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ORIGINALS  
THERAPY BY DRUGS

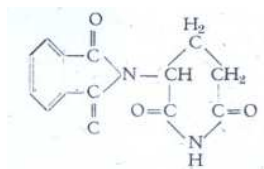
Of the neurological wards of the Wilhelminen- and Kaiserin-Elisabeth-Spitals of the city of Vienna  
(Chairman: Prim. Dr. W. Schober)

## Effect and ways of application of the glutamin acid derivative Contergan

By W. Schober

The treatment of psychosomatic and somapsychic disorders always asks for the application of combined pharmacotherapeutic and psychotherapeutic measures. Because of the continuously increasing over-consumption of the so-called psychotropic agents within the medicinal treatment area it is necessary to strictly diagnose the psychosedating ingredients whereas in each single case the personality of the patient and the significance of the pharmaceutical product should be taken into consideration when deciding on the overall treatment plan. The pharmacopsychic effect by itself, i.e. the sole application of the drug without any supporting psychotherapeutic measures does never reach the complete therapeutic goal.

If we ignore organic diseases such solitary measures within the functional area of dysfunction may be fitting to cope with the patient's pursuit of safety but from the doctor's side they only result in an anonymity in the relationship between doctor and patient which cannot be helpful for the treatment climate as was stated by *Stern* in a different context. Taking all these aspects into consideration the glutamin acid derivative Contergan has been clinically tested by us in the years since 1956 after suitable pre-tests justified that.



Pharmakologically is Contergan a N-phtalyl-glutamic acid imide in this structure:

The medicinal product was properly experimentally tested by *Kunz, Keller, and Mückter*. As a result it was found out that it was practically lacking any toxicity. Therefore the authors were unable to find out the lethal dose in tests with mice. Even during an application over 30 days no intolerance appeared in animal testing. Blood morphology, urine and weight checks stayed within the standard borders. The cat's pupil reaction stayed unchanged, heart rate, blood pressure and breathing were not affected. Movement coordination and retaining reflexes were not disturbed even when using higher dosages.

The named authors could proof in animal tests that the medicine had a significant deadening effect to the central nervous system and by using higher dosages had a sleep-prone effect. In all cases the sedative effect was characterised by a fast beginning and the missing of an initial phase of agitation. Narcotic effects were absent. A central analgetic or anticonvulsive effect could not be shown.

The observations described below result from the experience with Contergan tested on 100 in- and outpatients.

During an exploratory analysis of a small group of patients no case of toxic or allergic side effects could be detected. Though it happened in single cases that patients

complained about feeling dizzy, heaviness of limbs and sometimes slight restlessness and tremors but those symptoms always passed quickly. Mostly patients were thus affected who reacted often with organic sensations to other medicines, too. By reducing the dosis those discomforts disappeared or could not be observed anymore. In isolated cases higher dosages resulted in obstipation.

There never was a significant interference with the autonomic nervous system. Haematopoiesis and cardiovascular system remained unaffected.

We had the medicine available in the form of Contergan<sup>1</sup> (25 mg) and Contergan forte (100 mg). It could be applied as tablets, coated tablets, syrup and suppositories. We considered the tablet as the most pertinent way of application. Evidence for addiction or euphoria could not be provided during the whole period of observation not even in the case of using it as cure treatment. Especially patients suffering from cerebral sclerosis liked to take the drug.

A single dosis used as daily sedative was 25 mg given once or twice in which case the dosis of 25 mg turned out to be the best. In rare cases, for example patients suffering from chronic alcoholism the dosis had to be increased up to 100 mg or even 200 mg several times a day. A dosis of 100 mg or higher given to non-alcoholics resulted in a sleep-prone effect.

The sedation beginning after about 12 to 15 minutes effects the affektivity, i.e. anxiety state, irritability, inner unrest and tension. It approximates the effects of neuroleptics described by *de Boor*. An initial motility<sup>2</sup> stimulation could not be observed. It seems that contergan influences the last "symptomatic final common path" (*Freyhan*), which is the common factor in a lot of disorders, in regard to the emotional side. That might show that the effect is subcortical<sup>3</sup>.

By using Contergan it was possible to influence primarily disorders favorably where the aim was to get rid of emotional tension. That is how a convenient initial position for psychotherapeutic measures was created. The various types of neurosis and depression mostly reacted well to the drug. Psychoses and severe cases of agitation were excluded from the treatment. Especially physically caused depressive moods during menopause and those of Hyperthyreosis and hypothyroidism reacted favorably. The initial position regarding the autonomic nervous system was unimportant in those cases as effects on the cardiovascular system were not readable. We also successfully applied Contergan in cases of emotional reactions of the nervous heart, we reported already somewhere else how the nervous heart acts as signal. In the case of agitated cardioneurosis we found the therapeutic sleep treatment with psychotherapy nested in especially effective. We restricted the duration of sleep to 3 to 4 days. On the evening before 100 to 200 mg of Contergan forte was given, during the next days 100 mg were sufficient per day to keep up the sleep from which it was always possible to wake up the patients.

To sedate with the help of Contergan has been proven of value in cases of slight agitation. Especially in the cases of chronic alcoholism with its tension and agitation phases in connection with insomnia the use of Contergan forte for longtime in-patients has been applied successfully to prevent severe abstinence phenomenon symptoms.

Even after successful dehabitation it did a good job in connection with psychic guidance of the patient. In one case even a slight abstinence delirium could be mastered completely.

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<sup>1</sup> We would like to thank the company Interchemie (Grünenthal) for supplying us with a batch of the compound for testing purposes. In Austria the drug will shortly be on the market under the name of Softenon.

<sup>2</sup> Automatic body movement like intestinal movement (MBW)

<sup>3</sup> Of or pertaining to the subcortex, the portion of the brain located below the cerebral cortex (from Wiktionary)

In one case of *Alzheimer's* disease the female patient got rid of the empty restlessness through the use of Contergan. There was no positive result when using it in cases of high restlessness or paralysis agitans<sup>4</sup>.

One important area of indication of Contergan forte was the result of treatments of old people suffering from insomnia. Especially in those cases of vascular diseases of the brain the medicine proved to be reliable if it was included into the complex therapy<sup>5</sup> of those disorders. In the cases of cerebral sclerosis, hypertonia, hemiplegia, and senile restlessness it is best to avoid drugs like barbiturates, atropine, and morphine as those aggravate the mental disorders even more (*Meyer*). In the same way Contergan showed its effectiveness in the pre- and postoperative phases of old people suffering from Insomnia and nightly unrest.

Further areas of application are those of commotio cerebri<sup>6</sup> and posttraumatic state of shock. In this case we mostly gave the drug in combination with the usual sympathicolytic<sup>7</sup> substances.

Concluding and to give the complete facts we like to mention that Contergan may also be used as provocation agent in the cases of focal epilepsy. In cases of temporal lobe epilepsie we were able to reach a moderate degree of activation in the pathological electroencephalogram. In this connection we would like to point to the research of *Walkenhorst*. To provoke sleep artificially we used 200 mg Contergan for each case, too.

Additionally we would like to point out that Contergan proved its worth as sedative and hypnotic in cases of symptomatic disorders in the internal neurologic borderland. Because of its non-existing toxicity it may even be given in the case of liver damage (*Jung*).

#### *Summary*

Point and width of effect of the daytime sedative and hypnotic Contergan has been examined in the cases of 100 patients. We abstained on purpose from giving a detailed description. The practically non-existing toxicity and the missing of an initial agitation phase combined with an instant result recommend the use of the medicine for treatment of out- and in-patients. Nevertheless its application should always happen in combination with pharmacotic and psychtherapeutic measures within the frame of an overall therapy plan.

Special areas of indication for temporary use as well as cure treatment are given. Euphoria or addiction have not been observed.

#### *Literature*

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<sup>4</sup> Parkinson's disease

<sup>5</sup> literal translation of „Komplextherapie“

<sup>6</sup> craniocerebral injury

<sup>7</sup> vasodilatory (?)