

- Convention, Boston, Mass, May 16, 1966).*
7. DOWNING, ROBERT W.; COMER, NATHAN L. and EBERT, JOHN M.; "Family Dynamics in a Case of Gilles de la Tourette's Syndrome." *J. Nerv. Ment. Dis.*, 138: 548-57, 1964.
  8. DUNLOP, J.R.; "A Case of Gilles de la Tourette's Disease (*Maladie des tics*): A Study of Intra-familial Dynamics." *Amer. J. Psychiat.*, 130-44, 1960.
  9. EISENBERG, A.; ASCHER, E. and KANNER, L.; "A Clinical Study of Gilles de la Tourette's Disease (*Maladie des tics*)." *Amer. J. Psychiat.*, 115: 715-23, 1959.
  10. FAUX, EUGENE J.; "Gilles de la Tourette's Syndrome." *Arch. Gen. Psychiat.*, 14: 139-42, 1966.
  11. FENICHEL, OTO; "*The Psychoanalytic Theory of Neurosis*." New York: Norton, 1945.
  - FERNANDO, S.J.M.; "Gilles de la Tourette's Syndrome." *Brit. J. Psychiat.*, 113: 607-17, 1967.
  13. Gilles de la Tourette; "Etude sur une affection nerveuse caracterisee par 1' in-coordination motrice accompagnee d'echolalia et decoprolalie." *Arch. Neural. (Paris)*, 9: 158-200, 1885.
  14. HEUSCHER, J.E.; "Intermediate States of Consciousness in Patients with Generalized Tics." *J. Nerv. Ment. Dis.*, 117: 29-38, 1953.
  15. MACDONALD, IAN J.; "A Case of Gilles de la Tourette's Syndrome with some Aetiological Observations." *Brit. J. Psychiat.*, 109: 206-10, 1963.
  16. MORPHEW, J.A. and SIM, MYRE; "Gilles de la Tourette's Syndrome: A Clinical and Psychopathological Study." *Brit. J. Psychol.* 42: 293-307, 19
  17. SEIGNOT, M.J.N.; "Un cas de maladie des tics de Gilles de la Tourette que par le R1625." *Ann. Medico-psychol.*, 119: 578-79, 1961.
  18. SHAPIRO, ARTHUR K. and SHAPIRO, ELAINE; "Treatment of Gilles de la Tourette's Syndrome with Haloperidol." *Brit. J. Psychiat.*, 114: 345-50, 1968.
  19. SHAPIRO, ARTHUR K. and SHAPIRO, ELAINE; "Clinical Dangers of Psychological Theorizing: The Gilles de la Tourette's Syndrome." *Psychiat., Quart.*, 45/2: 159-71, 1971.
  20. SNYDER, SOLOMON H.; TAYLOR, KENNETH M.; COYLE, JOSEPH T. and MEYERHOFF, JAMES, L.; "The Role of Brain Dopamine in Behavioural Regulation and the Actions of Psychotropic Drugs." *Amer. J. Psychiat.*, 127: 119-207, 1970.
  21. WAGNER, EDWIN, E.; "Results of Psychological Testing on a Child with Gilles de la Tourette's Disease." *J. Clin. Psychol.* 26: 52-57, 1970.
  22. YATES, AUBREY J.; "The Application of Learning Theory to the Treatment of Tics." *J. Abn. Psychol.*, 56: 52-82, 1958.
  23. YATES, AUBREY, J.; "*Behaviour Therapy*." London: John Wiley and Sons, Inc., 1970.

## A CLINICAL TRIAL OF R6218 IN THE TREATMENT OF OBSESSIVE-COMPULSIVE NEUROSIS

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In this paper a clinical trial of the new neuroleptic Janssen R6218 (fluspirilene) in the treatment of obsessional states, involving 8 male, Malaysian, patients is reported. The patients ranged in age from 14 to 32 years with a mean of 23 years and the duration of their illness ranged from 1 to 11 years with a mean of 6 years. They had previously been treated with benzodiazepines, tricyclic antidepressants and in some cases with Haloperidol and other drugs with amelioration in anxiety and depression without the basic symptoms of the illness being affected directly as a result of drug therapy and those who spoke

English (and thus could converse with the therapist) had had an exposure to various forms of psychotherapy, chief among their being paradoxical intention with defocussing technique, but for one reason or another had failed to derive any benefit from it.

In this trial, which was mainly exploratory in nature, a new chemical compound was being tested, for the first time perhaps, to determine if it could basically alter the dominating symptoms of these patients, viz. their obsessive thoughts and compulsive actions. As such, the conditions of trial were (except in the case of one patient -T.S.D.)

totally uncontrolled. There was no drug-free period as one individual subject was taken off his former medication and placed on the new drug and concurrent use of other drugs could not be withheld in all cases because of such factors as his response to the trial drug, its side-effects and the prevailing effect of the patient. Both the doses and the interval between any two doses of the drug varied, there being no guide lines in this respect — the manufacturers only indicate that it should be used with caution in endogenous depression, Parkinsonism and possibly epilepsy — and the total period of trial varied from two weeks in one to the maximum of sixteen in another.

Only one patient on low dose therapy did not show any response to the new drug (his case has been left out from discussion), while seven benefited from it. Among those whose condition improved, one subject had failed to respond to the drug when given in low doses but as experience with the use of the drug built-up he was, after a lapse of eight weeks, once again included in the trial on a high dosage level and rated weekly on four different rating scales for assessment, of progress. Progress made by other subjects was recorded weekly, based on the interview findings: individual subjects and their relatives were asked to make a crude assessment of change in the intensity of prevailing symptoms in terms of variation in the number of times a ritual was carried out, and the time spent on it and finally as a proportion of the base line 100.

The cases are described briefly in the order in which they entered the trial as this point has an important bearing on both the determining of the effective dose of the drug and as to how the experience gained from one subject was utilized in the handling of the case that followed him.

Four patients showed marked improvement in their symptoms; one who was making satisfactory progress dropped out of the trial possibly because of the side-effects of the drug; one was taken off the drug immediately after he gave a false alarm of suicidal thoughts, although he clearly indicated that he was benefiting from the new drug; one on low dose found no change in his condition; and the most resistant of the cases, who was included twice in the trial, found about 30 to 40% improvement in his condition on the conclusion of the trial.

Side-effects encountered in all cases were the same as those seen in schizophrenia patients being treated with fluspirilene, chief among them being

weakness, muscular restlessness and extrapyramidal side-effects which appear within 24 hours of the administration of the drug and disappear after 2 to 3 days. For these side-effects, anti-parkinsonian drugs and methylphenidate were given, where indicated, in small doses for 2 to 4 days after the periodic intramuscular administration of fluspirilene.

There was no waning effect of the drug noticed by the patients in the interval that elapsed between two doses nor did they find any positive change which could be attributed to the use of anti-parkinsonian drugs like dextimide and benzhexol hydrochloride or to methylphenidate which was given to counter the distressing symptoms of fatigue and weakness.

Fluspirilene or Imap is a new chemical compound belonging to the diphenylbutylpiperidine family of drugs, structurally different from haloperidol and belonging in the same class as pimozide and penfluridol. Its selective action on the striatal dopamine — it is a potent antidopaminergic agent — is its most interesting property. It inhibits the stereotypic chewing movements in rats induced by the administration of amphetamine. This latter property is to a variable extent shared by other neuroleptics which are not so specific in their site of action, but is more marked in this series of drugs.

Other actions of fluspirilene noted in animal studies are:

1. In jumping-box the interval between the onset of buzzing and the flight reaction i.e. the latency is extended in animals treated with this drug and this failure for the flight reaction.
2. Similarly, in Sidman Shock-avoidance test in rats the number of responses to escape shock by pressing the lever drops after the administration of fluspirilene.

The drug has been tried extensively by the present investigator at the University of Malaya Hospital, Kuala Lumpur in the treatment of \*schizophrenia, where it is given in 4–12 mg. doses i.m. and seems to be specifically effective, like pimozide, in those forms which was dominated by autism, delusions and repetitive stereotypic traits in thinking and/or movement.

Based on those observations, it was felt that the drug may have a place in the treatment of obsessional states and allied conditions which have been a matter of great concern to therapists of all ages.

Talking of the prognosis and treatment of

obsessional states, John Pollitt observed in 1957: ".....the obsessional state has a much better prognosis than is usually thought and the view that it has an inevitable gloomy outcome can no longer be held." However, the same author writing twelve years later, when both psychotherapy and behaviour therapy had made sufficient progress admitted: "True obsessional states are among the few illnesses which can still torture patients almost for a lifetime." The disappointment with various forms of treatment is apparent and goads one to seek new methods of treatment for one of the most crippling forms of these known to mankind.

#### *Material, Method and Outcome*

The eight subjects included in this study had the primary diagnosis of obsessive-compulsive neurosis and their symptoms were not part of any other illness, schizophrenia, psychotic depression and organic states having been ruled out. The range of their age at the onset of illness was 12 to 26 years with a mean of 17. The symptoms they described were innumerable as, although all obsessive compulsive patients may look alike in being tortured in their obsessions and compulsions, each individual patient is tortured by symptoms which he considers as specific to him.

The dominating traits are here classified under the following headings:

1. Obsessive thoughts concerning health, death and allied themes.
2. Other ruminations.
3. Checking rituals (doubts) and repetitions.
4. Washing/purification/ablution.
5. Complicated rituals and obsessive.
6. Insistence on precision and orderliness.
7. Other compulsions.

For the sake of brevity, the patients' response to fluspirilene therapy is given at this stage.

Case No. 1, G.K.S., a Cantonese-speaking 27-year-old factory worker with 2 years' duration of illness and suffering from obsessive thoughts of death due to accident or tetanus, compulsive hand and leg washing and checking rituals, was given 4 mg. of fluspirilene by mistake by the investigator instead of two, as the starting dose. In the first week, he became extremely depressed, complained of insomnia and severe weakness but mentioned that in less than one week all his symptoms had dropped by at least 50% and although checking behaviour did not come to an end completely, his checking of locks had stopped altogether. He received a total of 13 mg. of fluspirilene over a period of 10 weeks given in 6 doses with an average of about 2.2 mg per

dose. His excessive leg washing stopped after the second dose, while after the fourth dose he said all his symptoms had gone down by 85–90%. While continuing to dislike the new drug because of its unpleasant side-effects, he admitted that for the first time instead of being calmed down, his basic symptoms had yielded to treatment. Eight weeks after the commencement of therapy, he could control himself from doing things against his wish and could "forget" his compulsions. His wife admitted that there had been a definite improvement in his symptoms.

Results: His obsessive thoughts of death had improved by 80% in the fifth week of treatment and were absent after eight weeks onwards. Other ruminations were less by 90% in the fifth week of treatment. Checking rituals were absent in the fifth week and excessive handwashing stopped in the ninth week.

Case No. 2, J.N.M., a 25-year-old English-speaking Malay bachelor, had the onset at the age of 14. He had found little relief from conventional therapy and had been putting up "a tremendous fight" against his symptoms. His complicated obsessive thoughts decreased by 90% in the tenth week of treatment, checking rituals became less by 80% in ten weeks, washing and purification rituals diminished by 75% in the fifteenth week. He received a total of 18.5 mg. of the drug over a period of sixteen weeks in 11 doses. His were the most complicated rituals and obsessive thoughts. Checking behaviour showed a gradual fall after the first dose and the patient stopped counting the number of times a ritual had to be carried out after 3 days of its administration. After the eight dose he conceded reluctantly: "The main change in me is that I can now ignore compulsions without worry."

After the ninth dose he was smiling but in the following week he developed free-floating anxiety which coupled with akathisia was contributing to his miserable condition. It became apparent that having few leisure interests, no aim in life and without obsessions and compulsions were removed he had become painfully aware of the existential vacuum in him.

Case No. 3, L.K.T., a Hainanese-speaking puny boy of 14, had developed severe obsessions and rituals after a bus accident in which no one was hurt.

He received a total of 18.5 mg. fluspirilene in 11 doses spread over a period of 11 weeks, average dose being 1.7 mg.

Results: His obsessive thoughts of violence,

death and drowning had gone down by 90% in 10 weeks, checking behaviour by 65% in 11 weeks, washing and purification rituals by 87% in 9 weeks and the extremely complicated rituals and other compulsions were negligible (less than 10%) after 9 weeks.

Throughout the treatment, he disliked injections but admitted that his obsessive thoughts had started diminishing after the second dose.

Overall assessment of improvement by the patient after the sixth dose was 70% and by his mother 50%.

Case No. 4, H.Y.F., a 26-year-old English-speaking clerk of Chinese origin with onset of illness at the age of 16, received a total of 10 mg. of fluspirilene over four weeks, averaging 2 mg./dose.

His obsessive thoughts diminished by 30% in the fourth week, other ruminations by 40% in the third week and doubts by 75% in the fourth week. He preferred the trial-drug to any previous form of therapy but was dropped out of trial after the fifth dose as he gave a false alarm of suicidal thoughts.

Case No. 5, T.W.K., a Chinese 32-year-old English-speaking lawyer's clerk, received only 2 doses of 2 mg. each with an interval of 1 week in between. Within one week, his obsessive thoughts were lessened by 20%, checking by 56% and other complicated rituals by 50–100%. However, his response to the side-effects was out of all proportion for, although he did not seem to have any extrapyramidal signs, after the second dose he defaulted treatment.

Case No. 6, C.C.B., a Hokkien-speaking 21-year-old young man, received a total of 6 mg. of fluspirilene in 4 doses, each of 1.5 mg. over a period of 12 weeks.

Results: After the first dose, his checking rituals had gone down by 80% and obsessive thoughts by 70% after the third dose.

Case No. 7, T.S.D., a 19-year-old school student, did not respond to treatment on low dose — average 2 mg. — but after being stabilized on imipramine and diazepam for eight weeks he was placed on combined therapy i.e. a high fluspirilene dose with imipramine and diazepam. He received a total of 48 mg. in 11 doses, average dose 4.36 mg., spread over a period of 11 weeks. He rated himself weekly on a 13-symptom self-inventory, on Lung Scale for depression and Hamilton Scale for anxiety. The Maudsley Obsessive-Compulsive inventory proved to be of very little help in assessing any change in his condition.

After four weeks on combined therapy i.e. fluspirilene with imipramine and diazepam, it became afferent that he was not responding to fluspirilene even in high doses and thereafter the other two drugs were stopped.

Results: On self-rating scale comparing the score when he was on combined therapy for four weeks with the last four weeks on fluspirilene alone, he showed an overall improvement of 21.04%.

Comparing the same two blocks of treatment, it was found that for the last 4 weeks when was on fluspirilene there had been an overall improvement in anxiety, on the Hamilton Scale, of 25.46% and in depression of 14.14% on the Lung Scale as compared to the 4 weeks when was on both an anxiolytic and an antidepressant — i.e., both anxiety and depression diminished after his basic symptoms began to show improvement without recourse to symptomatic treatment of the former.

On the Maudsley Obsessive-Compulsive Inventory, the patient was found to have lost his unwanted thoughts of harming other people after the fourth dose of fluspirilene.

On his 13-symptom Self-Inventory scores showed that not all symptoms respond at the same rate and whereas some remain static, either constantly or for a considerable period, others are quicker to respond. In his case items such as imagining things moving on floor associated with the compulsive action of turning round to see to reduce the ensuing anxiety and, compulsive reading of parts of newspaper over and over again were the ones which showed the most favourable response: the former stopped altogether after the seventh dose. Such symptoms as unwanted obscene thoughts intruding into his prayer did not show any change over a period of 11 weeks.

Nine out of thirteen symptoms on his self-scale showed graded improvement setting in at different stages of the treatment and it may be argued that with persistences whilst allowing drug-free periods to prevent the development of cumulative effects, the more resistant symptoms, too, might have shown change.

As in cases 1, 2 and 5 the basic change in his case was in the attitude towards the symptoms: instead of fighting the symptoms, he began to take a stand of ignoring them from the fifth week onwards. Incidentally, this patient with a good premorbid personality, having many leisure interests and definite aims in life, did not develop the existential vacuum as his symptoms started lifting off but then, unlike other subjects with less

desirable personalities, his symptoms were perhaps the most stubborn encountered in this study.

His overall assessment of improvement was 51% in respect of obsessive thoughts involving death themes, and about 86% as regards other ruminations.

#### COMMENTARY

Case No. 1 showed immediate response to the trial drug, given in a moderate initial dose of 4 mg., with an overall 50% subjective assessment of improvement setting in within the first week of treatment and with cessation of checking locks as its main feature. After the second dose, his excessive leg-washing stopped; obsessive thoughts concerning death and disease and other ruminations became appreciably less in the fifth week of treatment — when his other checking rituals were found to be absent — and excessive hand washing disappeared in the ninth week.

Case No. 2, showed a decline in his checking rituals after the first dose of the trial drug and stopped counting the number of times a ritual had to be performed after three days of its administration. His morbid obsessive thoughts disappeared in the sixth week of treatment, insistence on precision and orderliness became significantly less in the eighth week when he had begun to ignore this compulsion, and, excessive washing had diminished a great deal in the fifteenth week. However, he was less successful in ignoring the obscene thoughts that kept intruding into his prayers till the end of the trial period when his therapeutic gains had become greatly clouded by the mounting agitation and anxiety.

Case No. 3 showed an early favourable response to the drug by beginning to lose his morbid thoughts after its second dose; thereafter, his obsessive thoughts and compulsive actions responded equally well, albeit slowly, to the new treatment. He stopped being unnecessarily concerned about personal hygiene after about 8 to 9 weeks of treatment when losing his fear of being touched by others he could once again enjoy sitting in his mother's lap.

Case No. 5 lost some of his insistence on orderliness and precision together with some reduction in morbid obsessive thoughts within one week of the first dose of fluspirilene; his checking behaviour and other complicated rituals showed even greater response to this form of therapy.

Case No. 6 lost almost completely his checking rituals after the first dose of the trial drug; the effect on obsessive therapy concerning his health was comparatively tardy and not so complete.

Case No. 7 after showing no response to the trial drug in small doses lost at least one obsessive thought and one compulsive action completely when the same drug was given in relatively high doses. His obsessive thoughts based on religious beliefs turned out to be most resistant to treatment; other obsessive thoughts, ruminations and compulsive actions showed varying degrees of response becoming manifest in different weeks of treatment.

This one patient did not show any response to fluspirilene given in a low fixed dose regime.

Of the seven who derived definite benefit from the treatment: four patients showed amelioration in their condition after a single dose, in two this change became apparent after the second dose and one patient took longer (after the fourth dose) to exhibit any positive change in his symptoms. The same four patients who benefitted from the drug within the first week of treatment did so by shedding some of their compulsive actions chief among their being the checking rituals. Only one patient (L.K.T.) lost his morbid obsessive thoughts in advance of any change in the severity of his compulsive actions.

Two patients preferred tricyclic antidepressants and benzodiazepine anxiolytics to fluspirilene therapy because of the pleasantness of the former though persisted with the latter form of therapy because of its efficacy; two patients preferred fluspirilene to the anxiolytic-antidepressant therapy because of its effectiveness in assuaging their obsessive-compulsive symptoms though did not comment on the pleasantness or unpleasantness of either; two subjects while deriving benefit from the new drug became agitated and defaulted treatment, the response of the remaining two patients from this angle could not be ascertained.

#### DISCUSSION

Feelings of anxiety and tension have been described as characteristic of obsessional neurosis and together with a sense of impending doom are seen as the worst of patients' suffering by clinicians and other investigators alike working in this field. It is therefore no surprise that treatment of anxiety and depression has been considered a fundamental aim in treatment with the added hope that any reduction in anxiety may be followed by a lessening of the main symptoms of the obsessional phenomenon. The latter aim is seldom fulfilled though there is some justification for this form of therapy on the grounds that patients too seem to seek immediate relief from anxiety rather than hoping for any change in their

obsessions and compulsive actions with which by the time they come up for treatment they have learnt to live. The patients in this study repeatedly reported that while on anxiolytics and antidepressants they had felt calmed down and although they liked this form of therapy, their basic symptoms had shown us change. Furthermore they remain aware of the fact that such treatment is at least symptomatic and suffer from the foreboding that it is bound to fail in the end. In contradistinction to this form of therapy treatment with neuroleptics is fought with the danger of precipitating a severe bout of depression as happened in the case of G.K.S.

On the other hand, as pointed out in the case of T.S.D. — the patient who was included twice in the trial — anxiety and depression may fail to respond to conventional form of therapy and begin to diminish only as obsession and compulsions begin to lift off. Obsessive patients treated with fluspirilene seem to lose their anxiety and depression as a function of the effect of the drug on their basic symptoms.

Premorbid personality, leisure interests and the existence of aims in life determine to a variable extent the prognosis in almost all forms of psychiatric illness; in obsessive patients following treatment with fluspirilene, no less than those who have been leucotomised, this aphorism becomes more convincing once the subjects begin to lose their obsessions and compulsions. Anxiety experienced at this stage is quite different from the anxiety seen when the patient is busy fighting his symptoms and is very much similar to the anxiety reported in such conditions as compulsive gambling following successful treatment. If this fact is not taken into consideration, it is likely that further treatment may not be suited to the needs of the patient — who may decide to opt out of the treatment — or the mounting tension and anxiety may be wrongly interpreted as deterioration of condition and the treatment considered a failure both by the patient and the therapist. In this study, four subjects interpreted this agitation as worsening of condition: two patients (L.K.T. & T.W.K.) defaulted treatment when beset with anxiety of this sort and one patient (G.K.S.) could continue with treatment only after a great deal of persuasion. It has been the experience of the present investigator that continued support and other psychotherapeutic measures become more important at this stage of treatment and helping the patient develop a healthy attitude towards his problems instead of adhering to his

erstwhile habit of introspection may help him tide over this period of severe agitation.

It may be added that as the effects of fluspirilene in the treatment of obsessive compulsive neurosis varie from patient to patient and not all symptoms respond to the drug at the same dosage level, using high doses and persisting with the treatment for sufficiently long periods, where indicated, may be two important guide lines for further studies. It is felt that in such resistant cases, the dose should be gradually built up starting from a low dose and gaps allowed in treatment to prevent the development of akathisia, agitation and other disturbing side-effects.

It has been mentioned above that the study was uncontrolled — except in the case of T.S.D. — and the subjective assessment by patients may not be conclusive in deciding the efficacy of the drug in the treatment of obsessional states. The very fact that patients suffering from obsessive compulsive neurosis, tend to be extremely parsimonious when describing any positive change in their condition as a result of treatment minimizes any bias from this angle. It has been the experiences of the present author that unlike the patients suffering from schizophrenia and their relatives who almost always begin the interview with "no complaint" and then go on to describe one symptom after the other, the first response of the obsessive patients is "no change" and then any reduction in the intensity of symptoms is admitted with some reluctance.

It is also worth noting that language barrier between the therapist and the patient which was complete in the case of C.C.B. and allowed very little rapport in two more cases (L.K.T. & G.K.S.) served a useful purpose in assessing the therapeutic efficacy of the drug as whatever benefit these three patients derived from treatment may only be attributed to the drug.

#### SUMMARY

Seven out of eight subjects suffering from obsessive compulsive neurosis found relief in their symptoms, without being calmed down, following fluspirilene therapy; the only patient who could find no change in his condition had been kept on a fixed low dose regime. Patients who derived benefits from this form of treatment reported either losing a symptom completely or developing an attitude of ignoring it.

This exploratory strictly suggests that fluspirilene has perhaps some place in the treatment of obsessive compulsive neurosis where it acts on

### Summary of Findings

	G.K.S.	J.N.M.	L.K.T.	H.Y.F.	T.W.K.	C.C.B.	T.S.D.
Obsessive thoughts concerning health death and allied themes.	80% (5) ... Absent (8)	80% (4) ... Absent (6)	90% (10)	30% (4)	20% (1)	70% (13) after 3 doses	51% (11) ... of harming others Absent (5)
Other ruminations	90% (5)	15% (2)	—	40% (3)	—	—	86% (11)
Checking rituals (doubts) and repetitions	only checking locks 0% (1) ... Absent (5)	80% (10)	65% (11)	75% (4)	56% (1)	80% (6) after dose	14% (11)
Washing/purification/ablution	Excessive leg-washing 0% (2) Absent (9)	75% (15)	87% (9)	—	—	—	37.5% (11)
Complicated rituals and obsessions	—	90% (10)	90% (10)	30% (3)	some 50% others absent (1)	—	14% (11)
Insistence on precision orderliness	—	75% (8)	—	—	Less	—	12.5% (11)
Other compulsions	—	—	90% (9)	—	—	—	some 28.5% other compulsions 71.5% (11)

Percentage denote benefit derived from fluspirilene therapy; figures in parentheses represent the week when assessment was made.

the basic symptoms of the illness and that its efficacy is dose related affecting different symptoms at different dose levels and at different stages of treatment. Furthermore, in this condition its action is antagonized by the concurrent use of anxiolytics and antidepressant agents.

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#### BIBLIOGRAPHY

- FRANKL, V.E.; *"Psychotherapy and Existentialism: Selected Papers on Logotherapy."* New York: Washington Square Press, 1967.
- POLLITT, J.; "Natural History of Obsessional States." *Brit. Med. Journal*, 1: 194–96, 1957.  
(1969) "Obsessional States." *British Journal of Hospital Medicine*, 1146–50, June 1969.  
Unpublished report on R6218 (IMAP), Janssen Pharmaceutica, Beerse, Belgium.