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EFFICIENCY OF INHALATION AS A MODE OF
ADMINISTRATION OF HEROIN IN ADDICTS

by

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M.B., Hwa-Nam Medical School, 1956
T H E S I S

Submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

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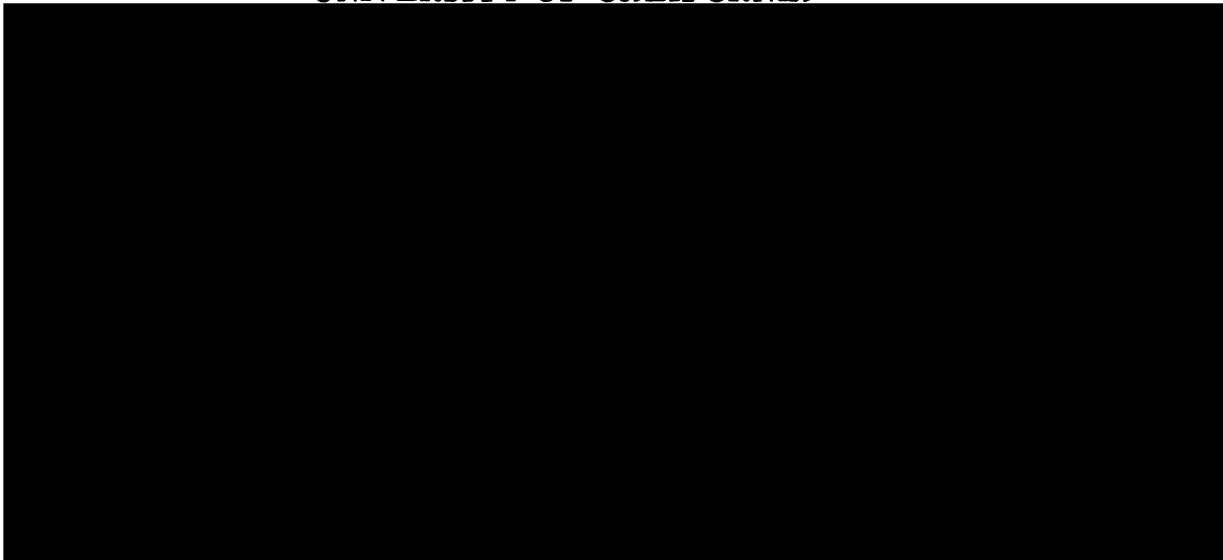
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INTRODUCTION

Hong Kong has been synonymous with narcotics ever since its birth in 1841 as a direct result of the Opium War fought between China and Britain. For reasons that opium addiction was economically and morally devastating China, the Chinese wanted to ban free trade of opium. On the other hand, the British wanted free trade of opium for economic reasons. The war resulted and China lost. In addition to paying indemnities China ceded Hong Kong which was then used as a port for facilitating shipments of opium and other goods into China.

The narcotic problem has continued to plague Hong Kong and is still a very serious one. The problem is also the consequence in large part of the peculiar economy of Hong Kong. Hong Kong is a free port and its economic well-being is dependent upon the free flow of commodities through the territory. To encourage this, it has been the policy of the Hong Kong Government to exercise a minimum of control over the movement of goods in and out of Hong Kong. International traffickers in narcotic drug have exploited the liberal trade regulations and port facilities of Hong Kong to make Hong Kong one of the more notorious centers for narcotic traffic and abuse.

Because of the easy availability of heroin, narcotic addiction remains a serious problem in Hong Kong, despite the Hong Kong Government's intensified efforts to combat this problem. A Hong Kong Government report (1959) indicated an incidence of about 150,000.

There are many aspects of morphine addiction in Hong Kong. One

facet of particular interest to the pharmacologist is concerned with the various modes of administering the narcotics. Opium smoking, which was extremely popular is now on the wane. The peculiar opium pipe, the antique-like opium lamp and the characteristic mahogany opium-smoking bed are no longer the main symbols of this vice in Hong Kong. Nowadays, heroin is used instead of opium by the majority of the addict population. Even opium smokers sometimes resort to the taking of heroin because of its availability and simplicity of administration.

Although the intravenous route of administration is used by "mainliner" some, the more common mode of administering heroin is by inhalation. There are a number of reasons for the popularity of this method: the high potency of heroin, its relative ease of conveyance, the simplicity of the implements required, the fact that the inhalation process is less time consuming than opium smoking and the possibility that the majority of the addicts are still shy of the needle. There are two principle techniques being used for the administration of heroin by inhalation. In the addicts' own parlance they are known as "chasing the dragon" and "ack-ack".

Dragon chasing is the more sophisticated technique. It is believed to have been introduced to Hong Kong, prior to the war. In this technique several granules of heroin generally dyed red ("red chicken") are mixed with several parts of barbital on a piece of tin foil which has been folded longitudinally. The mixture is heated gently with a lighted match or taper, and as it melts it is made to

run slowly up and down the tin foil by alternately tilting each end. As the molten mass is rolled slowly back and forth on the tin foil, the addict inhales the fumes which are evolved. The fumes take the shape of the undulating tail of a dragon, hence, the phrase "chasing the dragon". The fumes may be inhaled without the aid of an instrument, but generally a straw, rolled paper or bamboo tube is used. If the fumes are inhaled through a rectangular match box cover, this variant is called "playing the mouth organ". The inhaling process generally is completed within a few minutes but some of the more adroit inhalers maintain that they can chase the dragon for hours at a time. Dragon chasing usually begins when tolerance to ack-ack develops, and usually ends when the addict drifts to heroin injections to sustain his addiction. However, many addicts have been satisfied with chasing the dragon and have maintained this particular habit for years without any need to resort to heroin injections.

Ack-ack or "firing the anti-aircraft gun" is believed to be a milder form of heroin addiction by inhalation. In this procedure, the lighted end of a cigarette is dipped into heroin powder or small granules. In order to keep the heroin from falling off, the smoker tilts his head slightly backwards so that the lighted end of the cigarette points upwards. This position resembles that of an anti-aircraft gun, hence the name ack-ack. A variant of ack-ack is the smoking of cigarettes containing heroin concealed in the tobacco. Many addicts claim that they were unknowingly introduced to the habit in such a manner.

For inhalation purposes, heroin is distributed in two forms. The coarse granular form, used in dragon chasing, consists of irregular granules approximately 1.5 - 2 mm in diameter. It is called "red chicken" due to the fact that the granules are dyed red. The other form, used in ack-ack and in intravenous injections, consists of a fine powder or fine granules, and is called "white powder" or "No. 4 powder". No. 4 powder is seldom used in dragon chasing because upon heating the fine heroin powder, it has a tendency to melt into a single mass which chars easily with a minimum of smoke being evolved.

Both red chicken and No. 4 powder are dispensed in small packets containing 40 to 80 mgm of heroin. The packets cost, respectively, 18 cents and 35 cents. The barbital used in dragon chasing is dispensed free with the red chicken either in the same packet or in a separate packet.

Gruhrit (1958) estimated that the average dragon chaser inhales over 100 mgm of heroin per day and that some individuals can inhale as much as 300 mgm per day. A search of the literature, failed to yield any quantitative data concerning the efficiency of inhalation as a method of administering heroin. Clinical observations indicate that heroin inhalation is more effective than opium-smoking; and chasing the dragon is more effective than ack-ack. It is the purpose of this study to investigate the efficiency of these two different modes of inhaling heroin in addicts given a known daily dose of heroin. The urinary excretion of morphine was used as a measure of the efficiency

of heroin utilization by the two methods using the excretion value for intravenous heroin as the base-line for making comparisons.

MATERIAL AND METHODS

Urinary excretion studies

Confiscated batches of heroin were obtained from the Hong Kong Police Department. Two types of heroin were made available:

1) "Red chicken", used by the dragon chasers, consists of granules dyed red about 2 mm³ in size. The purity of a pooled sample from several batches was assayed to be 64%.

2) "No. 4 powder", powdered crystalline heroin hydrochloride, is used by the ack-acker and the mainliner. The sample of the No. 4 powder used in this study was found to be better than 92 percent pure.

Sixty-five male addicts between the age of 18-58 years old were used in the study. All were known heroin addicts with a history of addiction for 5 to 30 years. They were hospitalized at the Castle Peak Mental Hospital, Hong Kong, which is a modern 1000-bed government hospital operated in close association with the University of Hong Kong Medical School. A separate 30-bed block is maintained for housing drug addicts.

The addicts participating in this study were volunteers who were selected by a team consisting of two social workers (almoners) and a physician. The preliminary screening was carried out by the social workers. The criteria for selection was based on the premise that the addict should possess a sincere desire to give up addiction, a fair degree of trade skill, a stable family environment, access to a relatively constant income and a negative past history of serious organic disease or psychiatric disturbances.

The selected volunteer was then interviewed in the outpatient clinic by a physician who also took a case history concerning the addict's past physical and psychiatric condition. Particular attention was paid to the addiction history with respect to the addict's duration of addiction, economic status, mode of taking heroin and total daily intake of the drug. At the same time a preliminary physical examination was done to rule out overt organic disease.

After satisfying these preliminary requirements, the addict was given an appointment to be hospitalized. Upon admission, another more intensive physical examination was conducted for lung, liver, and kidney pathology. X-ray examination of the chest, blood serological tests and routine urinalyses were performed. Only addicts with negative findings were used in this study. The addiction history of the patient was re-checked to confirm his stated daily need and to set his daily dose for this study.

The subjects were divided into three groups, according to their mode of administering heroin. One group consisted of those taking heroin by intravenous injection, the second of those inhaling heroin by dragon chasing and the third, those inhaling heroin by the ack-ack technic.

The intravenous group consisted of 16 addicts. The daily heroin intake varied from 150 - 450 mgm with the most frequent dose being between 225 - 300 mgm, administered in equally divided parts three to four times daily. The No. 4 powder was dissolved in 2 ml distilled water by a member of the nursing staff and the injections of the drug were done by either the nurse or the addict himself under close

surveillance. While the nurse tended to deliver the dose rather cautiously the addicts preferred to inject the drug rapidly as a "slug".

There were 35 subjects in the dragon chasing group. The daily dose, ranging from 150 - 450 mgm, was divided equally into three or four equal doses and given three or four times a day. Appropriate amounts of heroin granules (red chicken) were distributed to the addicts together with 3 parts of barbital together with the paraphernalia for dragon chasing. The addicts did not always use up all the barbital. They varied the ratio of barbital to heroin according to what they called "the flavor of the smoke" evolved. The inhalation was made with either a straw, a foil tube with a larger bore than a straw or the outer cover of a rectangular match box. The addicts, under close supervision, were allowed as much time as needed to "chase the dragon". This usually required about 30 minutes.

There were fourteen subjects in the ack-ack group. The daily dose of No. 4 powder, ranging from 225 - 600 mgm, was dispensed with cigarettes in 3 to 4 equally divided doses. Usually the addicts smoked their heroin ration with one cigarette making two to four insertions of heroin.

A three-day observation period was used for all three groups. The addicts under study were isolated in a ward in the addiction block. Total 24 hour urine specimen of each addict was collected daily and the total volumes measured. A 15 ml aliquot was assayed for total (free plus conjugated) morphine content by the method of

Fujimoto, Way and Hine (1954). The total morphine present in 24 hour urine was expressed in terms of morphine base equivalent. The percent recovery of heroin from urine was calculated by comparing the total amount of morphine base equivalent recovered from the 24 hour specimen against the original amount of morphine base equivalent in the given daily dose of heroin hydrochloride. The average morphine excretion of each individual for the three days is expressed as mean % recovery. The daily mean % recovery at each dose level for each method of administering heroin was also calculated as well as the grand mean % recovery for all doses over the 3-day period for each method.

Assessment of the availability of heroin under laboratory conditions simulating "dragon chasing" and "ack-ack"

Both procedures involve volatilization of heroin under high temperature and trapping the heroin vapor in acid for estimation.

1) Procedure for evaluating "dragon chasing" - Three flow-towers containing 500 ml of 0.5 N H_2SO_4 were connected in series with polyethylene tubing so that by applying reduced pressure at one end, gas flow in the system would enter the flow-head and bubble through the acid (Fig. 1). The air-flow in the system was monitored with a flow-meter and kept relatively constant at a rate of 10 L/min. The volatilizing unit for the heroin consisted of a test tube fitted with a stopper which had a short inlet and a long outlet. The latter was connected by a ball and socket joint to the inlet end of one of the flow-towers.

Approximately 12 mgm heroin hydrochloride, weighed with a

1. The first step in the process of identifying a problem is to recognize that a problem exists. This is often done by comparing current performance against a desired state or goal. For example, a company might notice that its sales are declining or that its customer satisfaction is low. Once a problem is identified, the next step is to define the problem more clearly. This involves determining the scope of the problem, the causes, and the consequences. For example, a company might determine that its sales are declining due to a lack of marketing efforts or that its customer satisfaction is low due to poor customer service. Once the problem is defined, the next step is to develop a plan to address the problem. This involves identifying the resources needed, the actions to be taken, and the timeline for implementation. For example, a company might develop a plan to increase sales by launching a new marketing campaign or to improve customer satisfaction by training its customer service representatives. The final step in the process is to evaluate the results of the plan. This involves comparing the current performance against the desired state or goal to determine if the problem has been solved. If the problem has not been solved, the process may need to be repeated.

2. The second step in the process of identifying a problem is to define the problem more clearly. This involves determining the scope of the problem, the causes, and the consequences. For example, a company might determine that its sales are declining due to a lack of marketing efforts or that its customer satisfaction is low due to poor customer service. Once the problem is defined, the next step is to develop a plan to address the problem. This involves identifying the resources needed, the actions to be taken, and the timeline for implementation. For example, a company might develop a plan to increase sales by launching a new marketing campaign or to improve customer satisfaction by training its customer service representatives. The final step in the process is to evaluate the results of the plan. This involves comparing the current performance against the desired state or goal to determine if the problem has been solved. If the problem has not been solved, the process may need to be repeated.

3. The third step in the process of identifying a problem is to develop a plan to address the problem. This involves identifying the resources needed, the actions to be taken, and the timeline for implementation. For example, a company might develop a plan to increase sales by launching a new marketing campaign or to improve customer satisfaction by training its customer service representatives. The final step in the process is to evaluate the results of the plan. This involves comparing the current performance against the desired state or goal to determine if the problem has been solved. If the problem has not been solved, the process may need to be repeated.

4. The fourth step in the process of identifying a problem is to evaluate the results of the plan. This involves comparing the current performance against the desired state or goal to determine if the problem has been solved. If the problem has not been solved, the process may need to be repeated.

precision of 0.01 mgm, were placed in the volatilizing tube. The heroin was used alone or as a mixture with 3 or 6 parts of barbital. The tube was then placed in a heating block and while maintaining air flow, volatilization of the mixture was effected at temperatures of 200°C, 225°C or 266°C for 30 minutes. This time was sufficient for complete volatilization of the contents in the tube.

The connecting tubings were then rinsed three times with the acid solution in the flow-towers. An aliquot of 5 ml of the acid solution was analysed directly for total and free phenol content by the method of Way et al (1960).

The ^{percent} recovery of total phenol in terms of free morphine base equivalents, was then obtained by comparing the amount of total phenol recovered from the acid solution against the amount of heroin present initially in the volatilizing tube. The relative composition of the total phenol recovered as free and conjugated phenol was also calculated.

Heroin hydrochloride, being relatively labile, undergoes hydrolysis to monoacetylmorphine and morphine. The total phenol, therefore, represents a mixture of heroin, monoacetylmorphine and morphine; the conjugated phenol, that is the difference between total and free phenol, represents unchanged heroin and the free phenol represents a mixture of monoacetylmorphine and morphine.

2) Procedure for assessing ack-ack - A glass cigarette holder was fitted to the male portion of a ball and socket joint; the female joint was joined to a flow-tower which also had an attached outlet tube that could be used as a mouth piece for smoking (Fig. 2). The

tobacco leaves were removed for about 2 cms from the tip of a cigarette, a known amount of heroin powder inserted and the tobacco was replaced. The cigarette was inserted in the holder and smoked by a subject inhaling from the "pipe stem" connected to the flow-tower. Two modes of smoking were used; a slow but almost continuous suction with occasional shorts stops simulating a thoughtful smoker in deep meditation. This took about one and a half minutes. The second technique consisted of short quick puffs, mimicking an excited smoker and took about 1/2 to 3/4 of a minute. The smoke was passed through 150 ml of 0.5 N H_2SO_4 contained in the tower. After rinsing the connecting tubing the acid volume was made up to 250 ml. A 5 ml aliquot was extracted and analyzed for free and total phenol content as described by Way et al (1960). A cigarette containing no heroin was also carried through the same procedure to obtain a blank phenol value for correcting free and total phenol readings. The calculations for recoveries were the same as in the simulated dragon chasing experiments.

RESULTS

Urinary excretion of heroin as total morphine. In the group using intravenous injection the ^{mean} % recovery was, as shown in Fig. 3, relatively constant at various dose levels and the grand mean % recovery for all doses was $68\% \pm 2.12$ S.E. This value was obtained from 47 urine specimens collected from 16 addicts.

In the dragon chasing group the heroin accounted for was only a little more than 1/3 as much as that for the intravenous group. The grand mean % recovery of total morphine, obtained from 96 urine specimens of 35 addicts was 26.2 ± 0.74 S.E. (Fig. 4). While the mean % recovery of each individual from day to day and between individuals varied to a greater extent than that for the intravenous group, the mean % recovery for each dose level was relatively constant.

With the ack-ack group the heroin accounted for was only one-half as much as that in dragon chasing. The grand mean % recovery of total morphine obtained from 41 urine specimens of 14 addicts was found to be $14\% \pm 0.75$ S.E. (Fig. 5). The individual values varied even more than those of the dragon chasing. Although the mean % recovery for each dose level showed somewhat greater fluctuations, it still remained relatively constant.

Regardless of doses level, the daily mean % recovery for each method of administration is relatively constant (Fig. 6). There were individual variations among subjects and by the same subject from day to day with respect to total amounts of morphine excreted, but the mean percent heroin accounted for as morphine by each method and

for each day was relatively constant (Fig. 6).

Effect of temperature and barbital on the availability of heroin.

A. Dragon Chasing: The heroin sample used in the study was found to be 92 percent pure, the remaining 8 percent being chiefly monoacetylmorphine and a trace of morphine (Fig. 7). On heating the heroin in the volatilizing unit at various temperature levels, there were distinct changes in total recovery as well as in the relative proportion of unchanged heroin to hydrolysed heroin. The mixing of barbital with the heroin sample also affects the total heroin recovery quantitatively and qualitatively. In general the higher the temperature and the greater the amount of barbital added to the heroin samples, the greater were the effects.

At 200°C, heroin alone gave a total heroin recovery value of 17%. The total heroin recovery values went up to 34% and 68% as the heroin sample was heated respectively with 3 parts and 6 parts of barbital. On the other hand, although the total heroin accounted for was increased, the proportion of free to conjugated phenol was increased slightly.

At 225°C the total heroin accounted for was increased about 10 percent. The effect of barbital addition on total heroin recovery was similar to that at 200°C. The recovery of heroin alone was 29%, that of the heroin-barbital 1:3 mixture 46 percent and that of 1:6 mixture, 75 percent. Not only was total heroin recovery increased but the hydrolysis of heroin was inhibited by the barbital. The percent of unchanged heroin went up from 16 percent for heroin alone, to 67%

for the 1:3 mixture and 74% for the 1:6 mixture.

At 266°C, the effects of barbital on the total heroin recovery were less obvious but still significant. Although the total recoveries for heating heroin alone and with the two barbital mixtures were all around 70 percent, the fraction of free phenol present was about one-half that for heroin alone whereas for the heroin-barbital mixtures it was about one-fourth.

B. Ack-ack: Both the total recovery and the percent of unchanged heroin were lower than those of dragon chasing and were dependent on the manner of smoking the heroin (Fig. 8). Greater values for total recovery and percent unchanged heroin were obtained by slow, almost continuous smoking than by quick short puffs. The total heroin accounted for was 29 percent for the slow method of which unchanged heroin constituted 19 percent, while with rapid method the total recovery was but 15 percent and only 12 percent represented unchanged heroin.

DISCUSSION

On the basis of previous data on the metabolism of heroin and our present findings, it appears that urinary recovery of heroin as morphine may be used as a reasonable index for approximating the efficiency of heroin utilization. The metabolic fate of heroin has been reviewed by Way and Adler (1962). Heroin is rapidly deacetylated in the body, yielding first MAM and shortly thereafter, morphine. Little if any heroin or MAM, however, appear in the urine and by far the major fraction of a given dose of heroin can be accounted for in the urine as free morphine and as morphine conjugated as the glucuronate.

The views of Way and Adler were based in part on several earlier studies. Shen (1936) reported that he was unable to extract any heroin from the urine of rabbits or addicts after giving heroin. Since he was only able to detect morphine in the urine, he concluded that the heroin must have been changed into morphine on passing through the human body. Goris and Fourmont (1931) also reported that the excretion product of heroin was morphine. Oberst (1941) reported that about one-half the dose of heroin in morphine addicts after subcutaneous administration could be accounted for in the urine as morphine and its conjugate. In a follow-up study, Oberst (1943) found almost identical results. In addicts receiving 108 mgm of heroin hydrochloride daily to sustain physical dependence to 200 mgm of morphine sulphate, he found that he could account for 57.3% of the heroin dosage as extractable morphine.

In our present study, the total amount of morphine (free and

conjugated) excreted in 24 hr. urine by the intravenous heroin group accounted for 68% of the daily dose. The minor discrepancy with Oberst's results can be reconciled on the grounds that his and our studies differed with respect to dose and mode of administering heroin as well as in the ethnic extraction of the addict groups. In view of these differences, the agreement between the two studies are not incompatible and can be considered reasonably good. Our intravenous findings, therefore, serves as a reliable base for evaluating the efficiency of heroin utilization by the inhalation techniques of dragon chasing and ack-ack. It is also of interest to note that the daily mean urinary excretion of total morphine for all three methods of administering heroin remained relatively constant. This finding suggests that there is little or no significant morphine carry-over from day to day and also that the dose assigned to each addict was compatible with his stated daily needs. The relatively constant excretion data from day to day also indicate that the addicts are skilled enough to reproduce the manipulative procedures of heroin inhalation with a high degree of consistency. It appears valid, therefore, to compare these excretion values with those after intravenous heroin administration for assessing the efficiency of the inhalation procedures.

With intravenous heroin administration, in which absorption of the compound can be regarded as complete, the mean urinary recovery of heroin as morphine was 68%. If this figure is assumed to represent 100% utilization of a given dose of heroin, then the 26% morphine

urinary recovery by "dragon-chasing" would indicate that approximately two-fifths of the heroin was utilized. Similarly, the 14% morphine recovery by "ack-ack" would indicate that about one-fifth of the heroin dose was utilized. Thus the efficiency of dragon chasing is about twice that of ack-ack .

The standard deviation of the total morphine recovery in the intravenous group after heroin administration was only $1/5$ of the grand mean whereas in the dragon chasing group it was $1/3.6$ and that in the ack-ackers $1/2.9$ of the grand mean. There are several factors which might explain why utilization of heroin in dragon chasing and ack-ack is less complete and more variable. Physiologic, pharmacologic, physical, chemical as well as mechanical factors are all involved, often inter-related, and some of them are subject to control by the addict.

An obvious source of loss of available heroin with the inhalation techniques is that not all the heroin smoke evolved can be inhaled. Except in a close circuit, the administration of a gas by inhalation is inevitably accompanied by a partial loss of the administered gas through incomplete inhalation. This phenomenon is appreciated by the more sophisticated dragon chasers who use the outer cover of a match box rather than a straw for inhaling heroin because of the former's greater cross section. The greater fluctuation, in our excretion values for morphine in dragon chasing are due in part to the fact that this group consisted of subjects who used different types of inhalers for obtaining heroin effects and varied in their adroitness in chasing the dragon.

二、(一) 本國之法律，對於外國人，在同等條件下，應予同等之保護。此項原則，在國際法上，稱為「國民待遇」。其意謂：外國人應享有與本國國民同等之權利。此項原則，在國際法上，稱為「國民待遇」。其意謂：外國人應享有與本國國民同等之權利。

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It may be taken for granted that in dragon chasing and ack-ack, absorption of heroin takes place chiefly in the respiratory tract. There is, however, lack of information concerning the absorption of heroin by this mode of administering the drug. In consideration of the fact that inspired heroin in the alveoli is in very close contact with plasma, it is justifiable to presume that most of the absorption takes place in the alveoli.

Effective alveolar uptake of inspired heroin depends on a uniform distribution of the inspired heroin in the alveoli in order that a large surface area of the alveolar membrane can be utilized. An adequate pulmonary circulation is also mandatory for any poorly perfused area of the alveoli would hardly take up much drug, no matter how well it is ventilated with inspired heroin. In the absence of adequate function of any one of these two factors, heroin uptake would be impaired. Effective alveolar uptake of heroin, therefore, is dependent on optimal pulmonary ventilation and perfusion conditions which may vary in and between individuals. Moreover, during the process of dragon chasing or ack-ack, pulmonary ventilation can be influenced by such factors as inspiratory volume, duration of breath holding, functional residual capacity and expiratory volume, all of which are subject to some control by the addict.

Alveolar uptake of inspired heroin may be presumed to be incomplete, although direct evidence is lacking. If one considers that inspired heroin as a gas and compares its probable alveolar uptake with that of O_2 , partial loss of inspired heroin by exhalation is easily under-

standable. Direct qualitative evidence to support the idea of heroin loss by exhalation can easily be demonstrated by trapping the expired air in acid solution after heroin inhalation, and detecting the presence of heroin or morphine in the acid solution by thin layer chromatography. Quantitative data would be troublesome to obtain since it is rather difficult technically to administer a fixed amount of heroin in its volatilized or gaseous form by inhalation and these problems will be brought in later discussion.

Apart from physiological and pathologic considerations, there are also pharmacologic aspects which may affect the exchange of heroin by inhalation. It is common clinical knowledge that an ordinary therapeutic dose of morphine can be dangerous to the asthmatic. While the exact mechanism of action remains to be elucidated, one possible explanation is that morphine causes bronchospasm by virtue of its histamine-releasing property. The fact that high concentrations of narcotics can be provided locally in the respiratory tract by inhalation, increases the probability that the inspired heroin could exert effects on alveolar ventilation in normal subjects or addicts with or without the overt manifestation of bronchospasm. This constitutes a significant problem for future study.

The high local concentration of heroin provided by inhalation, may effect regional changes in pulmonary circulation that could also alter the ventilation^{and} perfusion of the lung. Recent evidence indicates that the pulmonary vasculature is not unsusceptible to changes in physical or chemical conditions of its environment. It is well-known that narcotic drugs depress respiration with resultant hypoxia and

hypercapnia. It is now known that a decrease of O_2 tension and a rise in alveolar CO_2 tension can raise pulmonary arterial pressure independently, presumably by increasing the pulmonary vascular resistance (Fishman, 1961; Comroe et al, 1962). Furthermore, it has already been shown recently that pulmonary circulation can be affected by chemical agents acting locally as evidenced by the report that acetylcholine has been found to dilate pulmonary vessels when injected into the pulmonary artery of some patients with pulmonary hypertension (Harris, 1957). Whether morphine has any effects on the pulmonary vessels in normal subjects and in addicts needs to be studied. Such information could be of general clinical significance and might well enhance our understanding of the mechanisms involved in alveolar absorption of inhaled heroin.

Of all the possible factors responsible for low urinary recoveries of total morphine by inhalation, however, by far the most important appears to be the physical-chemical ones concerned with the volatility and stability of heroin under the conditions of inhalation. The amount of heroin available for absorption hinges on these two properties which in turn was found to be greatly influenced by temperature and by mixing with barbital.

In the simulated dragon chasing experiments the total volatilized heroin accounted for was increased as temperature was increased from temperatures 20 to 45 degrees lower than the melting point of heroin to a temperature 20 degrees higher. However, although the amount of heroin accounted for as total phenol was increased, it was accompanied

by considerable hydrolysis of heroin to 6-monoacetylmorphine and morphine which are still pharmacologically active, although less so than heroin. Barbitol was found to enhance the volatility of heroin at the temperatures below the melting point of heroin and concomitantly to depress the hydrolysis of heroin. At temperatures above heroin's melting point the influence of barbitol became of less consequence; heroin volatility was not greatly affected but there was some depression of its hydrolysis. It is of interest to mention that dragon chasers generally do not apply continuous heat to barbitol-heroin mixture on the foil but prefer to use a paper taper or match instead of a candle for a source of heat. They informed us that heating the heroin on the foil with too intense heat or without barbitol results in a burned-charcoal flavor, and the greater this flavor, the less the effect.

It is to be expected that as the temperature is increased considerably beyond the melting point of heroin, decomposition more extensive than hydrolysis would ensue and this is indicated by the very low total morphine recoveries in the simulated ack-ack experiments. While the actual temperatures to which the heroin was exposed in these experiments were not recorded, the reported temperatures for the burning area of a cigarette have been reported to be 746°C while unsmoked and 774°C while being smoked (Harlow, 1956). It is not surprising, therefore, that urinary recoveries for heroin are low for ack-ack.

It should be recalled that in the laboratory study the maximum

availability of a given dose of heroin after heating was only about 75% in simulated dragon chasing and 30% in ack-ack. Assuming that the laboratory conditions reproduce closely those of the actual inhalation procedures, and basing calculations on the amount of volatilized heroin available rather than the administered dose, the urinary recovery of morphine in dragon chasing would represent 51% utilization instead of 38% and that of ack-ack 67% instead of 20%. This suggests that loss of heroin by exhalation is rather minimal.

It is not surprising to find that utilization is greater by ack-ack since the procedure involves less skill and less mechanical loss of fumes containing heroin. The main loss of heroin by ack-ack can be attributed rather to its exposure to conditions of high temperatures with resulting extensive decomposition. While utilization of available volatilized heroin is less efficient in dragon chasing than in ack-ack, more heroin is made available to the addict in dragon chasing as a consequence of more favorable temperature heating conditions and by the addition of barbital. This would explain the greater urinary recovery of morphine with dragon chasing as well as greater pharmacologic effects of dragon chasing over that of ack-ack.

Clinical observations and descriptions by addicts indicate that the pharmacological effects of dragon chasing on addicts are much more pronounced than those of ack-ack. After developing tolerance to heroin, the ack-acker generally shifts to dragon chasing for greater heroin effects; a novice in the latter technique often experiences symptoms of morphine overdose. Sophisticated dragon chasers mention that

ack-acking generally fails to sustain their daily needs for heroin. Many addicts also state that they experience less severe withdrawal symptoms from ack-ack than from dragon chasing and this phenomenon was supported by the observations in the ward. Greater physical dependence to dragon chasing than ack-ack can be correlated with the more severe abstinence signs resulting from withdrawing heroin. The greater narcotic and addicting effects produced by dragon chasing over ack-ack can be accounted for by the greater availability of a given dose of heroin as evidenced by the finding of greater amounts of unchanged heroin present in the volatilized smoke and higher urinary recoveries of total morphine.

Another consideration to explain the more pronounced effects of dragon chasing over those of ack ack is that the barbital present in the dragon chasing mixture may also exert pharmacologic effects. Gruhzeit (1958) has previously expressed this belief and reported that 1% of the dragon chasers in his series developed convulsions. In our study, one dragon chaser, whose addiction history revealed the use of a relatively high dose of barbital and in whom past history of epilepsy was excluded, developed convulsions during withdrawal and had "nightmares" for almost a week. Two other dragon chasers who used high doses of barbital also described having nocturnal hallucinatory episodes for varying periods of time after withdrawal. This phenomenon can be interpreted as an indication of moderate barbital withdrawal. Ordinarily one would not expect that the dose of barbital used in dragon chasing would have significant addicting effect. The daily dose used ranged from 0.45 gm -- 1.35 gm, with the most frequent

range between 0.6 -- 0.9 gm, and these doses, as described in the method section, were often not used entirely by the addicts. Assuming that the actual utilization of barbital is about 50%, most of the daily doses within our daily range would be sufficient to produce some sedative effects and its effects tend to be cumulative. Consequently, the combination ^{of} barbital and heroin on a long term basis could result in enhanced addictive and narcotic effects of either one or both drugs.

SUMMARY

- 1) The efficiency of administering heroin by two unique modes^{of} inhalation was studied in conjunction with intravenous injection using 24-hour urinary excretion of total morphine as a means of comparison. The more sophisticated inhalation method, called dragon chasing, consists of heating heroin granules and barbital with a lighted taper on a piece of tin foil and inhaling the fumes which emanate with a straw or a rectangular match-box cover. The other method "ack-ack" or "anti air-craft gunning" involves the smoking of a cigarette to one end of which heroin powder is loaded. In order to prevent the heroin powder from falling off the cigarette, the addict smokes the cigarette with his head tilted backwards.
- 2) Urinary excretion of heroin as free and conjugated morphine in 24-hours urine samples was determined for three days in 65 male heroin addicts to whom a known amount of heroin was given by intravenous injection, dragon chasing and ack-ack.
- 3) The urinary excretion of total morphine after intravenous injection was found to be fairly compatible with previously reported studies. Although individual results in the dragon chasing group and the ack ack group showed greater fluctuation, the daily mean recovery of total morphine for each of the three methods of administering heroin and the mean recovery for each dose level in each method were relatively constant. In the group of 16 addicts, using intravenous injection the mean % recovery of heroin as total morphine in 24-hour urine of 47 specimens was found to be $68\% \pm 2.12$ S.E.

of the given dose. In 96 urine specimens from 35 dragon chasers the mean urinary recovery of morphine was 26.2 ± 0.75 while that of 41 specimens from 14 addicts of the ack ack group was $14\% \pm 0.74$. Thus, using excretion value in intravenous injection as the baseline, the efficiency of dragon chasing was estimated to be two-fifths that of intravenous injection and twice that of ack ack.

- 4) Availability of volatilized heroin for inhalation in dragon chasing and ack ack was found to be the important factor in limiting the pharmacologic effects and urinary excretion of heroin. Simulated dragon chasing and ack ack experiments were carried out in the laboratory and it was found that availability of heroin was found to be temperature dependent. Below or slightly above the melting point of heroin hydrochloride (244°C), increases in temperature increased heroin volatility and availability. At very high temperatures such as in ack ack in which the temperature of a burning cigarette is reported to be 746°C , availability of heroin is decreased by extensive decomposition of heroin. The maximum availability of heroin in dragon chasing was 75% of the given dose and that in ack ack less than one-half as much.
- 5) It was found that under conditions of dragon chasing, barbital increases heroin availability by inhibiting heroin decomposition by heat and facilitating heroin volatilization.
- 6) Other factors accounting for the decrease in efficiency of dragon chasing and ack ack are also discussed.

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Legend

- Fig. 1. Apparatus for recovery of heroin under conditions simulating dragon chasing.
- Fig. 2. Apparatus for recovery of heroin under conditions simulating ack ack.
- Fig. 3. 24-hour urinary excretion of morphine in addicts after ~~intravenous~~ administration of heroin hydrochloride.
- Fig. 4. 24-hour urinary excretion of total morphine in addicts after inhalation of heroin hydrochloride by the dragon chasing method.
- Fig. 5. 24-hour urinary excretion of total morphine in addicts after inhalation of heroin hydrochloride by the "ack-ack" method.
- Fig. 6. Comparison of daily urinary excretion of total morphine in addicts receiving heroin by different routes of administration.
- Fig. 7. Recovery of heroin by inhalation under conditions simulating "Dragon chasing".
- Fig. 8. Recovery of heroin by inhalation under conditions simulating "ack-ack".



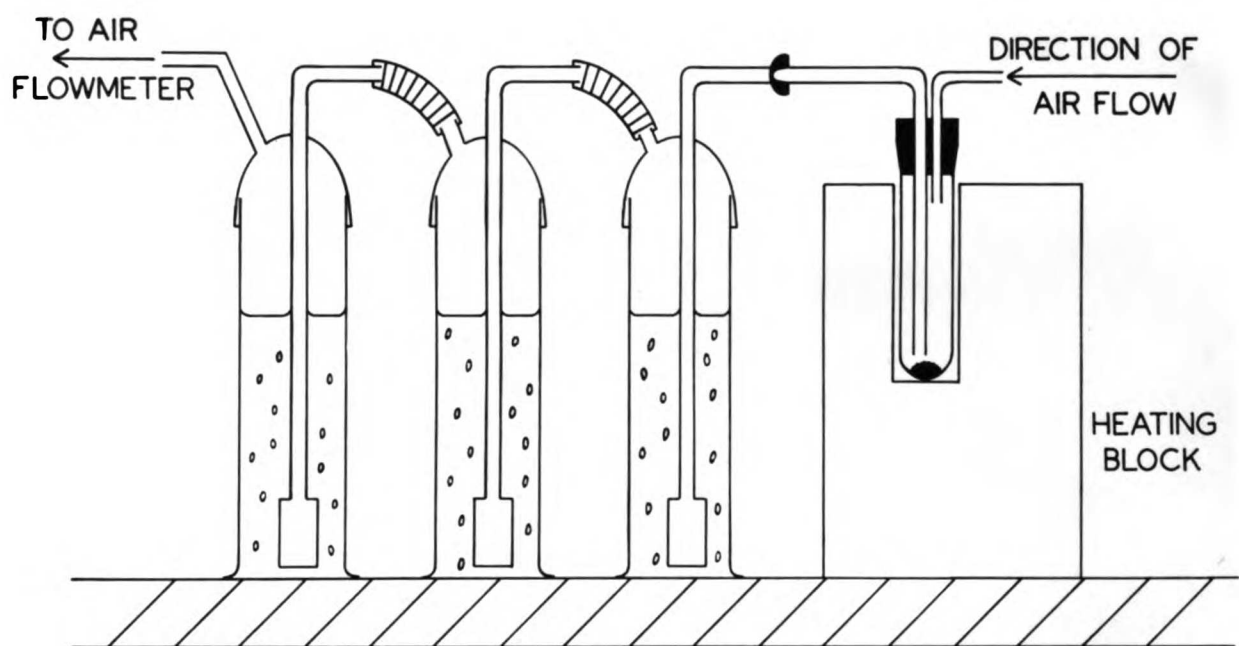


Fig. 1

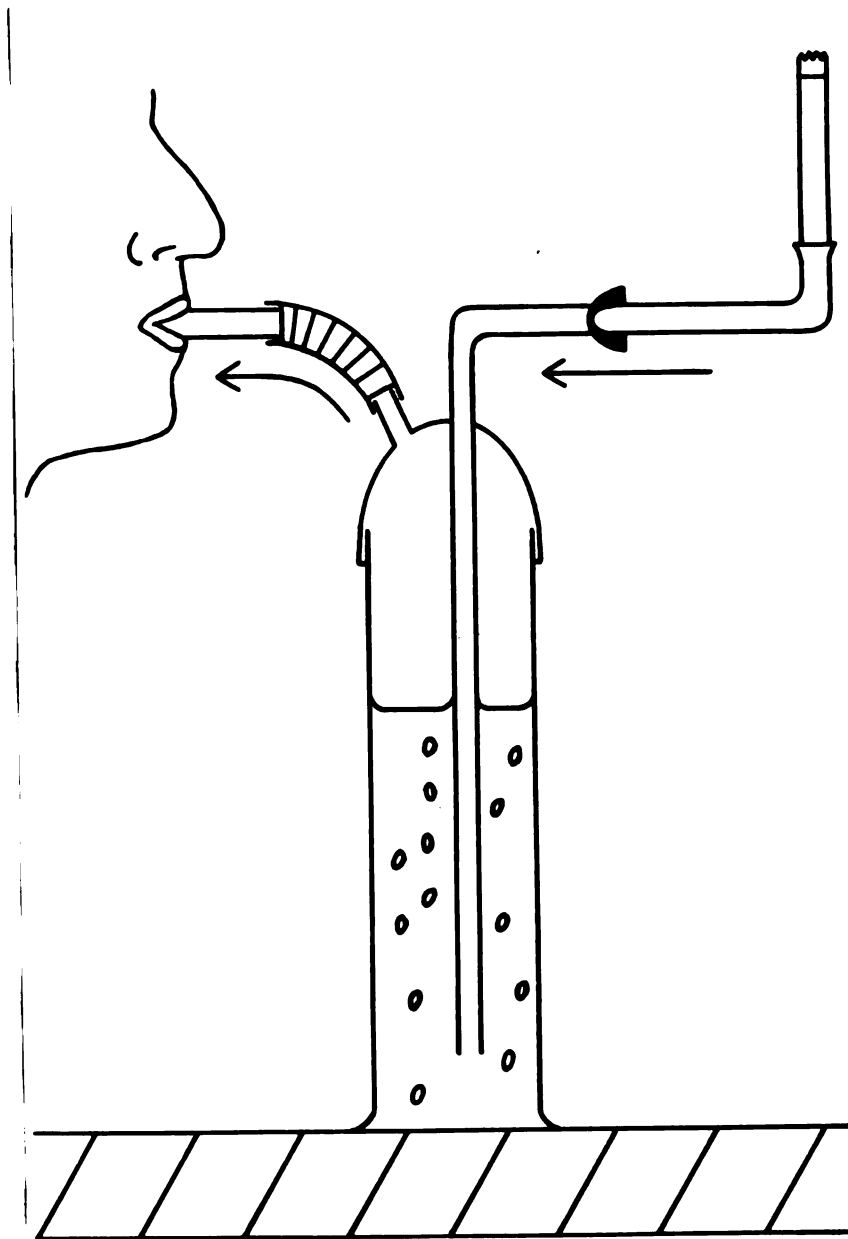


Fig. 2

**24-HOUR URINARY EXCRETION OF MORPHINE IN ADDICTS AFTER
INTRAVENOUS ADMINISTRATION OF HEROIN HYDROCHLORIDE**

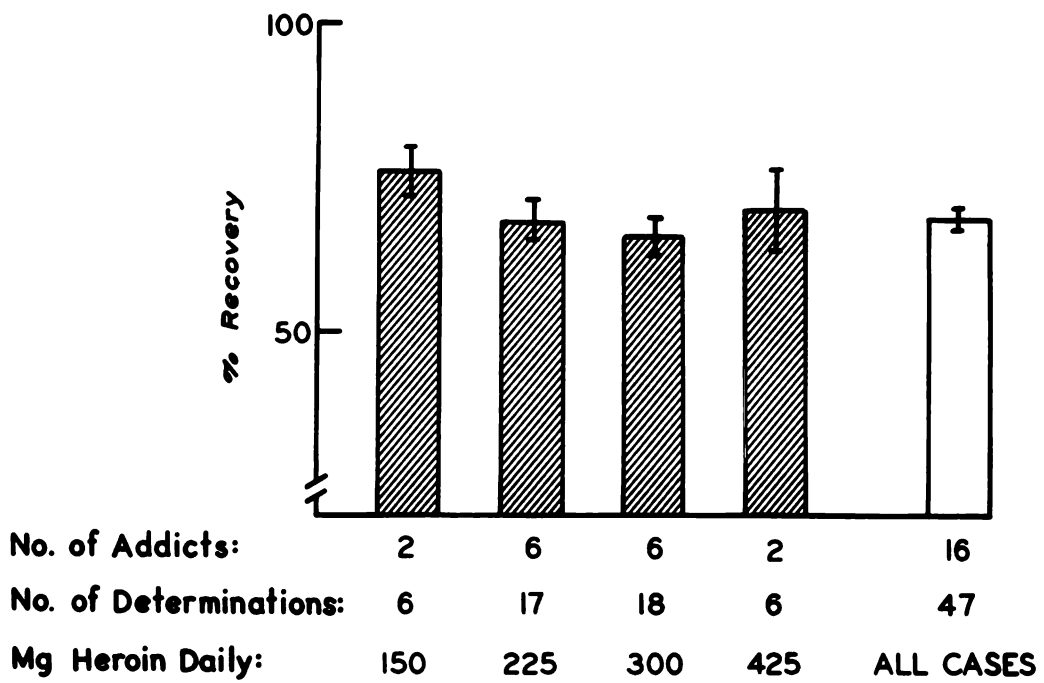
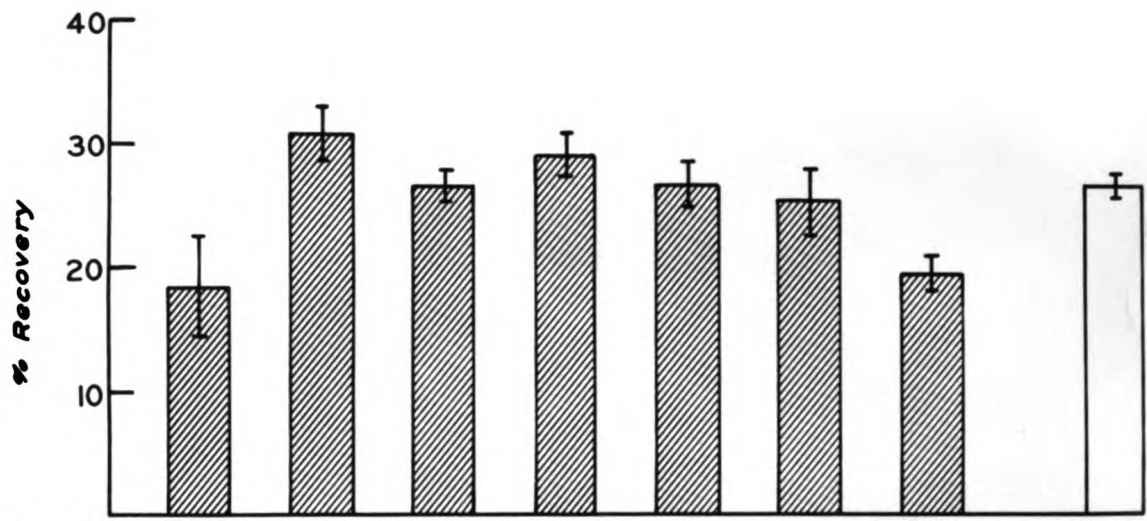


Fig. 3

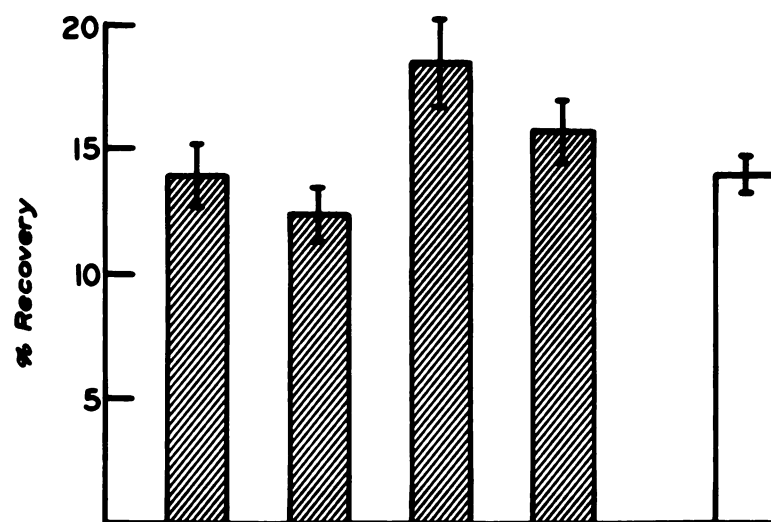
**24-HOUR URINARY EXCRETION OF MORPHINE
IN ADDICTS AFTER INHALATION OF HEROIN
HYDROCHLORIDE BY THE "DRAGON-CHASING" METHOD**



No. of Addicts:	2	5	10	5	6	4	3	35
No. of Determination:	6	15	26	13	18	9	9	96
Mg Heroin Daily:	100	150	200	250	300	400	450	ALL CASES

Fig. 4

24-HOUR URINARY EXCRETION OF MORPHINE IN ADDICTS AFTER INHALATION OF HEROIN HYDROCHLORIDE BY THE "ACK-ACK" METHOD



No. of Addicts:	4	6	2	2	14
No. of Determinations:	12	18	5	6	41
Mg Heroin Daily:	225	300	375	600	ALL CASES

Fig. 5

COMPARISON OF DAILY URINARY EXCRETION OF
HEROIN HYDROCHLORIDE IN ADDICTS BY DIFFERENT
ROUTES OF ADMINISTRATION

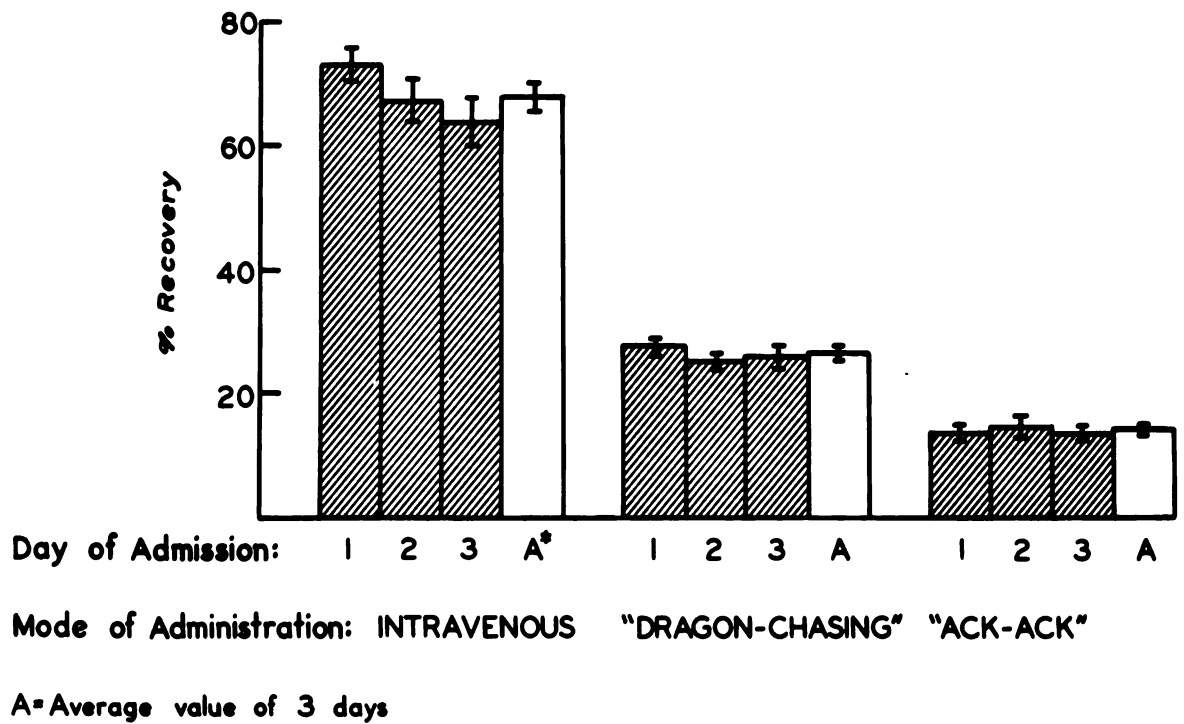


Fig. 6

RECOVERY OF HEROIN BY INHALATION UNDER
CONDITIONS SIMULATING "DRAGON CHASING"

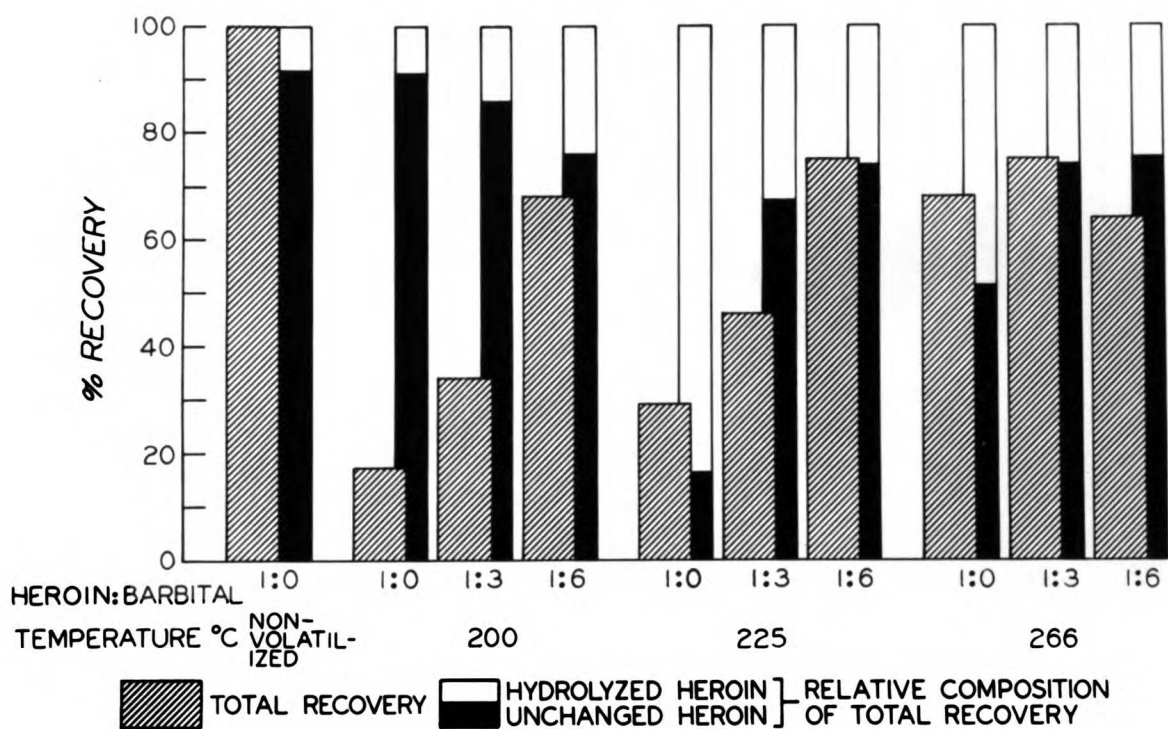


Fig. 7

RECOVERY OF HEROIN BY INHALATION UNDER CONDITIONS
SIMULATING "ACK-ACK"

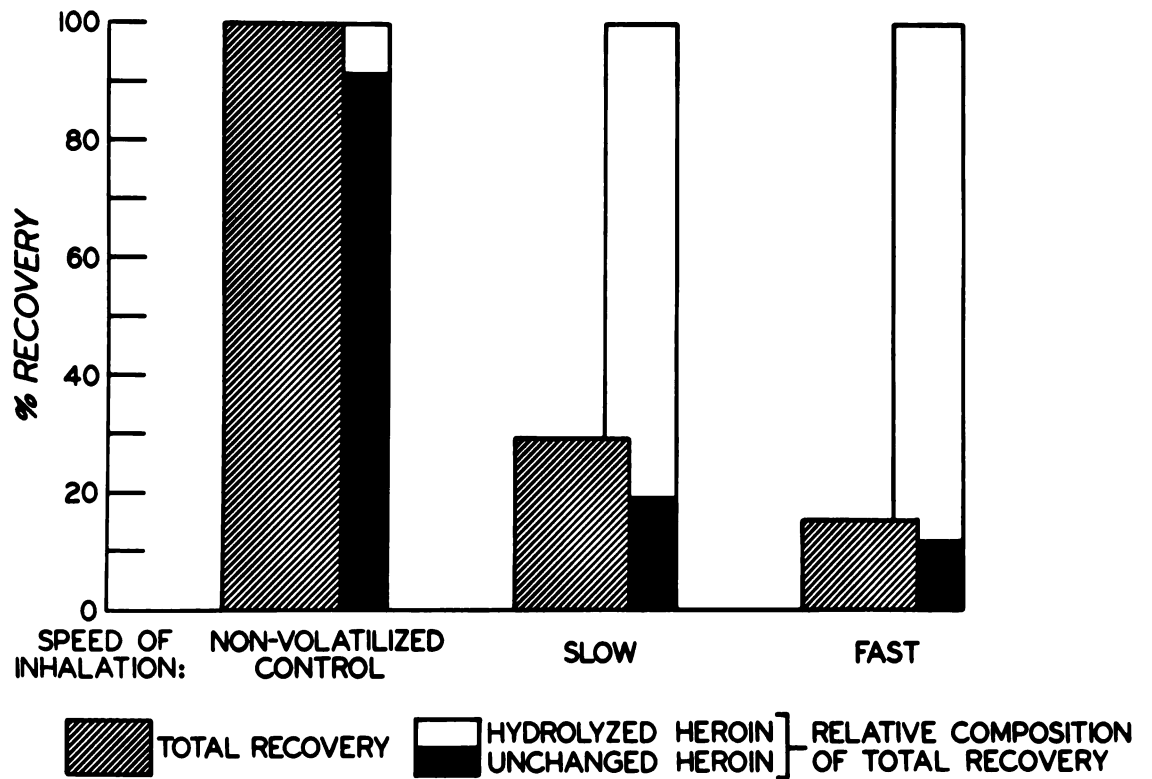
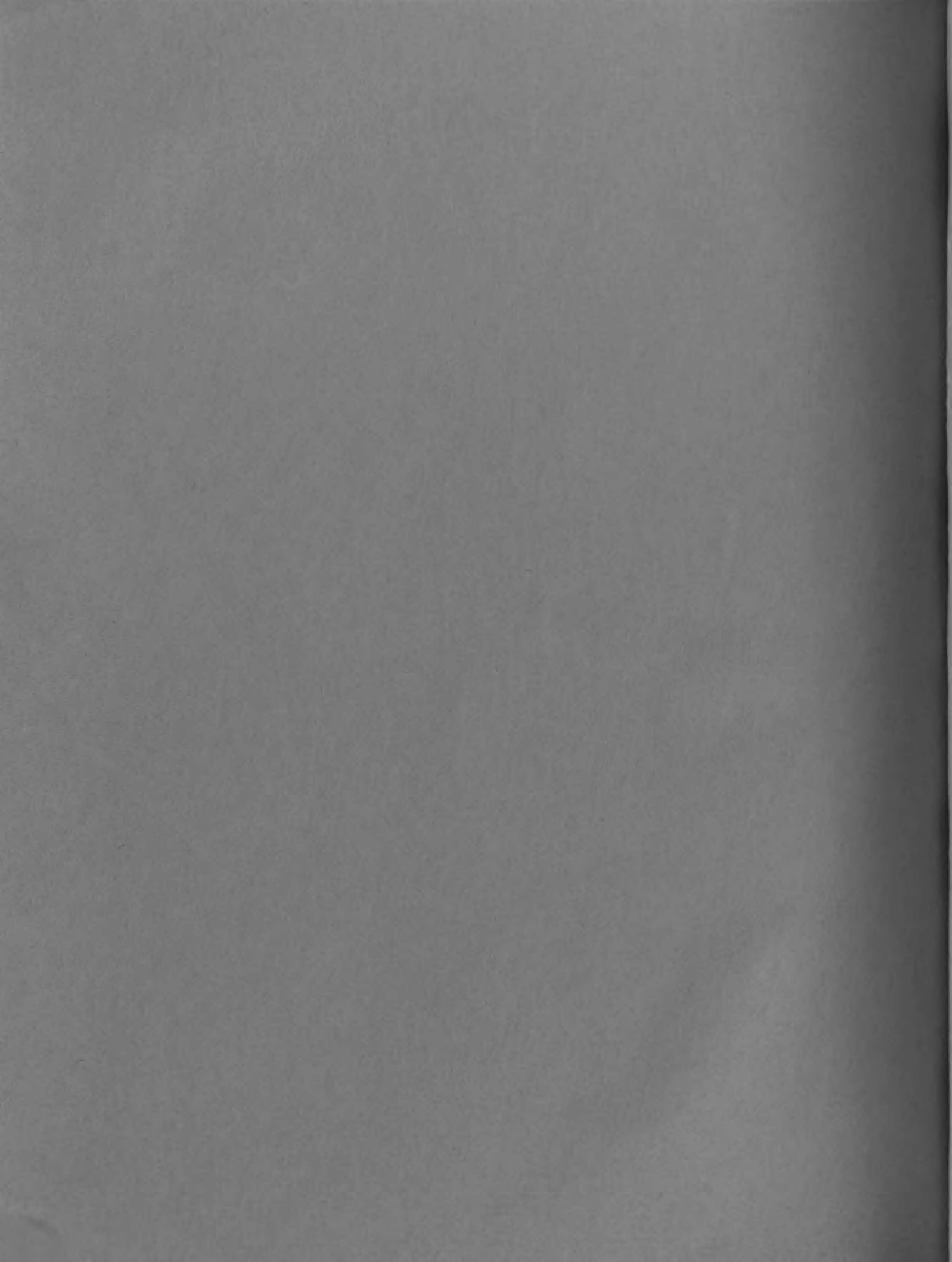


Fig. 8





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