

A REVIEW OF THE PATHOGENESIS OF CHLOROMYCETIN (CHLORAMPHENICOL)

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Introduction

"Chloramphenicol" is an useful drug of modern school of medicine being initially extracted from cultures of streptomycetes venezualae, *chloramphenicol*, or *chloromycetin* are obtained today by synthetic methods. It appears in the form of white, colourless crystal with an extremely bitter taste, not very soluble in water (0.25% at 25°) but soluble in propylene-glycol (15%g ethanol). It is the only antibiotic which contains chemically peculiar molecule of Nitro Group (NO₂). It has toxic effect resulting in vomiting, meteorism, cyanosis and irregular respiration terminating in death by collapse of the vasomotor system in children and adults. In adults it creates serious disturbances of the bone-marrow leading to leukaemia, aplastic anaemia, hypoplastic anaemia, reduction in the number of platelets and granulous leucocytes.

Keeping in view its toxicology, Hahnemannian proving of chloramphenicol was conducted upon ten provers under the Drug Proving Research Scheme at Midnapore Homocopathic Medical College and Hospital, Midnapore, West Bengal in the year 1960-61 through grant in aid from Government of India and also by O.A. Julian from January to March, 1970 in which six provers including three women participated.

The syptomatology which was established by those provings is very interesting from clinical point of view. Hence the present authors undertook an analytical study of both the provings and have compiled the peculiar and interesting symptoms. Apparently the signs and symptoms attributed to Chloramphenicol have not been clinically verified or confirmed on

many occasions. It is, therefore, imperative that these be clinically verified so as to establish a complete drug picture of Chloramphenicol. Principal symptoms which emerge from the comparative study of both the provings have been tabulated.

Method

In this study, both the provings of Chloramphenicol were reviewed in order to compile its principal symptoms and to evolve its drug picture for therapeutic application. The first attempt was made to find out those symptoms which were obtained during both the provings. Secondly, an attempt was made to verify the symptoms which were found in most of the provers under Drug Proving Research Programme, Midnapore, from the provers day-books at the present author's disposal. The provers day-books concerning Dr. Julian's proving were not available. Hence, they could not be studied for verification.

An interesting feature of the study was that there were many peculiar symptoms in either of the two provings. Both the provings which, if clinically verified represent the characteristic and individualistic indications of this drug. Such symptoms have been superscribed with an *Asterisk* in the main compilation.

The main symptoms which were found in both the provings, were also observed on a number of provers who participated in proving at Midnapore.

In the following symptoms manifestation of both provings are mentioned.

OBSERVATION

Pathogenesis of Chloromycetin

Generalities

- Pallor (T)¹
- Pronounced asthenia (T)
- Discouragement in morning* (HS)²
- Euphoria (HS)

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- Weak and prostrated feeling, tired and loss of body weight (DM)³
- Great general uneasiness (DM)

Mind

- Delirium, mental confusion (T)
- Hallucination (T)
- Extreme sleepiness around 5 O'clock in the afternoon* (HS)
- Sleepiness, drowsy feeling in morning* (DM)
- Feeling of tiredness, great prostration with great aching of the body* (DM)
- In bed, at night, discomfort throughout the body* (HS)
- Restless, must move, gets out of bed, because he feels too hot, forced to uncover himself and walk* (HS)
- Heat or impression of heat over all parts of the body* (HS)
- Fidgety, and heat in the entire body, compelling him to move* (HS)
- Agitation with the need to move a great deal* (HS)
- Apathy, extreme muscular weakness, depression (HS)
- Feels sad, despairing, but the condition improves on rising (HS)
- Sad, gloomy, inactive mind, aversion to work (DM)
- Mentally tired with great general uneasiness (DM)
- Vexation without cause. Unintelligible expression* (DM)
- Mentally restless and morning weakness (DM)
- Great dullness (DM)
- Confusion in mind with cloud of ideas, could not retain anything in memory* (DM)
- Loss of inspiration to work* (DM)
- Irritability with disturbed sleep* (DM)
- Lack of concentration* (DM)

Head

- Frontal headache with heaviness and vertigo, better in open air and after bathing (DM)
- Recurring headache* (HS)
- Congestive frontal headache better by pressure, cold application (DM)
- Pain and hammering at vertex and sides of the head,

- improved by pressure from the hands and by holding the head high (HS)
- Headache with prostration and weakness followed by aversion to work* (DM)
- Prolonged bouts of vertigo* (HS)
- Waking at night from 2 A.M. to 5 A.M. with a throbbing headache* (HS)
- Severe headache with nausea* (DM)
- Dull headache by closing eyes* (DM)
- Left sided headache* (DM)

Digestive System

- Bleeding gums (T)
- Dryness of mouth, with bad breath, bitter taste (HS)
- Bitter taste of mouth (DM)
- Nausea after eating, inclination to vomit but no vomiting (DM)
- Dryness of mouth with thirst (DM)
- Hungry with feeling of distress in stomach (DM)
- Nausea with thirst* (DM)
- Coated tongue with foul smell (DM)
- Loss of appetite (DM)
- Bad taste of mouth (DM)
- Anorexia, nausea and vomiting (T)
- Morbid hunger, causing pain in the morning especially between 11 A.M. and noon* (HS)
- Hunger with hollowness in stomach in the afternoon and 5 P.M. (HS)
- Glossitis (T)
- Stomatitis (T)
- Inflammation of lips (T)
- Thirst for cold water (DM)
- Feeling of well being in stomach* (HS)
- Thirst for cold beer (HS)
- Haematemesis (T)
- Euphoria after meals, with giddy feeling in head* (HS)
- Extreme sleepiness after meal (HS)
- Aversion to sugar and sweets (HS)
- Diffuse abdominal pain (T)
- Intestinal spasms towards evening (HS)
- Constipation, vomiting, pain in peritoneum (T)
- Cholera type syndrome (T)
- Diarrhoea (T)
- Colic and diarrhoea following the indigestion of sweet pies (HS)
- Stools thin, dark, scanty* (HS)
- Urge to stool with tenesmus* (HS)
- Urge for stool, not improved by stool* (HS)
- Persistent tenesmus with cramping pain in lower region of stomach* (HS)
- Anal burning, inflammation of anus and rectum (T)

1. (T)=Toxicological symptoms. 2. (HS) = Hahnemannian symptomatology (both T & HS have been taken from Julian's *Materia Medica of New Homoeopathic Remedies.*). 3. (DM) = Drug Proving Research Scheme, Midnapore.

*These symptoms were obtained during the proving and therefore need to be verified clinically.

- Icterus (T)
- Pain in lower abdomen, better by heat and pressure (DM)
- Colicky, griping (DM)

Eyes

- Sensation of burning in eyes, better cold application (DM)
- Pressure of eye ball (DM)
- Inflammation of eyes, better cold application (DM)
- Optic neuritis (T)
- Paresis of accommodation (ciliary muscle) (T)

Respiratory System

- Sudden pain in chest with difficult breathing* (DM)
- Wheezing, not altered by changing position* (HS)
- Redness in throat with difficulty in swallowing (T)
- Dyspnoea without cause (T)

Nose

- Epistaxis (T)

Ears

- Disorders of the cochlea (T)

Urinary and Genital Organs

Urinary

- Dysuria (T)
- Frequent micturition (T)
- Frequent micturition with hurry to act immediately, burning during (DM)
- Flow cannot be retained with back pain and shuddering, temperature of 100°F* (DM)

Genital-Male

- Pain and soreness of left testis* (DM)

Female

- A colicky pain in lower abdomen before menstruation* (DM)
- Scanty menses (DM)

Circulatory System

- Aplastic anaemia (T)
- Echymotic and petechial purpura (T)
- Hypothermia (T)
- State of collapse with cyanosis (T)
- Vascular hypertrophy with bouts of arterial tension (HS)
- Pulse accelerated* (HS)
- Tachycardia alternated by changing position (HS)
- Thermal regulation, fever hovering between 38°-40° (T)

Skin

- Profuse sweat (DM)
- Hair seems to grow darker (HS)
- Vesicular, papular and macular erythema (T)

Extremities

- Aching pain in limbs better hard pressure (DM)
- Feeling of great muscular weakness and exhaustion (DM)

Principal Symptoms

(These following symptoms are found in both the provings and repeated in most of the provers during drug proving conducted at Midnapore).

- Pallor, pronounced asthenia, weak, prostrated, tired and loss of body weight.
- Great general uneasiness.
- Asthenia, great muscular prostration and aching pain all over the body.
- Sad, gloomy, inactive mind and aversion to work.
- Mentally restless and morning weakness.
- Confusion of mind, cloud of ideas, cannot retain in memory.
- Frontal headache with heaviness and vertigo, better in open air.
- Congestive frontal headache better by pressure and cold application.
- Bitter taste and bad taste of mouth.
- Dryness of mouth with thirst.
- Hungry with feeling of distress in stomach.
- Coated tongue with foul smell from mouth.
- Thirst for cold water.
- Extreme sleepiness after meal.
- Constipation, vomiting and pain in the peritoneum.
- Diarrhoea with colicky pain in lower abdomen.
- Pain in lower abdomen, better by pressure.
- Burning sensation in eyes, better cold application.
- Pressure feeling in eye balls.
- Dyspnoea without cause.
- Frequent micturition, hurry to act immediately, burning during.
- Fever with intense general heat of the body.

Discussion

It is observed that "Chloromycetin" or "Chloramphenicol" in its attenuated form has produced many common symptoms to certain diseases and drugs as well as many uncommon individualistic symptoms. Many of the common symptoms have been found to be repeated upon a number of provers. The uncommon symptoms which are observed either in "Julian's" proving or in the proving of Drug Proving Research Unit, Midnapore upon some of the provers and those

attributed to toxicological source need clinical verification.

It is interesting to note that there are many pathological conditions such as aplastic anaemia, degeneration of reticular system of leucocytes and of blood platelets, prolonged bleeding and irreducible blood clot attributed to the pathogenetic properties of chloramphenicol. These are suggestive of its deep and wide sphere of action, and call for further investigation and clinical confirmation.

Considering its pathognomonic symptoms, the clinical conditions where it may be of use, appears to be typhoid fever, colitis, urticaria and arthritis.

Arsenic album, Veratrum album and Rhus toxicodendron appear to have symptomatic relationship with chloramphenicol.

It is suggested that an organised proving of chloramphenicol following double blind method may be made

in order to obtain its true drug pathogenesis data. Simultaneously, the available symptomatic data may be clinically verified.

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