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Addiction to Diazepam

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Abstract

Literature is reviewed which raises the question of diazepam's addicting potential. To explore this issue, 50 subjects referred from medical, surgical, and psychiatric clinics were evaluated by interview regarding their use of diazepam. Replies to a standardized interview were combined with physicians' ratings of addiction under two conditions: without and then with the knowledge that the drug in question was diazepam.

A computer-aided analysis of these data, including a correlation matrix, revealed surprisingly strong evidence for diazepam's capacity to elicit tolerance and withdrawal in this sample. Psychiatric patients were no more "addiction-prone" in this regard than patients given diazepam for medical conditions. Of equal significance, physicians' impressions of addiction were significantly altered toward a more favorable view when they learned that the drug in question was diazepam. Implications for

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psychiatric and medical practice are discussed, and suggestions for further controlled research offered.

A cursory reading of the available literature would lead one to a sanguine view of diazepam addiction. Indeed, the "Warnings" section of the Valium package insert admitting to the occurrence of withdrawal symptoms leads one to believe that addiction can only occur should the usual doses be exceeded or the user be an alcoholic, drug addict, or "addiction-prone," a state further undefined.

In a fashion similar to chlordiazepoxide, diazepam has engendered a host of articles attesting to its freedom from addicting properties. A careful scrutiny, however, raises serious questions about such optimistic conclusions. Of 27 articles (Constant and Gruver, 1963; Grayson, 1962; Katz, Aldes, and Rector, 1962; Kelley, 1962; Cromwell, 1963; Levy, 1963; Burdine, 1964; Dorfran, 1964; Fowlkes, Strickland, and Peirson, 1964; Bowes, 1965; Burnett and Holman, 1965; Vilkin and Lomas, 1962; Randall et al., 1961; Susses, Linton, and Herlihy, 1961; Chesrow et al., 1962; Feldman, 1962; Kelley, 1962; Kerry and Jenner, 1962; Merliss, Turner, and Krumholz, 1962; Pignataro, 1962; Proctor, 1962; Cromwell, 1963; Dorfman, 1963; Love, 1963; McGovern et al., 1963; Rathbone, 1963; Ryan, 1963) reviewed in which diazepam was claimed to be free of addicting properties, *none* conducted sufficient controls to merit dismissing this question. Most such reports claimed, usually as an after-thought, "no evidence of addiction was observed" (Constant and Gruver, 1963). In fact, no trials of withdrawal with systematic observations were attempted (Constant and Gruver, 1963; Grayson, 1962; Katz, Aldes, and Rector, 1962; Kelley, 1962; Cromwell, 1963; Levy, 1963; Burdine, 1964; Dorfran, 1964; Fowlkes, Strickland, and Peirson, 1964; Bowes, 1965; Burnett and Holman, 1965) and no data regarding tolerance collected (Vilkan and Lomas, 1962; Randall et al., 1961; Susses, Linton, and Herlihy, 1961; Chesrow et al., 1962; Feldman, 1962; Kelley, 1962; Kerry and Jenner, 1962; Merliss, Turner, and Krumholz, 1962; Pignataro, 1962; Proctor, 1962; Cromwell, 1963; Dorfman, 1963; Love, 1963; McGovern et al., 1963; Rathbone, 1963; Ryan, 1963). Table 1 presents salient features of these studies in chartlike form.

The overacceptance of diazepam's safety in this regard has been surprising in the light of evidence that other minor tranquilizers can be addicting (Haizlip and Ewing, 1958; Phillips, Judy, and Judy, 1957; Anonymous, 1959; Arneson, 1961; Hollister, Motzenbacker, and Degan,

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Such acceptance may be falsely based upon a narrow concept of addiction: unless withdrawal symptoms mimic those of heroin or alcohol, a drug cannot be addicting; yet one of the most severe withdrawals, the depressed state following amphetamine abuse (Bartholomew, 1970), attests to a variety of possible withdrawal symptoms. An analogous situation exists for meprobamate: a cardinal symptom of withdrawal from this drug is anxiety (Haizlip and Ewing, 1958; Phillips et al., 1957; Anonymous, 1959).

Diazepam might also have been prematurely considered safe in this regard on the basis of optimistic earlier reports regarding its close congener, chlordiazepoxide. Scrutiny of such reports is of interest. Lawrence (1960), for example, has stated "no withdrawal symptoms to chlordiazepoxide were observed, *although all patients noted a recurrence of their original symptoms—anxiety or tension, craving for alcohol, etc. when . . . without medication for 24–48 hours*" (emphasis added). Moore (1962) discovered that gynecologic "patients asked that they be put back on chlordiazepoxide after it had been discontinued . . . but this was due to continued or renewed stresses rather than to any physiologic demand for the drug." We are not informed how the authors made this distinction. Further confusion is produced by Williams' (1961) statement that "there appears to be no addiction to chlordiazepoxide, though there is a tendency to develop dependence upon it. Between 24–36 hours after withdrawal of the medicine, there is recurrence of symptoms." There would be no *a priori* reason not to consider this a sign of withdrawal instead.

Indeed, several reports have raised questions concerning addiction to diazepam. Cromwell (1963), even while reaffirming diazepam's efficacy to tranquilize, noted that the drug was extremely "well-accepted" as evidenced by patients' regular request for a new supply. While Cromwell thought this "unusual," he failed to more fully evaluate such requests. Aivazian (1964) describes a patient who experienced seizures in abruptly discontinuing diazepam. Barten (1965) notes the occurrence of a toxic psychosis during withdrawal, while Edgley (1970) points to the more common manifestations of tremor and agitation among several patients on abrupt discontinuance. Hollister et al. (1963) also noticed withdrawal, including one seizure, in 6 of 13 patients whose drug was abruptly discontinued; however, these authors, as in a previous study of withdrawal from chlordiazepoxide (1961), used unusually high doses and administered the drug to schizo-

Table 1
Abstracts of Articles Reviewed Concerning Use of Diazepam

Author	Year	No. *Ss*	Type *Ss*	Av Age[a]	Usual dose	Duration of treatment	Criteria for addiction
Kelley	1962	109	Private psychiatrist	46	5–10 mg	tid 1–48 weeks (av 14 weeks)	"No signs . . . of habituation and addiction." No criteria
Cromwell	1963	31	Private medical	50	2–5 mg bid to qid	1–2 weeks	"No indication of . . . habituation." No criteria—too brief to determine
Pignataro	1962	67	"Chronic, refractory," psychiatrist	U. Modal age 30–39	5 mg bid to qid (Maintenance)	1–11 months	None
Ryan	1963	50	Headache patients	U	2 mg tid	U	None
Randall	1961	18	Psychiatric patients	U. Range = 21–70	20–30 mg/day	4–34 weeks	None
Grayson	1962	44	Private dermatologist	40.1	2.5–15 mg/day	11	"No indication of . . . habituation." No criteria
Burnett and Holman	1965	216	General practice: 98 emotional disorders, 47 psychogenic disorders, 71 organic with emotional "complications"	U	8–20 mg/day	4 days to 15 months	"No signs of . . . habituation." No criteria. Study originated with investigator's concern over addiction with barbiturates and meprobamate
Rathbone	1963	40	Private internal medicine patients in "psychological distress"	55	2.5 mg bid to 10 mg qid	1–8 weeks	Necessary to increase dosage when reinstating drug. No criteria; no mention of habit or addiction
Kerry and Jenner	1962	75	Clinical psychiatrist, patients complaining of anxiety	37	10 mg tid	2 weeks	No criteria
Feldman	1962	142	Chronic psychiatric inpatients	36	U	94 days	No criteria
Katz, Aldes, and Rector	1962	84	Muscular-skeletal disorders	U. Range 20–27	2.5–40 mg/day	Av of 4 weeks	"No indication of . . . habituation." No criteria
Merliss, Turner, and Krumholz	1962	80	Chronic state hospital patients	U. Modal 30–40	10 mg tid	6 weeks	No criteria
Proctor	1962	51	Private psychiatrist	U. Range 25–58	5–10 mg tid to qid	Av of 11 weeks	No criteria
Dorfran	1964	137	Private psychiatrist; most with "depression"	U	5 mg tid	1 week to 2 years	"No instances of addiction . . . most reduced their dosage. . . ." No criteria
Love	1963	74	46 Neurosis; 28 somatic disorders	Range 22–83	1–10 mg bid to tid	2 days to 3½ months	"Many patients reported the drug was 'wonderful' and sought repeated assurance that more would be available." No criteria

(*continued*)

Table 1 (continued)

Author	Year	No. *Ss*	Type *Ss*	Av Age[a]	Usual dose	Duration of treatment	Criteria for addiction
Dorfman	1963	U	Private psychiatrist	U	5 mg tid	U	No criteria
Susses, Linton, and Herlihy	1961	13	Medical school psychiatric clinic. Complaints of anxiety-tension	U. Range 22–46	15–30 mg/day	2 weeks to 6 months	No criteria
Bowes	1965	> 500	Private psychiatrist	U	5 mg tid and 10 mg hs	U	5 of 500 "overly dependent." All "addictive personalities." Gradual withdrawal was needed using chlordiazepoxide in hospital
Vilkin and Lomas	1962	83	Private psychiatrist	U. Range 14–78	5 mg tid	6 months	No examples of patients able to stop diazepam. No criteria
Constant and Gruver	1963	183	General psychiatrist	U. Range 14–78	6–30 mg/day	2 days to 11 months	"No evidence of . . . addiction or extreme dependence was observed." No criteria
McGovern et al.	1963	423	Private allergy patients	U. Range 1–75	Varied with age; modal 5 mg tid	1 week to 7 months (200 > 4 weeks)	No criteria
Levy	1963	151	Medical school dermatology clinic: "Emotional disturbances were . . . major causative or aggravating factors"	40	2.5–10 mg/day	2–17 weeks, av 6 weeks	No signs of habituation, addiction, or "psychological dependency" on discontinuance. No criteria
Fowlkes, Strickland, and Peirson	1964	33	Hospitalized patients with major neuromuscular disorders and spasticity	44	5 mg tid	2 years	"No evidence of tolerance." No criteria
Burdine	1964	108	General psychiatric patients (77 hospitals)	39	10–80 mg/day	3 days to 7 months	"No signs of habituation or drug abuse in those taking diazepam as needed." No criteria
Chesrow et al.	1962	58	Hospital psychiatric patients	72	2 mg tid	4–6 months	No criteria
Kelley	1962	> 100	Private psychiatrist	U	5–10 mg tid	U	No criteria
Cromwell	1963	50	Private medical	U	5 mg tid	U	No criteria

[a] U = Unspecified.

phrenics, not usually treated with "minor" tranquilizers. Clare (1971) describes a woman with evidence of withdrawal from diazepam, but her case was intertwined with barbituate and alcohol abuse as well. Even as strong a proponent of "minor" tranquilizer use as Bowes (1965) discovered five cases of diazepam addiction among his patients.

In the light of apparent confusion in the literature regarding the addicting properties of diazepam, and in the light of its wide distribution, we have made an attempt to answer the following questions:

1. Are patients able to adhere to prescribed doses of diazepam?
2. Are patients able to discontinue diazepam?
3. What symptoms occur upon abrupt discontinuance?
4. Can we predict which patients might develop tolerance or withdrawal if such conditions indeed exist?

METHODS

Subjects

Our subjects were collected from the records of a neuropsychiatry clinic on a military installation in the Southeastern United States. The study was conducted from August to December 1972. Subjects were also referred from physicians in medical, surgical, and general outpatient clinics. Such referrals were solicited by requesting information from physicians on any patients currently taking diazepam. We were thus able to uncover a wide range of patients taking this drug. The first 50 such referrals constituted our sample; no exclusions were made.

This sample included 31 female and 19 male subjects with an average age of 34.3 years (19–63). While just 12 had a history of psychiatric difficulties (including 9 referred from the Neuropsychiatry Clinic), 29 were given the drug for psychiatric reasons, usually anxiety secondary to an organic illness. The 12 subjects with a psychiatric history included 6 diagnosed neurotic, 5 personality disorders, and 1 schizophrenic. The large number of females in such a sample is of interest: recent reports indicate a higher incidence of women using "minor" tranquilizers (Mellinger, Balter, and Manheimer, 1971; Parry et al., 1973).

Structured Interview

Each subject underwent a structured interview, as presented in Table 2. The interview, devised by the authors, was designed to investigate subject

variables, use-of-drug data, and effects upon discontinuing the drug. It was conducted by social work and psychology technicians within the clinic setting. All interviewers were instructed in the operational definitions of terms, for example, agitation as the presence of an unpleasant increase in motor activity. Although other information and conversation were permissible and even encouraged, each interviewer attempted to elicit the basic information presented in Table 1. Because so much of the data collected in this manner was both subjective and retrospective, each interviewer attempted to corroborate these data by asking similar questions of at least one other person familiar with the subject, usually a spouse. Interviewers were successful in locating and interviewing such persons for 92% of the subjects.

Physicians' Analysis

Following completion of interviews, each form was reviewed by a group of four general practitioners, five general surgeons, three internists, and two orthopedic surgeons. Each was asked, "Do you believe this subject is addicted to the substance in question?" Each answered on a scale of 0 (not at all) to 4+ (very much) in a fashion similar to the last question asked of each subject on the structured interview (Table 2). No physician was informed of the nature of the drug in question. However, after answering this question blindly, each physician was informed of diazepam's identity and again asked to rate the degree of addiction.

Assessment

Frequency and Amplitude Data

A computer-assisted analysis of all data was undertaken to yield frequencies and amplitudes for this population for each variable, including complete population distribution statistics. Data were combined into three categories: use of diazepam (variables 6–9, see Table 2), addicting potential (variables 10–15), and physicians' ratings (variables 16 and 17). Reliability coefficients were determined for variables 14 (interviewer's withdrawal severity ratings) by assigning two other interviewers for each of 20 randomly-selected subjects, and for variables 16 and 17 (physicians' addiction rating) by assigning two other physicians for each of 20 randomly-selected subjects. In each case, reliability coefficients exceeded 90%.

Correlation Matrix

A correlation matrix for all variables was generated by computer in an effort to determine if individual variables could predict future difficulties with diazepam.

RESULTS

Frequency and Amplitude Data

Percentage data are presented in Tables 3–6. Complete data, including population distributions, are available from the author, but because of the large number of variables involved, in the main only means and standard deviations (SD's) will be discussed.

Use of Diazepam

Table 3 presents the data for variables 6–9. As can be seen, subjects took an average of 15.9 mg (SD 9.3) of diazepam daily, a dose considered routine. Only 14 of the 50 subjects took 20 mg or more of this drug daily. They had been taking this amount an average of 25.9 months (SD 20.1), with only 10 subjects taking diazepam for less than a year and 15 taking it 3 years or more. Over half (26) the subjects were using other minor tranquilizers, chiefly chlordiazopoxide and meprobamate. On a 0 ("no help") to 4+ ("very much") scale of assessing how helpful diazepam had been in alleviating symptoms for which it was prescribed, 3 subjects rated it 0, 16 1+ ("very little"), 16 2+ ("moderate"), 13 3+ ("much") and 2 4+ ("extreme"), yielding an overall mean rating of 1.9 (SD .99).

Table 3
Subjects' Use of Diazepam

	Mean	Range	Standard deviation	Standard error of mean
Variable 6. Amount taken, mg	15.98	5–50	9.31	1.32
Variable 7. Duration taking drug, months	25.98	1–96	20.15	2.85
Variable 8. Other tranquilizers			(26 yes, 24 no)	
Variable 9. Help from drug	1.90	0–4+	0.99	0.14

Addiction Potential

Tables 4a and 4b present the data for variables 10–15. Among all subjects, 30 (60%) did not decrease diazepam on their own. Of the 20 subjects who did, many recalled a recurrence of symptoms, chiefly anxiety and insomnia, and quickly increased their dose. Half of these subjects increased diazepam without asking their physicians, usually secondary to inability to cope with some external stress. Once increased, they found it difficult to taper: of the 25 subjects involved, only 10 subsequently decreased their dose to what was originally prescribed. Twenty-four subjects attempted to stop diazepam abruptly at some point. Twenty-two resumed the drug, usually within 1 week, while only two subjects (8% of those stopping the drug and just 4% of the total sample) were able to stop diazepam and remain without the drug for a period greater than several weeks. Interviewers, asked to judge withdrawal severity in these 24 subjects after questioning each on the symptoms experienced within 1 week of discontinuing diazepam, rated one subject as 0 ("none"), four as 1+ ("light"), nine as 2+ ("moderate"), eight as 3+ ("great"), and two as 4+ ("severe"). Thus 79% of this sample experienced withdrawal symptoms of moderate to extreme severity. Such symptoms are presented in Table 5 with the

Table 4a
Subjects' Abuse of Diazepam—Number of Subjects

	Yes	(%)	No	(%)
Variable 10. Decrease on own	30	(60)	20	(40)
Variable 11. Increase on own	25	(50)	25	(50)
Variable 12. Unsuccessfully stop ($N = 24$ who attempted to stop)	22	(92)	2	(8)
Variable 13. Successfully stop ($N = 24$ who attempted to stop)	2	(8)	22	(92)

Table 4b
Subjects' Abuse of Diazepam—Number of Subjects

	0 None	1+ Little	2+ Moderate	3+ Great	4+ Severe
Variable 14. Withdrawal severity	1	4	9	8	2
		Mean = 2.33			
Variable 15. Dependency self-rating	20	14	8	4	4
		Mean = 1.16			

Table 5
Major Symptoms upon Abrupt Discontinuance of Diazepam—Numbers of Subjects (N = 24)

Symptom	Number experiencing symptom	Percentage
Anxiety	23	95
Agitation	18	75
Insomnia	14	58
Tremor	10	42
Diaphoresis	7	29
Pain	6	25
Depression	4	17
Nightmares	4	17

percentage of these 24 subjects experiencing each. It will be seen that anxiety, insomnia, tremor, diaphoresis, and restlessness are prominent and form a common withdrawal syndrome. Despite the difficulties in discontinuing diazepam, a relative few of the total believed they were "dependent" on diazepam. Twenty subjects rated themselves 0 ("none") when asked about their dependency on the drug, 14 rated 1+ ("slight"), 8 rated 2+ ("moderate"), 4 rated 3+ ("great"), and 4 rated 4+ ("severe"). It is of interest that among the 10 subjects rated 3+ and 4+ by their interviewers for withdrawal severity, only 5 rated themselves equally distressed when undergoing abstinence from the drug.

Physicians' Ratings

Table 6 presents the data for variables 16 and 17. Without the knowledge that diazepam was the drug in question, the physicians' panel judged

Table 6
Physicians' Ratings of Estimated Addiction—Number of Subjects

	0 None	1+ Slight	2+ Moderate	3+ Great	4+ Severe
Variable 16. Ratings without the knowledge of which drug was involved	19	11	11	6	3
Variable 17. Ratings with the knowledge that the drug was diazepam	36	9	5	0	0

19 subjects as 0 ("no addiction"), 11 as 1+ ("slight"), 11 as 2+ ("moderate"), 6 as 3+ ("great"), and 3 as 4+ ("severe"); thus 20 (40% of the sample) were felt to be moderately addicted. On the other hand, once the panel discovered the name of the drug, they rated 36 subjects as 0, 9 as 1+, and 5 as 2+; in other words, in these latter circumstances just 10% of the sample was adjudged moderately addicted and one as severely addicted. Comparing the ratings done blindly and then with the knowledge of which drug was involved yielded statistically significant differences ($p < .05$, χ^2) at each level.

Correlation Data

Too large a number and variety of significant ($p < .05$) correlations were discovered to be commented upon fully here. A complete matrix is available upon request from the authors. The following are pertinent:

The older the subject, the greater the amount of diazepam taken ($r = .402$).

A psychiatric history was positively correlated with physicians' ratings of addiction, both open and blind ($r = .338, .298$); conversely, a purely organic history was negatively correlated with these ratings ($r = -.302, -.298$).

A history of purely organic problems was negatively correlated with subjects' evaluations of their dependency ($r = -.343$).

The greater the amount of diazepam taken, the less help it was reported to be ($r = -.312$).

The greater the amount taken, the greater the withdrawal severity ($r = .345$). However, the greater age of subjects taking higher doses was not significantly correlated with withdrawal severity.

The longer the drug was taken, the greater the withdrawal ($r = .350$).

The more diazepam helped the patient, the greater the probability in unsuccessfully stopping ($r = .350$).

The more the drug helped, the greater the withdrawal severity ($r = .354$).

The tendency to increase the dose was positively correlated with the withdrawal severity ($r = .469$).

The greater the withdrawal severity, the greater the physicians'

blind ratings ($r = .582$). On the other hand, once physicians learned the drug's identity, the withdrawal severity had no relationship to the addiction ratings ($r = .114$).

Several findings were of interest for their *lack* of correlation. Thus the presence of a neuropsychiatric history was correlated only with physicians' estimates of addiction, but not with any other criteria of dependency or addiction employed. Similarly, sex of subjects was neither positively nor negatively correlated with any other variable.

Computer attempts to group variables into a factor analysis were not successful, verifying what gross observation of the data suggested: no combination of variables seemed able to predict greater or lesser vulnerability to addiction.

DISCUSSION

The discussion that follows corresponds to the original questions asked in formulating this research.

1. *Are Patients Able to Adhere to Prescribed Doses of Diazepam?* Of 50 subjects, 42 adjusted their own dosage; of these, 25 consistently adjusted it upward. Diazepam may be vulnerable to self-manipulation because of its capacity to produce immediate positive effects, a trait it shares with addicting substances, such as alcohol or amphetamines, as opposed to nonaddicting psychotropic drugs, such as chlorpromazine and imipramine. The fact that half the sample increased their own dose suggests, but does not document, tolerance. When asked, 14 of these 25 replied they increased their dose because the prescribed amount was not as helpful as before.

2. *Are Patients Able to Discontinue Diazepam?* Of 24 subjects who attempted discontinuance, 22 were unsuccessful and returned to the drug. They unanimously commented that they wished to be free of reliance upon diazepam, but seemed unable to be so. These unsuccessful abstainers rated themselves significantly higher on dependency scores than the remainder of the sample.

3. *What Symptoms Occur upon Abrupt Discontinuance?* As Table 5 documents, most subjects experienced anxiety, restlessness, insomnia, tremor, and diaphoresis. Many subjects complained of the same symptoms upon abstinence for which the drug was prescribed. Yet the anxiety complained of initially was usually secondary to an organic illness; upon

discontinuance the physical complaint almost always was gone, yet the anxiety present. It appeared just as likely that the symptoms noted on abrupt discontinuance were secondary to an abstinence syndrome as they were related to an ongoing condition which the drug had suppressed. For example, several subjects complained of extreme anxiety upon abstinence, yet had been free of anxiety when the drug was initially prescribed. In addition, symptoms such as tremor, diaphoresis, and even insomnia, which had been rare prior to taking diazepam, emerged when the drug was stopped.

A reanalysis of our data reveals that of the 24 subjects discontinuing diazepam, 17 complained of symptoms not present before taking the drug. It would seem logical to assume that, rather than the onset of "psychic" distress at some point during the diazepam regimen, these symptoms developed *de novo* upon abstinence. It is unclear from these data whether gradual discontinuance would have mollified these symptoms.

What symptoms suffice to determine a physiological withdrawal? Withdrawals from amphetamines and tobacco differ qualitatively from alcohol or heroin withdrawal, yet such drugs are considered bona fide addicting substances nonetheless. Data from animal laboratories confirms addicting qualities of amphetamines and other minor tranquilizers as well (Schuster and Thompson, 1969; Findley, Robinson, and Peregrino, 1972). The distinctions between "dependence" and addiction may be vague in some cases, superficial in others.

4. Can We Predict Which Patients Might Develop Tolerance or Withdrawal? Those taking high doses of diazepam (greater than 15 mg daily) for long periods of time (over 12 months) who believe the drug has significantly helped them, and who have increased their dose on their own, stand a greater chance of developing serious symptoms upon its abrupt discontinuance. However, neither age, sex, psychiatric history, nor the presence of current psychiatric problems have the slightest relationship to drug use and abuse variables. It is disappointing to find no individual characteristics predictive of potential danger with diazepam. The "addiction-prone" individual would certainly seem to possess some past drug or alcohol history, at least a psychiatric history, and to be more commonly a woman. A review of our data revealed 7 of 50 patients admitting to prior drug or alcohol abuse; no differences were found between this subpopulation and the remainder. These data partially refute the "addiction-prone" concept and raise the possibilities of either equal addicting potential among all subjects, as animal data would predict (Schulster and Thompson, 1969; Findley, Robinson, and Peregrino, 1972), or susceptibility grounded in

factors not examined here (for example, marital status or genetic constitution).

When physicians were informed that the drug involved was diazepam, they modified their positions considerably in the direction of less addiction. Often physicians commented, with relief, that "it was only Valium," thus could not be dangerous. Nonmedical psychiatric specialists, performing the interviews, had relatively little preknowledge of diazepam's presumed safety and rated significantly higher addiction levels for almost all subjects.

The retrospective, uncontrolled nature of most of the data reported herein makes this study merely suggestive. Ideally, hospitalized normal subjects might be given diazepam, blood levels checked, and physiological withdrawal monitored, including EEG's. Such a prospective study is being planned. Nonetheless, these data support previous research (Aivazian, 1964; Barten, 1965; Edgley, 1970; Hollister et al., 1963; Clare, 1971) raising suspicions of diazepam's capacity to produce genuine addiction. Tolerance was partially demonstrated and symptoms of withdrawal occurred upon abrupt discontinuance; such symptoms were not always similar to those for which the drug was initially prescribed. Moreover, withdrawal symptoms seemed so uniform as to delineate a discrete syndrome, similar to that seen upon discontinuance of other minor tranquilizers.

In addition, many subjects not thought to be "addiction-prone" developed what appeared to be both tolerance and withdrawal. These subjects, given the drug for medical reasons and without a psychiatric history, were just as likely as psychiatric patients to develop tolerance and withdrawal. It appears as if the prescribing physician needs to cultivate as much care in prescribing diazepam as in other potential drugs of abuse.

Diazepam treats no specific psychiatric illness, as opposed, for example, to lithium or chlorpromazine. This is not to deny its value in certain neurologic syndromes (Tudo, 1971) or as a temporary aid in behavior therapy (Bandura, 1969). It is a common belief that reliance upon nonspecific tranquilizers may inhibit the acquisition of coping skills in the face of stress (Klerman, 1970; Anonymous, 1972). Beyond these issues, minor tranquilizer use, in adults, may predispose toward drug use in children (Smart and Fejer, 1972). Because of these factors and because of diazepam's addicting qualities, we have limited its use in our neuropsychiatric clinic and encouraged medical colleagues likewise. Prescriptions for diazepam and chlordiazepoxide in the military hospital supplying our base have decreased from 35,000 to 2,500 tablets weekly over the past 2 years. Our neuropsychiatric practice is presently minor-tranquilizer free without

serious sequelae. There is no reason to doubt diazepam's efficacy in reducing levels of anxiety, but it is believed the data offered herein raise the question of at what price?

SUMMARY

In order to further investigate the addicting properties of diazepam, 50 medical and psychiatric subjects were interviewed concerning their diazepam use. While this sample was not taking excessively high doses, nor using the drug great lengths of time, many had extreme difficulty in decreasing or discontinuing their dose, rather finding it easier to increase. Most who increased felt they required more to achieve the same benefits as previously. Most who decreased or stopped their drug abruptly experienced an array of symptoms thought of as withdrawal, including agitation, anxiety, insomnia, diaphoresis, and tremors; many such patients did not have similar symptoms before taking the drug.

Those taking more diazepam over longer periods, who felt it was more helpful and who needed to increase their dose, were the more likely to develop severe symptoms on abstinence and to be unable to do without diazepam. Yet age, sex, and the presence or absence of a history of psychiatric, alcoholic, or drug-related problems had no bearing on development of tolerance or withdrawal, thus raising questions about the validity of the "addiction-prone" concept.

Physicians, asked to rate the quantity of addiction, were far more sanguine once they learned the drug in question was diazepam. The reluctance to consider diazepam an addicting substance despite the evidence may stem from prior anecdotal reports. Yet scrutiny of the literature, coupled with the present data, argue for caution in prescribing and supervising diazepam pending further, more sophisticated study.

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