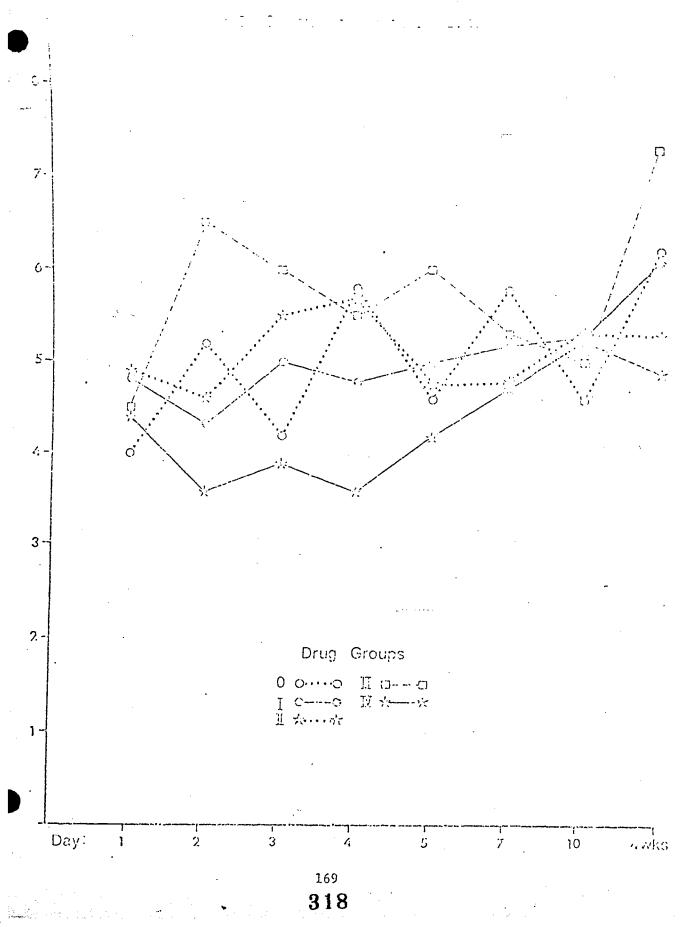




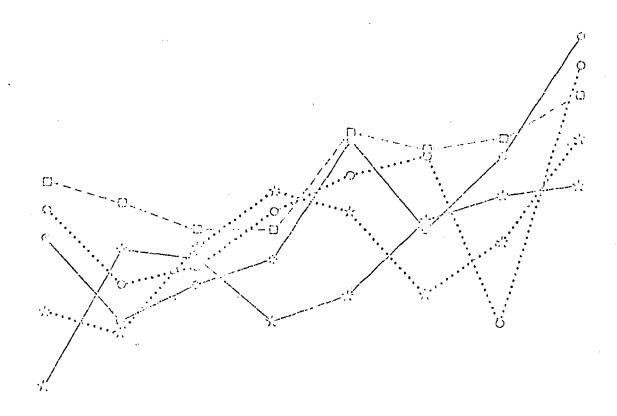




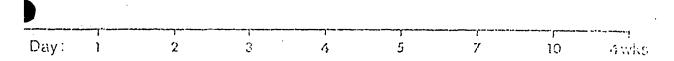




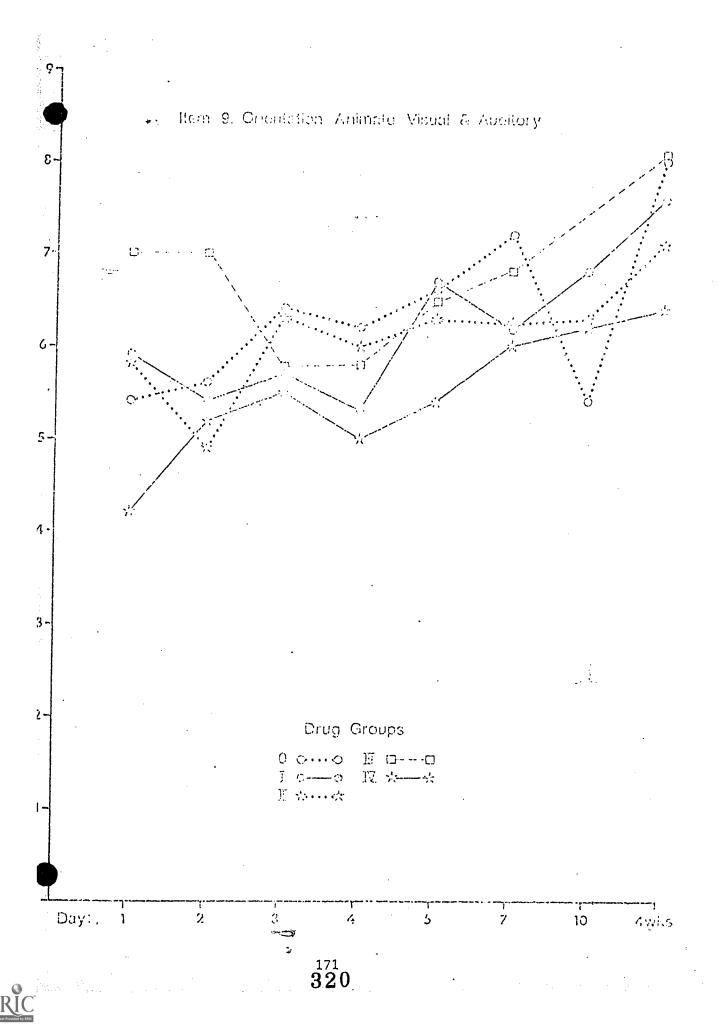
Item 7. Orientation Animate Visual

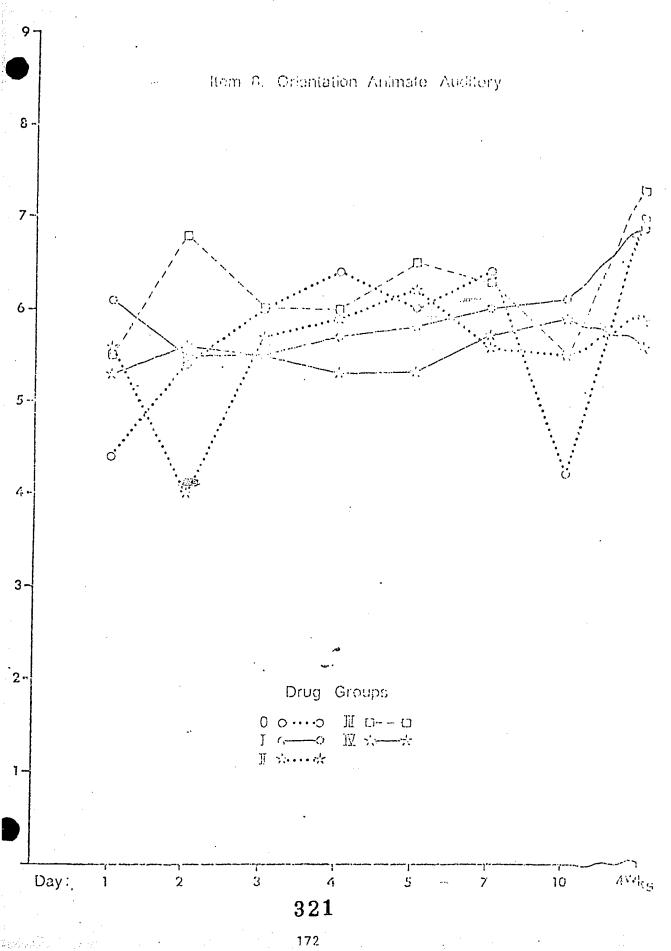


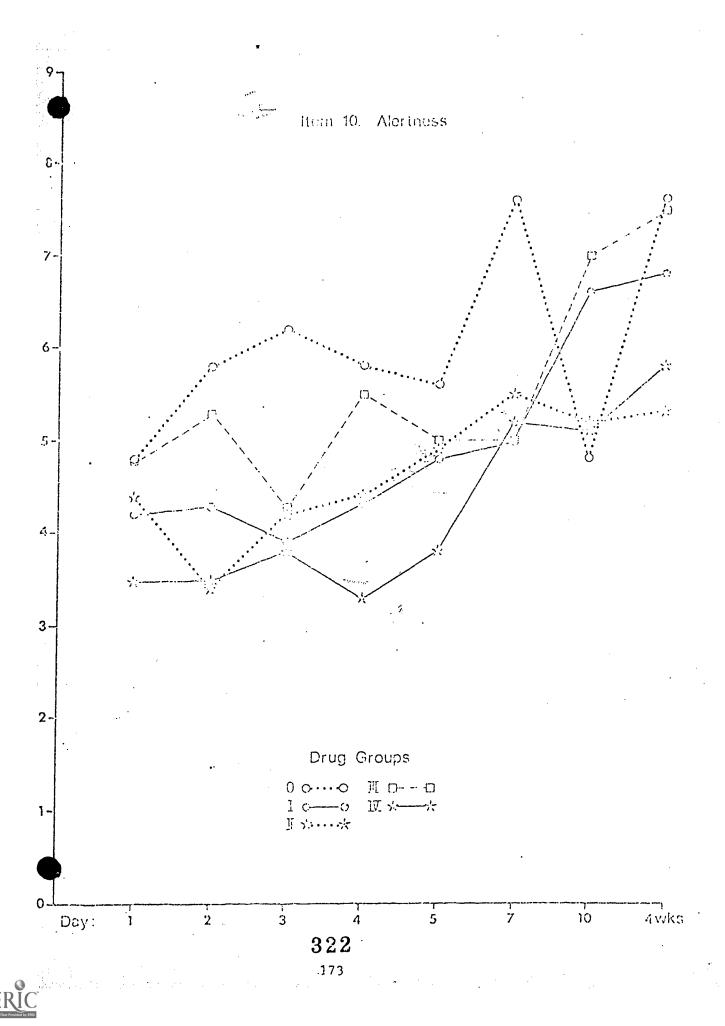
Drug Groups

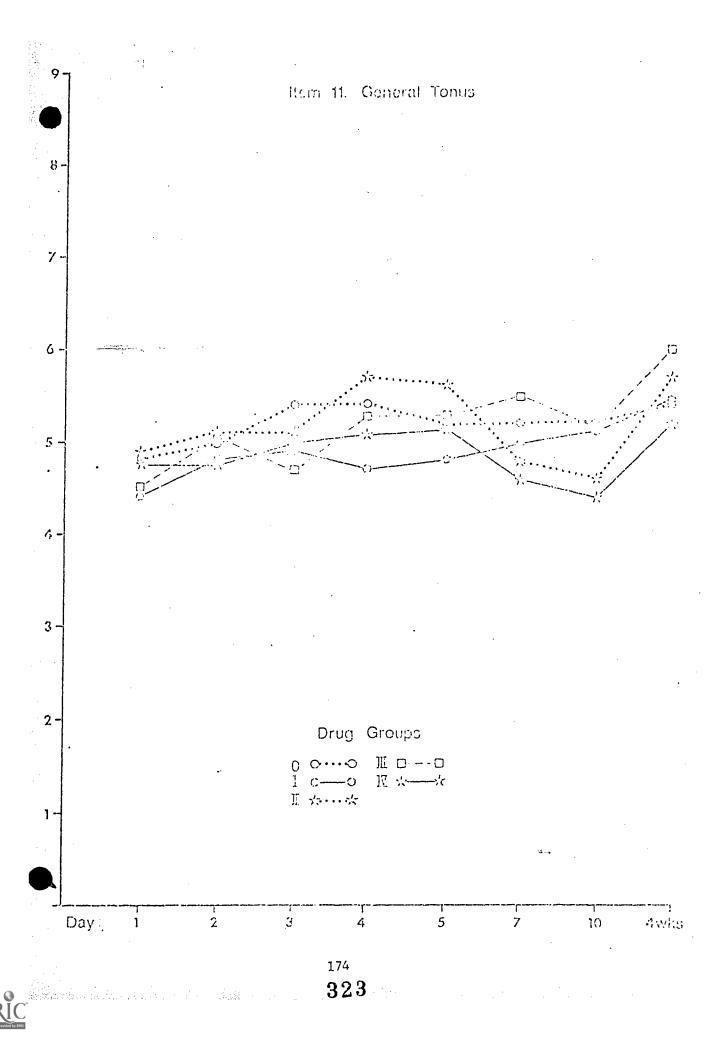


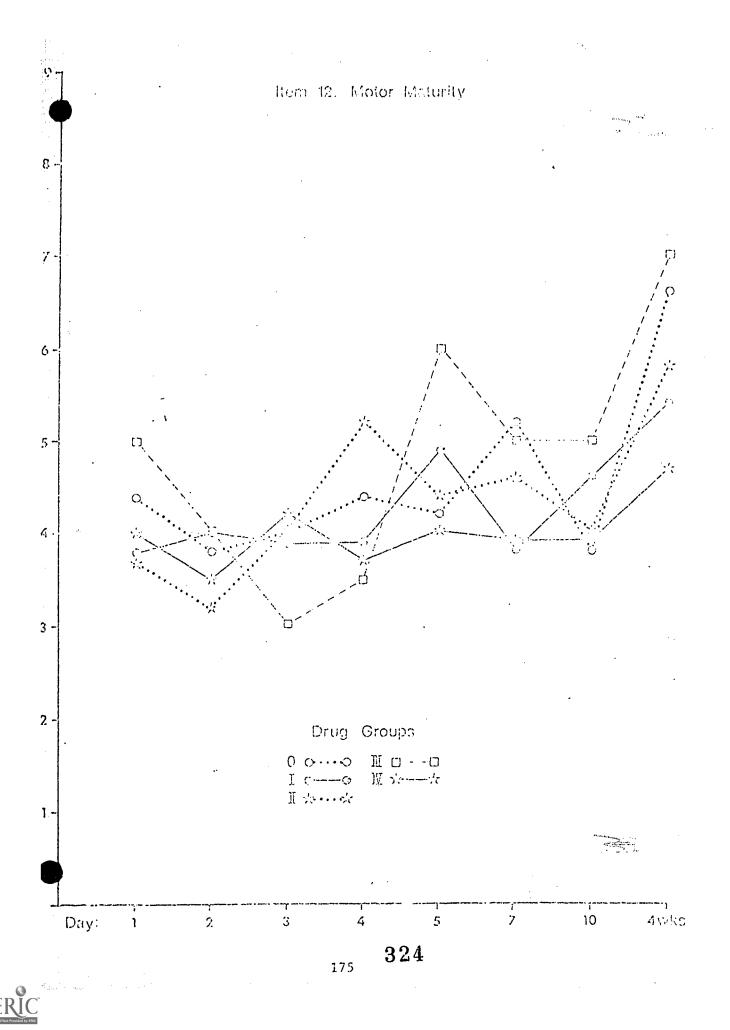
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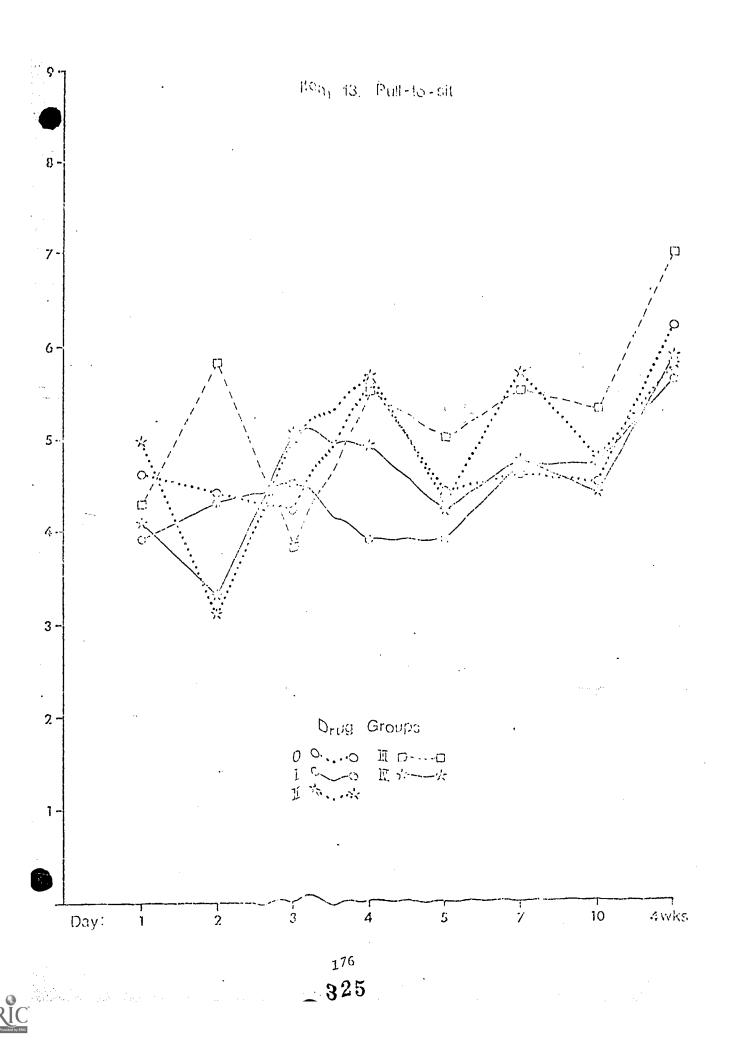


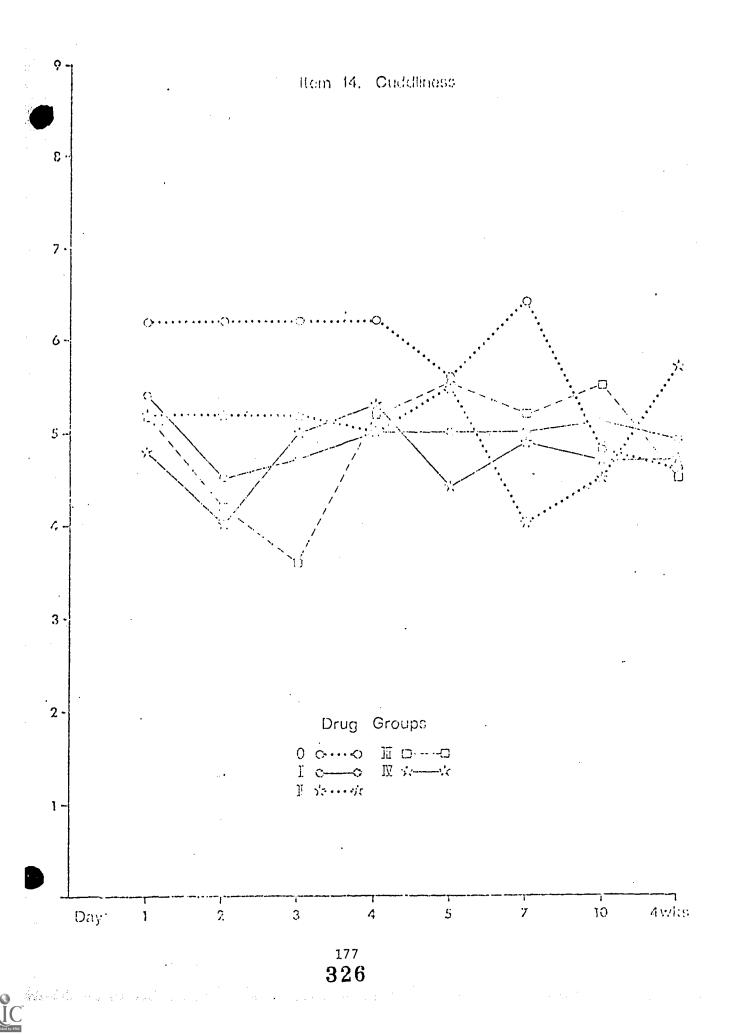


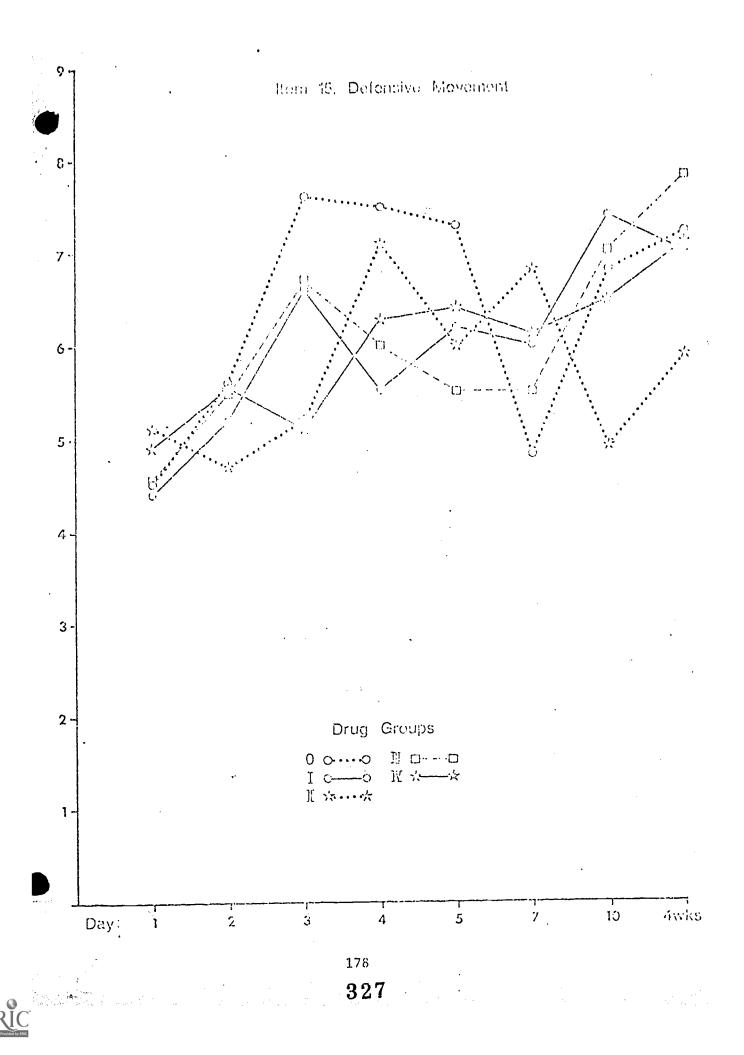


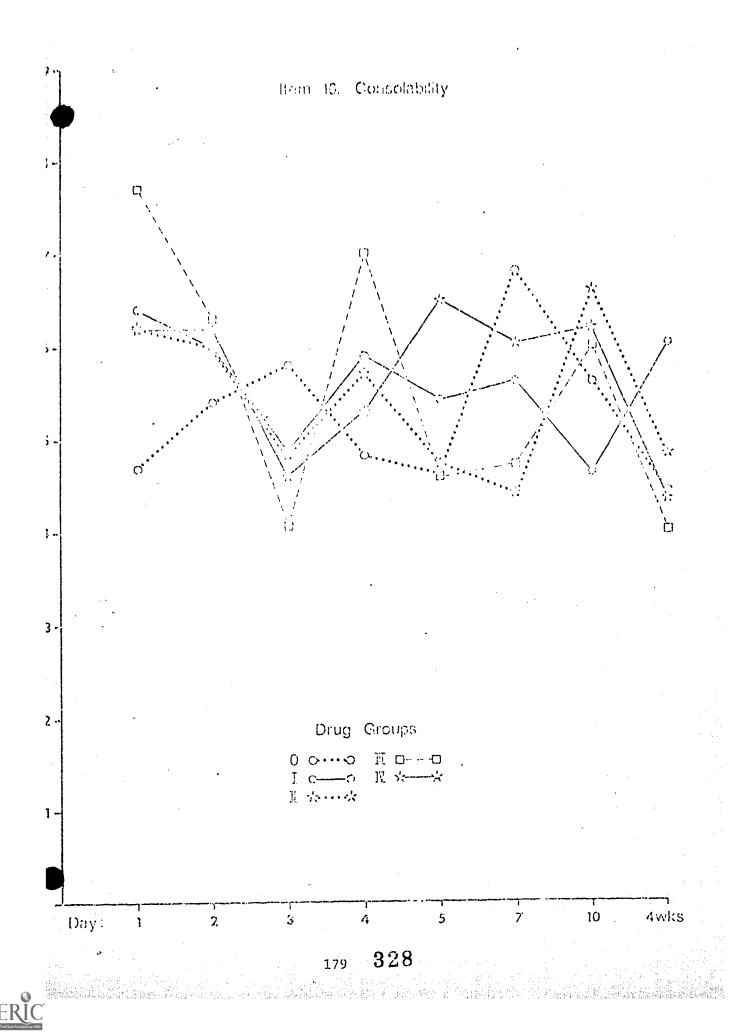






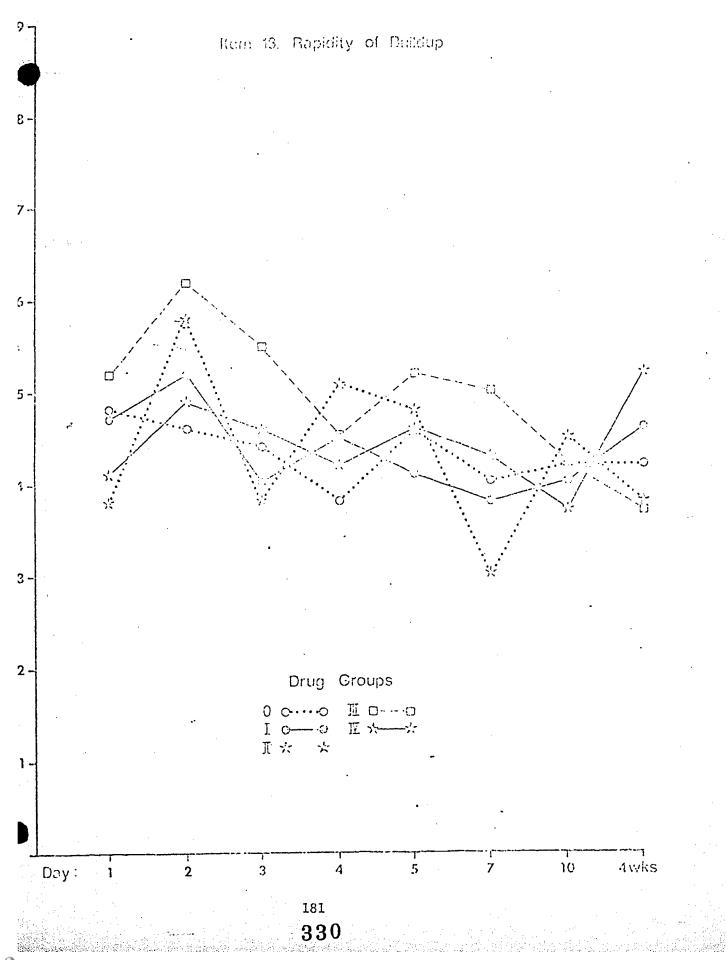




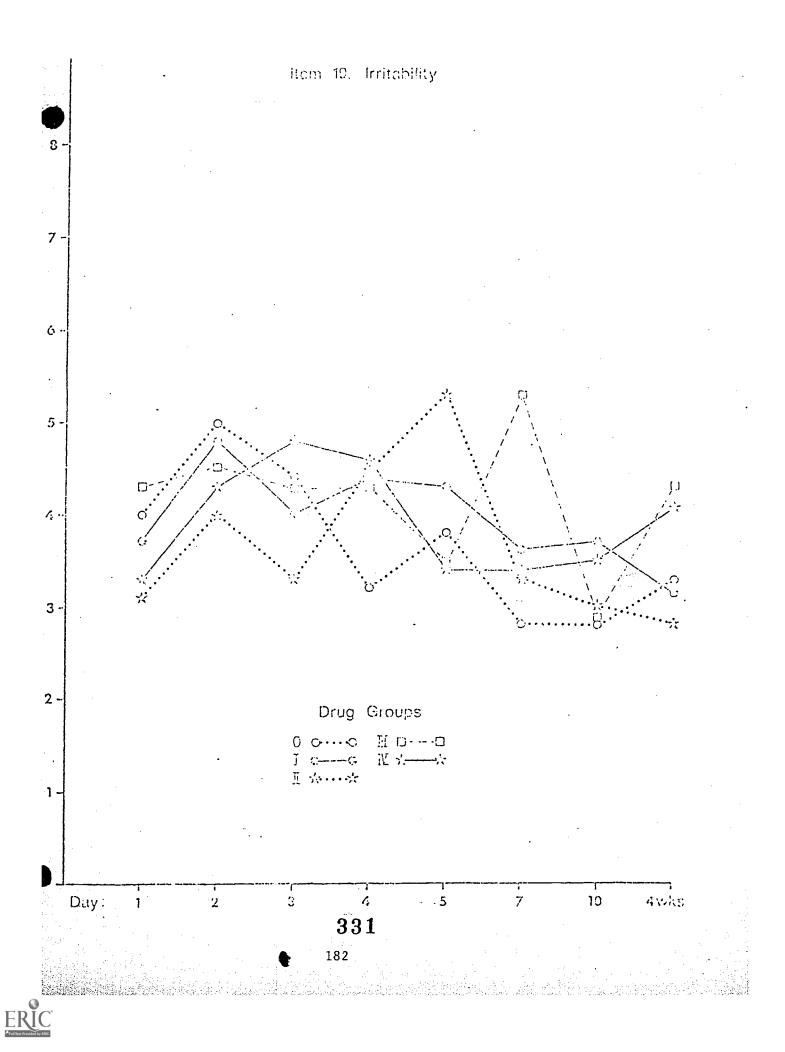


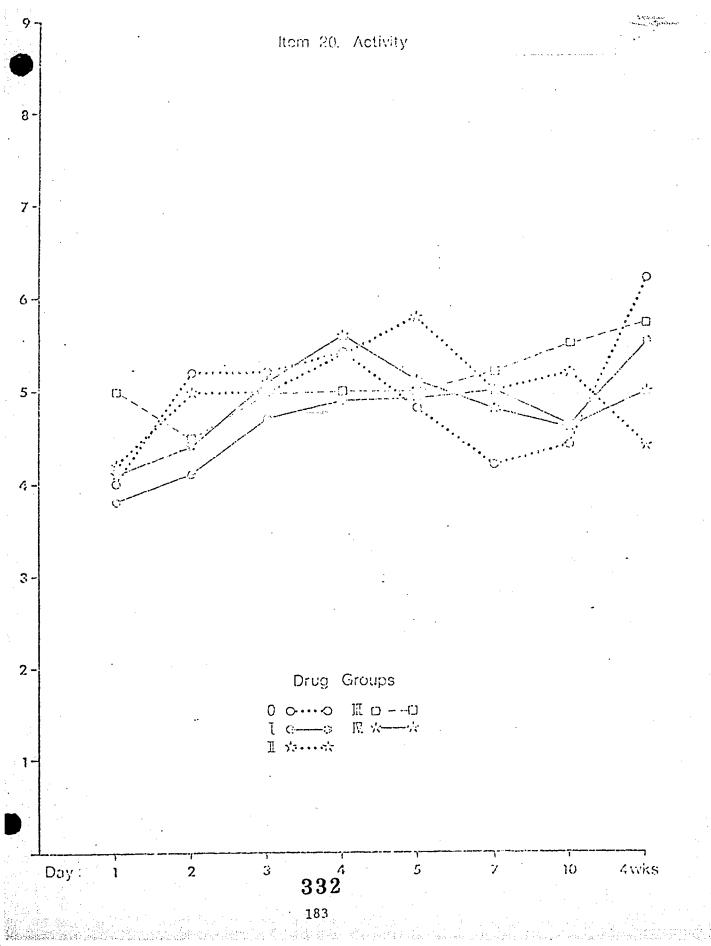
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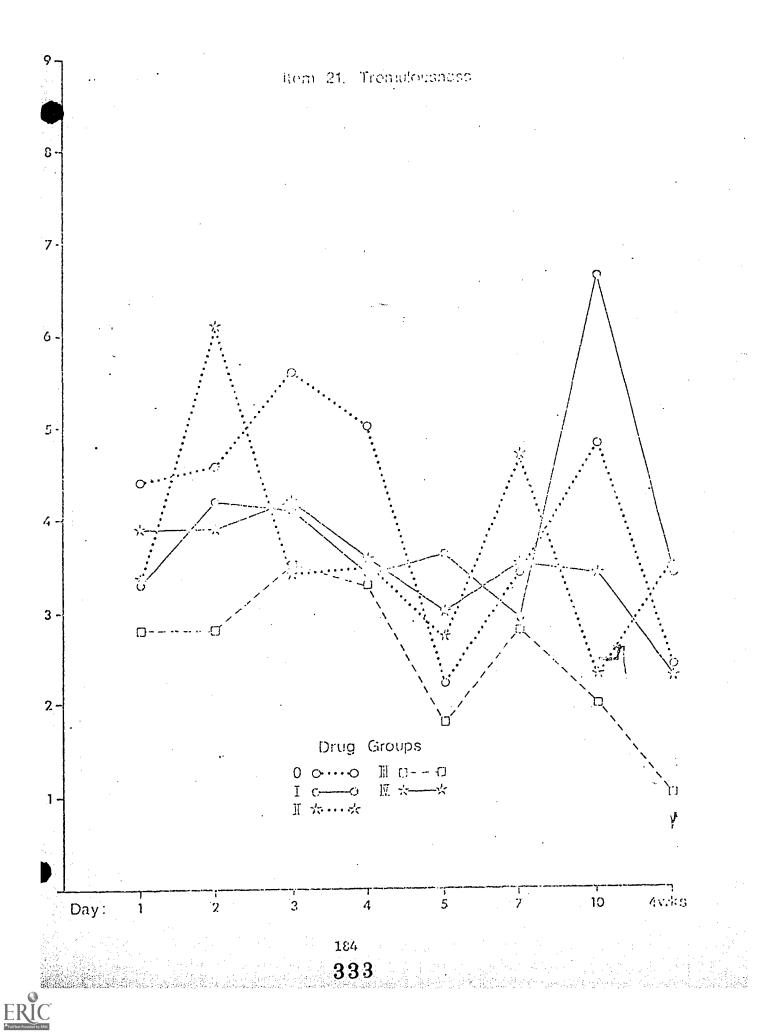


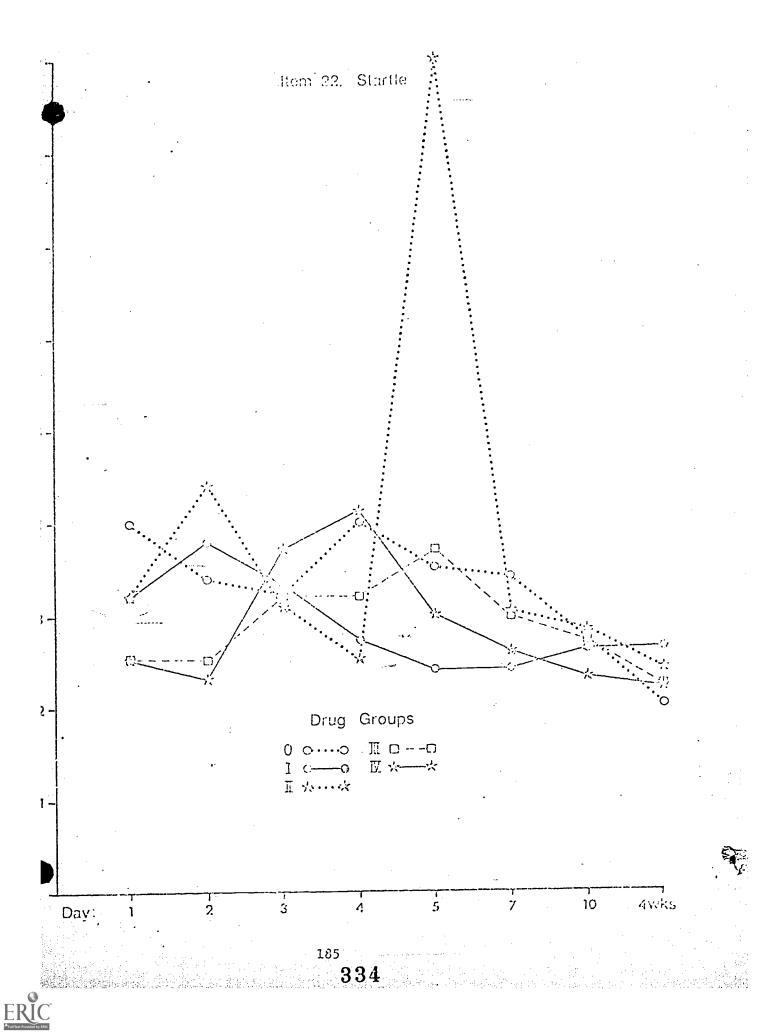


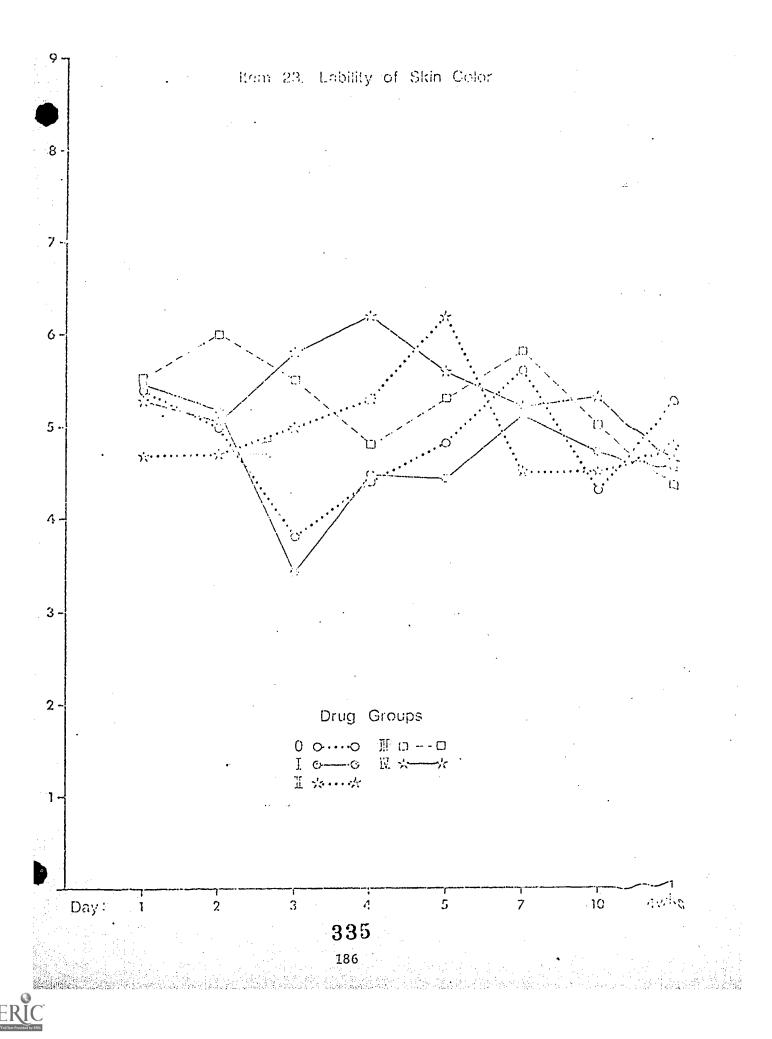


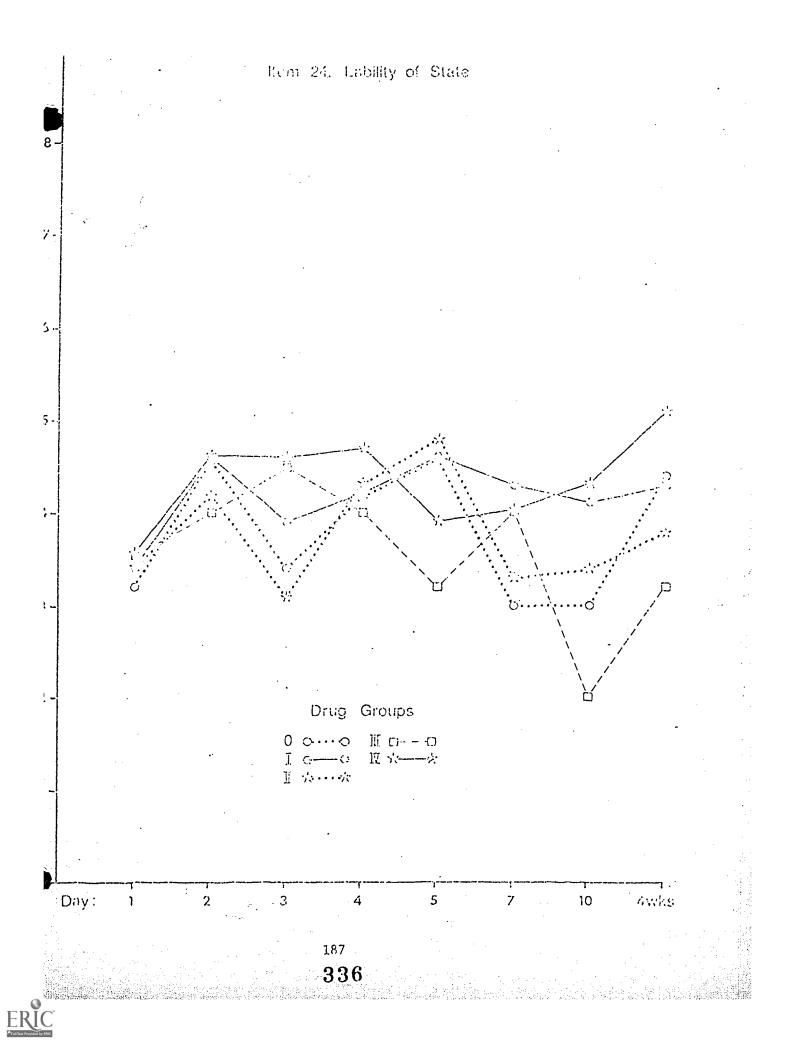


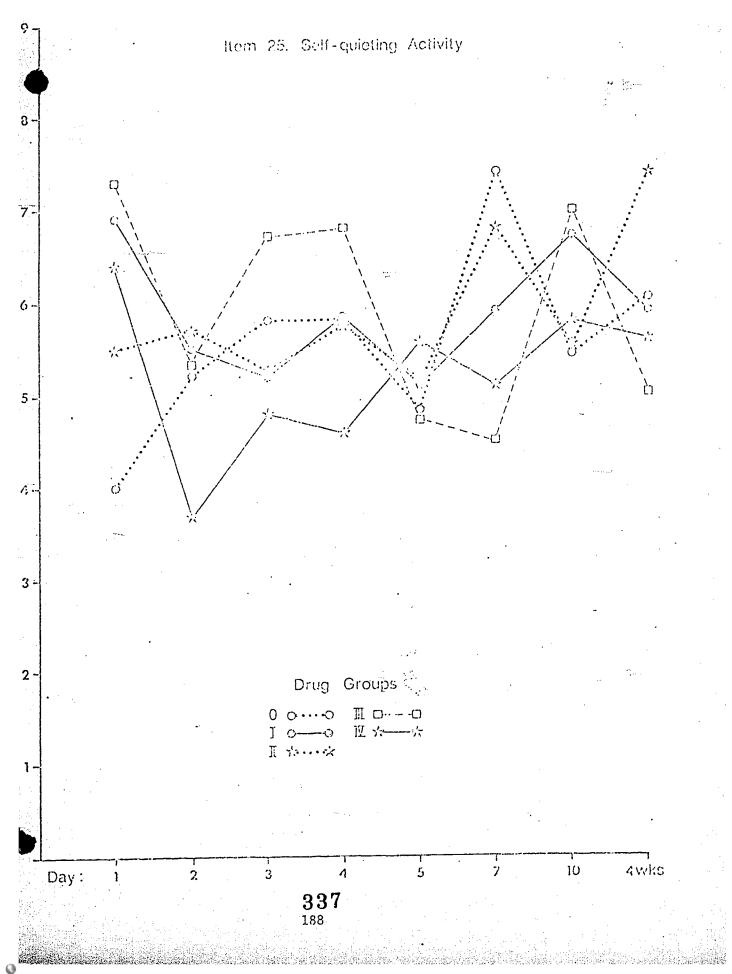


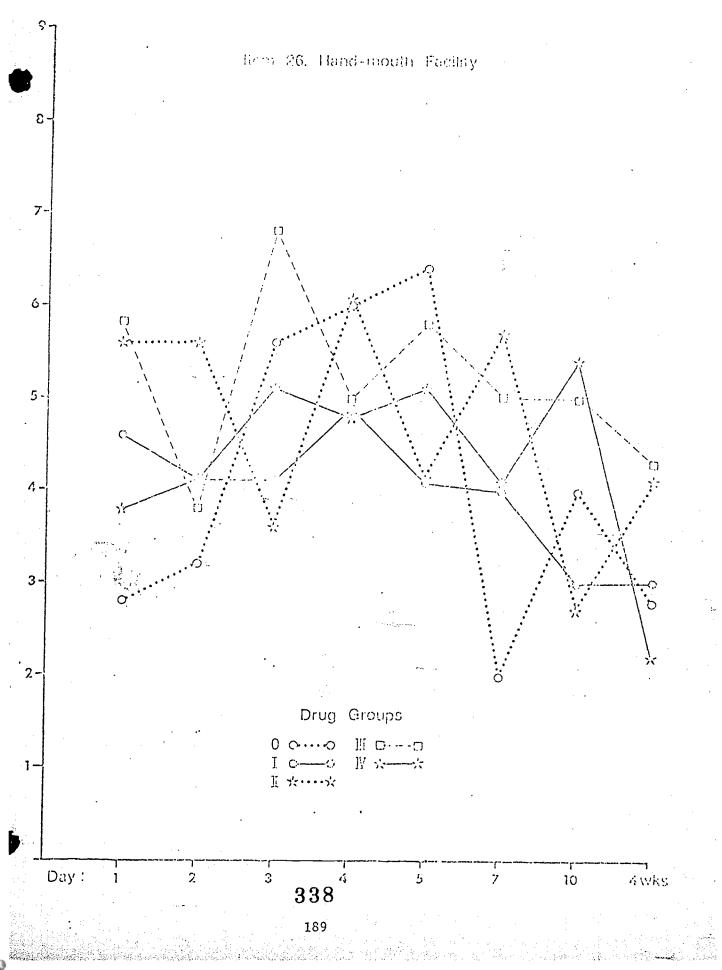


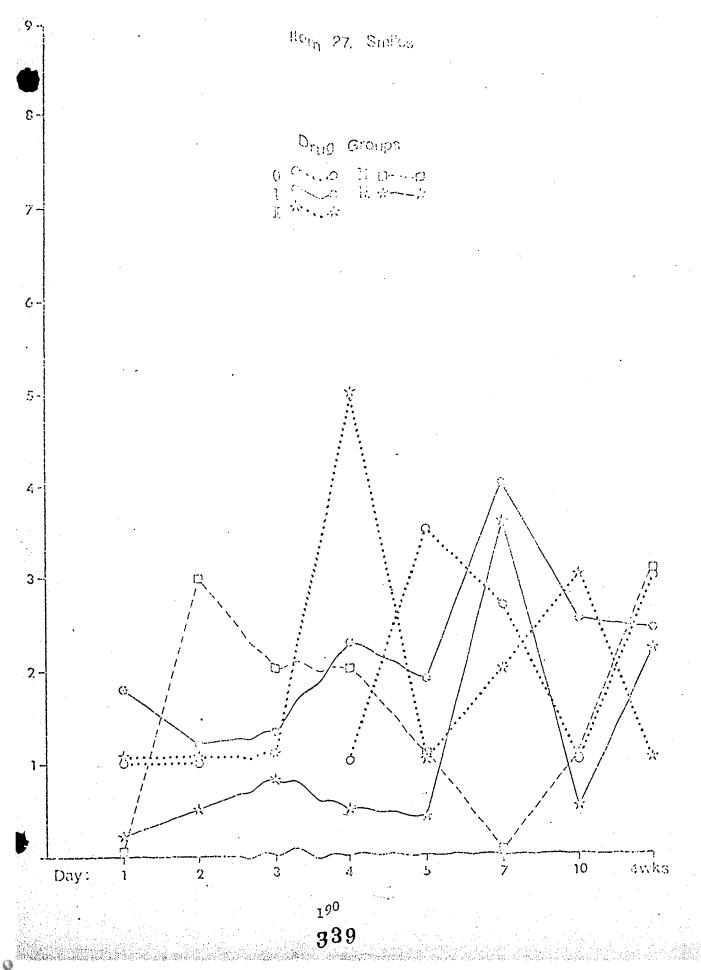












## APPENDIX I



APPUNDIX I

Profile Analysis for Drop Dosage Groups O, I, II, III, and IV Mean Scores for Marker from 9 Over Four Testing Days

DRUG DOSAGE			Pour DA	YS Seven	Twenty Light	TOTAL
GROUP	SEX	One			7.750	6,625
0	F	5.000	6.750	7.000	7.730	
	(N 224)	7.000	4.000	7.000	9.000	6.750
· -	(N-1)	. 5.400	6.200	7.000	8.000	6.650
I	(N=5) F	5,538	5.231	6.077	7.385	6.058
	(N=13) M	4.833	5.500	5.333	8.000	5.916
	(R=6)	5.315	5.316	5.842	7.579	6.013
II	(N=19) F	7.333	6.000	7.667	7.333	7.083
	(H=3) M	4.250	6.000	5.000	7.000	5.562
		5.571	5.000	6.143	7.143	6.214
111	(N=7) M	7.500	5.500	6.750	8.000	6.938
IV	(N=/t)	3.833	5.000	6.167	6.333	5.333
	(N=6) M	4.333	3.667	5.333	7.000	5.083
ur H	(N=3)	4.000	4.556	5.889	6.555	5.250
	(1i=9) ,	5,269	3.500	6.423	7.192	6.096
.2	$\frac{(N=20)}{}$	5.33			7.667	5.972
19 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	M (N=18)	5, 29				6.04

