

## CLINICAL

# Clinical Homeopathic use of RNA: evidence from two provings

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**Two homeopathic drug provings (HDPs) of RNA have been published. The methods are reviewed. Our method is double-blind and placebo-controlled, conforms to GCP and includes run-in and follow-up phases. Symptoms are selected from diaries according to predefined criteria. The results of the provings are compared with each other and with the homeopathic clinical use of RNA. At this stage it is difficult to draw conclusions concerning the clinical use of RNA. Further HDPs are required, they should follow GCP and standard, transparent protocols. Homeopathy (2005) 94, 33–36.**

**Keywords:** homeopathic drug proving; RNA; research methods; GCP guidelines

## Introduction

Two homeopathic drug provings (HDPs) of RNA have been published: Julian (1972)<sup>1</sup> and Riley and Zagon (2002).<sup>2,3</sup> We compare the results of these HDPs with each other and the clinical use of this remedy. Our research questions were:

Is there a role for HDPs in contemporary homeopathy?

How do the results of HDPs relate to the clinical practice of homeopathy?

This paper discusses the proving methodology and results of Riley and Zagon and compares them with those of Julian, and with the use RNA in homeopathic clinical practice.

Our HDP of RNA<sup>2,3</sup> followed the Good Clinical Practice Guidelines (ICH-GCP) for clinical research. Our group has conducted more than 70 HDPs between 1992 and 2003<sup>4–7</sup> Julian's methods are not clearly described and he published in the 1970s, predating GCP guidelines.<sup>1</sup> HDPs are pharmacological studies on healthy subjects similar in some respects to Phase I clinical trials. However, HDPs, particularly when using non-toxic homeopathically diluted substances, lack the toxicological risks of such trials. The definition of an

'adverse event' (AE), as it applies to conventional clinical trials is modified because of the unique qualities of a HDP in which each symptom or sign of discomfort is recorded and is a potential component of the homeopathic symptom picture for that medicine. Only severe health disorders requiring withdrawal from the trial, and inter-current illnesses are classified as adverse events in accordance with the GCP-Guidelines.

In homeopathy, the individual symptoms experienced by a patient are of primary importance. The complexity of homeopathic clinical research is increased by the fact that homeopathic medicines are often prescribed based on the individual symptoms that a patient with an illness experiences rather than the typical symptoms associated with that illness. Models for clinical research in homeopathy need to account for the individualization of homeopathic prescribing and not just the general symptoms of an illness. Recognizing the symptoms of an individual subject and matching them with the symptom pattern associated with a homeopathic medicine is considered the key to the successful practice of homeopathy.

Historically, the actions of homeopathic medicines have been evaluated in four ways: HDPs on healthy subjects, toxicological data, clinical trials<sup>8</sup> and clinical practice. Questions of placebo response and the role of non-specific effects in homeopathic research including HDPs continue to be a point of discussion.<sup>9</sup> Concentrations of the substances used in HDPs conducted by

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Hahnemann and in contemporary provings have ranged from mother tinctures to 30C and higher ('ultra-molecular' concentrations). Samuel Hahnemann, the founder of homeopathy, conducted more than 100 homeopathic drug provings in the process of investigating '... the peculiar actions of medicines on the health of man...' [Organon § 108].<sup>10</sup> He stressed the need for HDPs on healthy subjects as an important method for achieving a clear homeopathic symptom picture.

## Materials and methods

### Riley and Zagon 2002

The duration of the study was 6 weeks per subject (42 days). Data were collected in a diary with data entered daily. Twenty-five subjects, 18 females and 7 males age 16-72, were recruited between November 2001 and January 2002 by advertisement. Prior experience with homeopathy was not a pre-requisite for participation nor an exclusion criteria. Subjects included were at least 16 years of age, in a state of good general health and provided written informed consent as outlined in the IRB (ethics committee) approved protocol. They were excluded if they were in the midst of major life changes, receiving current or ongoing medical treatments, had surgery within the past 6 weeks, had used homeopathic medicines higher than a 30C or oral contraceptive pills in the past 3 months, were pregnant or lactating, or had a history of alcohol or drug abuse. Each subject attended two separate training sessions prior to entering the HDP.

The diary included both structured and open-ended entries. The structured section contained the chapter headings that are customarily used in homeopathic repertories with additional space for other information. Subjects were encouraged not to qualify the symptoms they noted, even if they thought they had an explanation for why the symptoms may have occurred, but rather simply to report the symptoms they experienced. A routine medical evaluation (history and physical) was performed on all subjects who participated in the HDP.

The medication used in this HDP was prepared in accordance with the methods outlined in the HPRS (Homeopathic Pharmacopoeia Revision Service) in a 2X potency. This was chosen because it conforms to the OTC/RX potency guidelines of the Homeopathic

Pharmacopoeia of the United States (HPUS). The RNA starting material was obtained from Oligos Etc. (Wilsonville, Oregon). Homeopathic production was supervised by Eric Foxman, R.Ph; a licensed pharmacist who has extensive experience in the homeopathic pharmaceutical industry including production.

All bottles were coded and the investigators were blind with respect to the verum or placebo coding until after the final report was written. Regime was ten drops, once daily beginning on Day 8 for the duration of the proving or until symptoms occurred. No food was to be eaten for 15 min prior to or after taking the medication. Subjects were followed up in person to evaluate any symptoms they may have experienced, the bottle of medication was returned at the end of the proving. Weekly in-depth interviews were conducted with data entry done at that time.

### Schedule

#### Day 0-7, run-in

Subjects noted their current state of health in a daily diary. After 1 week a pre-medication evaluation occurred in which their diary was evaluated by the investigator. They noted the subject's 'baseline symptoms', assessed their compliance and conducted a physical examination. The subject then received the investigational medication to be started on the next day (day 8).

#### Day 8-29, medication phase

The subject documented the occurrence of symptoms in their daily diary as well as the time they took the study medication. While taking the medication the subjects were interviewed daily at which time the symptoms experienced by the subject were reviewed. When symptoms occurred the homeopathic remedy was discontinued although subjects continued to document the occurrence of symptoms in their daily diary.

#### Day 30-42, follow-up

During this follow-up phase the subject were followed for the occurrence of any additional symptoms or adverse events. They did not keep a diary. (Table 1).

### Symptom selection criteria

The process by which the symptoms gathered in HDPs are selected is one of the most challenging parts

**Table 1** HDP schedule, Riley and Zagon (2002)

Proving timeline	Day 0	Day 7	Day 21	Day 28	Day 35	Day 42
Medical history	X					
Inclusion/exclusion criteria	X					
Informed consent	X					
Physical examination		X				
Diary data entry	X	X	X	X		
Delivery/return of medication		X		X		
Observation for adverse events		X	X	X	X	X

of a HDP.<sup>11</sup> We reviewed the symptoms experienced by each subject during the HDP. We use the following criteria in selecting symptoms: modalities, concomitants, timing of the symptom, localization, uniqueness of a symptom, intensity of the symptom, newness of the symptom, a symptom occurring after taking the medication on at least two occasions, a symptom experienced before the proving started which disappeared or was significantly ameliorated after the administration of the proving medication, a symptom experienced in more than one subject. Each symptom is identified with one or more numerical codes corresponding to the selection criteria noted above.

The task of symptom selection in a HDP is further complicated by the observation that some symptoms derived from historical HDPs initially appeared unimportant and may have been experienced by only one subject in a HDP. Some of these symptoms were subsequently verified clinically and are now major keynotes of homeopathic medicines. In order to extend our understanding of homeopathic medicines of which our knowledge may be incomplete, proving models should be methodologically consistent, clearly defined and transparent. It is probably not possible or even useful to perform a statistical analysis of newly arising symptoms in a HDP as there are no pre-defined target criteria for comparison. Instead, specific quality-related criteria should be used to evaluate and classify the symptoms that occur. We included a symptom in the homeopathic symptom picture if at least one of the above selection criteria was fulfilled. Ideally the symptom selection criteria used to extract a symptom experienced in a HDP should link a HDP with clinical practice and back. Thus providing, over time, verification on the validity and usefulness of the symptom selection criteria. The final arbiter of the validity of any symptom experienced in a HDP remains the clinical response of patients treated with the medicine.

#### Julian's Proving

Othon Julian was a French physician and homeopath who attended the Strasbourg School of Medicine, graduating in 1935. He incorporated homeopathy and chiropractic into his medical practice until his death in 1984 and conducted many provings over the course of his medical career.

His proving of RNA was published in 1972; it involved 22 subjects (20 male, 2 female) who took RNA in 30C, 7C and 3X potency. Placebo was used in a format described as 'single blind' but not clarified further. Further complicating analysis of the results is the fact that a self-proving of Dr Guiot of Wavre and clinical research from other Belgian homeopathic authors was included in the results without identification. The data from the proving was not stratified by homeopathic potency or placebo. No further information on methodology was available to us.

## Results

### Summary of essential characteristics from the homeopathic drug proving of homeopathic RNA *Riley/Zagon 2002*

- allergic symptoms (3 subjects),
- decrease and increase in appetite (3 subjects),
- arthralgias and arthritis, particularly in the large joints (4 subjects),
- dizziness and vertigo (1 subject),
- intense dreams (2 subjects),
- fatigue and fibromyalgia (3 subjects),
- flu and cold symptoms - viral infections (4 subjects),
- gastro-intestinal symptoms, including loose stools and acid reflux (3 subjects),
- severe headaches (1 subject),
- sexual dysfunction including symptoms related to the menstrual cycle (3 subjects),
- muscle pain in the lower extremity (2 subjects),
- internal heat - fever or early phase of an illness (2 subjects),
- skin rash - primarily eczema and dry, cracked skin (4 subjects).

### *Julian 1972*

- allergic reactions in general,
- acid reflux,
- appetite changes,
- arthralgias,
- biliary sycosis and entero-hepatic syndrome,
- depression,
- eczema,
- fatigue and fibromyalgia,
- herpes,
- infections, particularly of the skin and upper respiratory tract,
- insomnia,
- pain, particularly low back pain,
- sexual dysfunction,
- urticaria,
- weight gain and loss.

## Discussion

### Data on comparison of proving symptoms and clinical use

Clinical use of RNA as a homeopathic medicine was gathered by questioning 29 homeopathic practitioners who had graduated from the Hahnemann College of Homeopathy. Approximately 10% of those contacted had prescribed the remedy and only 1 of those had used it more than once. There is no report of usage based on the results of the 1972 proving done by Julian.

This problem is compounded by the fact that there is also no toxicological picture associated with RNA to

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**Table 2** Summary of symptoms reported in 2 HDPs of RNA, compared to reported clinical use

	Julian	Riley	Clinical use
Allergic reactions (including urticaria)	X	X	X
Appetite changes	X	X	—
Arthritis	X	X	X
Depression	X	—	—
Dreams	—	X	—
Fatigue	X	X	—
Fibromyalgia	X	X	—
Gastro-Intestinal symptoms	X	X	X
Herpes	X	—	—
Low back pain	X	—	X
Sexual dysfunction	X	X	—
Skin infections (eczema, dry skin, rash)	X	X	X
Upper respiratory tract infections	X	X	X
Weight gain and loss	X	—	—

guide potential clinical applications in homeopathy. Comparing the results of multiple provings with clinical usage may provide a clearer understanding of the similia principle<sup>12</sup> (see Table 2).

### Limitations

Although there is overlap between the symptoms of the two provings of RNA one cannot assume that homeopathic RNA is useful for the symptoms common to both provings. The methodology of the HDPs is different and the results do not lend themselves to statistical analysis. It is very difficult to distinguish among verum and placebo symptoms reported in an HDP, the subjects used in these two HDPs may not be comparable, and the potencies used were different. Comparisons are therefore not quantitative but only qualitative at best they point to the need for clearly defined standardized methods so that meaningful comparisons are possible.

### Conclusions

The use of homeopathic RNA in specific clinical situations is primarily of interest to homeopathic practitioners treating individual patients where this remedy might be considered. Results from multiple homeopathic drug provings and comparisons with

clinical applications would be particularly useful for remedies used frequently in the clinical practice of homeopathy. The information from these two HDPs may be of use in designing future clinical trials where a specific clinical indication is evaluated; it is not helpful in defining with any confidence a specific indication where this remedy might be useful. Despite these limitations this comparison between two HDPs and clinical use does point out the importance of conducting HDPs using a clear and transparent protocol to facilitate standardization of methodology, comparisons between HDPs, toxicological data, clinical trials and guide the clinical practice of homeopathy. Further studies linking homeopathic drug provings with clinical practice are needed.

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