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Repertory and likelihood ratio: time for structural changes

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If the likelihood ratio (LR) method is introduced, the repertory will gradually change as more symptoms are assessed. It will also change the use of the repertory: the most important medicines of each symptom rubric can be identified and relied on, even in large rubrics. This is also a good opportunity to correct structural shortcomings of the repertory, for instance, entries should be based on systematic analysis of materia medica instead of casual observations. *Homeopathy (2004) 93, 120–124.*

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Introduction

Is it possible to devise the perfect repertory, with complete symptom-rubrics, nothing but correct information and repertorisations that always put the effective medicine in the first place? Probably not, but the present repertory is far from perfect and not essentially improved during one century. The scientific basis of the repertory, proving as well as clinical data, can be improved. For clinical data the improvement should consist of using data from prospective, multi-centred research.¹ This could lead to the implementation of likelihood ratio (LR) indicating the increase (or decrease) of the likelihood that a medicine will be effective if a certain symptom is present (or absent).² With LR the content of the homeopathic materia medica and repertory will change, but will the use of these instruments also change? We expect that this will be the case if the kind of information introduced by LR is significantly different from that traditionally used. But in this case we should also reconsider the old information that has not yet been assessed by LR

investigation, because there are structural shortcomings in this information. What changes can we expect in the repertory and how might this affect our method? In this paper, we present two different procedures to find the right medicine. The first is a step-by-step procedure where symptoms are considered consecutively and likelihood for one medicine gradually increases. The second method is a one-step overview of a number of selected symptoms to make a differential diagnosis of several medicines. Both methods are placed in the perspective of the LR method.

Structural problems

For this paper, we use Kent's repertory as starting-point because it is the best known repertory.³ This repertory was developed manually in the late 19th and 20th century and originally contained about 65 000 symptom rubrics for about 650 medicines. A homeopathic repertory is essentially an index to the materia medica, symptom entries referring to corresponding symptoms in the materia medica. Each entry refers to one to hundreds of homeopathic medicines. The use of this index has developed into an art, as difficult as case-taking. There have been many editions and revisions. In this process mistakes have been made, many of them

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typing errors and semantic problems: for example different rubrics that are semantically comparable, but with different medicines (eg ‘Ataxia’ and ‘In-co-ordination’).

But there are also structural problems. Each symptom-rubric has to be considered with expert knowledge about its importance and reliability. This problem is multiplied in every case-taking because we generally need more than one symptom to make the right choice of medicine. There are some rules of thumb, eg the importance of a rubric is inversely related to the number of medicines in the rubric. But there are other complexities which make it very difficult to tell which medicines are the most important in any given rubric in spite of the system of typeface, where bold type should indicate the most important medicines. The methodology of this system is fundamentally wrong; bold type indicates that the symptom is more often seen in relation to the remedy (proving or cure). This, however, depends heavily on the frequency of use of that medicine; if a medicine is seldom used even its most important symptoms will not be mentioned in bold type in the repertory.

In a previous paper, we presented LR as the solution for this problem. LR is based on the relation between the prevalence of a symptom in the population responding to a medicine and the prevalence of the same symptom in the rest of the population. Therefore, it does not matter if the medicine is seldom or frequently prescribed. Another advantage of LR is that it gives a better representation of frequently used medicines in large rubrics. In the present repertory there are many inaccurate entries of ‘large remedies’ in large rubrics; the prevalence of the symptom is not greater than in the rest of the population ($LR = \pm 1$), so the symptom is no indication for that remedy.

Changing the repertory

When prospective studies using the LR method are performed, the repertory will change gradually as more symptoms are investigated and symptom rubrics become better assessed as the research progresses. In a separate paper, we show the outcome of a pilot-study on the symptom ‘loquacity’, which gives some indication of the outcome of a prospective study.⁴ Then, we place the new information on top of the old repertory. This is visualised in Figure 1 where hypothetical results of LR investigation of the symp-

tom ‘fear of death’ are added in red and between parentheses. These figures can only be interpreted in the context of the assessment, so the consensus of the research group and the prevalence of the symptom in the research population (with confidence interval) are added to the symptom. Thus, the user can compare the assessment with his interpretation of the symptom and his own population. Some medicines will prove to have $LR+ = \pm 1$, which means that the symptom is not an indication for these medicines (like *Aurum* in the example of Figure 1). One might ask if these entries in the repertory are superfluous. It is even possible that $LR+$ for a medicine is smaller than one and in that case the entry is wrong, because the symptom contra-indicates that medicine. Application of the LR method will also lead to medicines in the rubric. In the original repertory much data found in the materia medica is still absent (like *Latrodectus mactans* in this example). In most computer-repertories this is already corrected.

Many rubrics of the repertory will only change in the long run, especially the smaller rubrics because they represent infrequent symptoms. The assessment of these symptoms will take a very long time because the prevalence is low and the gain in assessing them is not so great because we already know that LR of these symptoms is high. But in small rubrics there may be medicines with different importance to the symptom, like *Aconitum* and *Argentum-nitricum* in the rubric ‘Fear of death, predicts the time’. These differences, represented by typeface, should be based on estimations using the LR method to make the repertory consistent. The estimations can be made by available information; the materia medica gives us indications about the importance of the symptom in relation to the remedy. This enables us to give a rough estimation of the prevalence of the symptom in the remedy-population. We can therefore divide the importance of the symptom in different classes: ‘not important’, ‘important’ and ‘very important’. But this leaves the problem of handling the second term of LR, the prevalence of the symptom in the rest of the population. We will deal with this subject in the section ‘Repertorisation’.

Step-by-step procedure with rubric analysis

The use of the repertory will alter with LR. There are two ways to use the repertory, the first is rubric

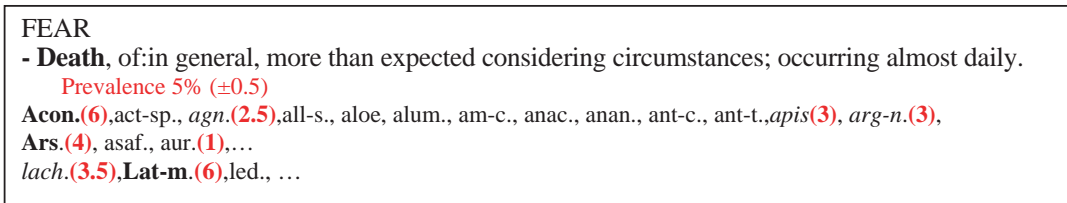


Figure 1 Repertory rubric with addition of (hypothetical) $LR+$ and context of assessment.

analysis (considering each medicine of a symptom rubric), and the second is making a repertorisation (combining symptoms in a spreadsheet).

At present, rubric analysis is only practical for small rubrics; in that case we can consider the likeness of each medicine in the rubric with the picture of the patient. In general, small rubrics are more important, ie LR is probably high for each medicine in that rubric. This means that every medicine in that rubric is worthwhile considering. For large rubrics this procedure is too time consuming and for many medicines in the rubric the LR is low, but until we have assessed LR we do not know for which medicines.

But if the LRs are known we can analyse any rubric, large or small, because we can select the interesting remedies (with high LR). A computer-repertory can easily produce a graph that shows the increase of probability that a medicine will work with the corresponding LR. Suppose we investigated the symptom 'fear of death, in 5000 patients, then we can be much more confident about the remedies *Aconitum*, *Agnus castus*, *Apis*, *Argentum nitricum*, *Arsenicum album*, *Lachesis* and *Latrodectus mactans* than about other remedies. If the other remedies do not show up in cases with good results it is unlikely that those remedies must be considered in cases with 'fear of death' as one of the most important symptoms. We can also estimate the number of symptoms needed for a reliable prescription. This is represented in a simplified way in Figure 2, where two such graphs are combined. Suppose that we have two patients, one with three symptoms with $LR+ = 6$ and one with four symptoms with $LR+ = 4$. If the prior chance that any medicine will work is 1% the probability of an effect will develop as shown in Table 1.

We see that we need three symptoms with $LR+ = 6$ or four symptoms with $LR+ = 4$ to get approximately the same certainty that the medicine will work. For example: if you have three strong symptoms for *Lachesis* with hypothetical $LR+ = 6$, like jealousy, left-sided complaints and aversion for clothing around the neck, you are fairly sure that the *Lachesis* will be effective. If the symptoms are less powerful, you will need more symptoms to be sure. There are, however, some precautions as we will mention in the discussion. This is a very straightforward example. Real cases have symptoms with different LRs. If, say in the second case (with four symptoms) symptom 4 had $LR+ = 6$ we could extend the last vertical red line in Figure 2 to the upper curve. Posterior chance would become 80%. (Figure 2).

One-step differential diagnosis: repertorisation

A repertorisation is a spreadsheet of different symptoms belonging to one case placed beneath each other,

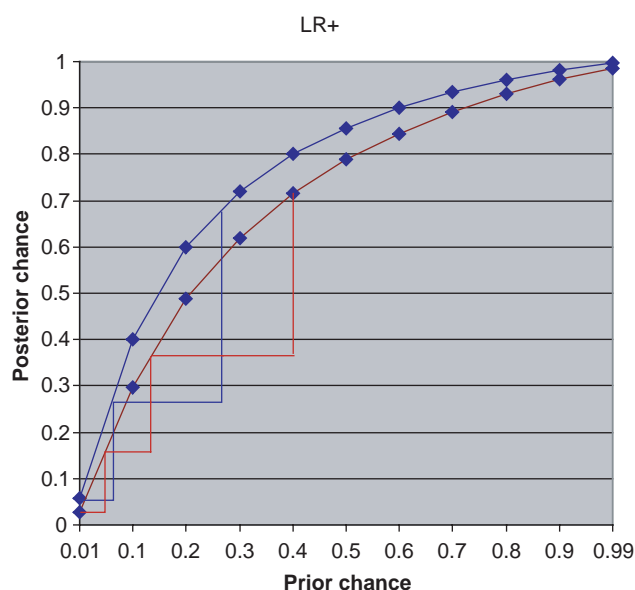


Figure 2 Step-by step development of posterior chance with 3 consecutive symptoms with $LR+=6$ (upper curve) and 4 symptoms with $LR+=4$ (lower curve).

Table 1 Change of 'posterior' probability of a remedy being effective according to LR and number of symptoms

Symptom	Certainty with $LR+ = 6$ (%)	Certainty with $LR+ = 4$ (%)
1	6	4
2	26	14
3	68	39
4		72

it indicates a number of remedies. Numbers replace typeface: 1 for plain type, 2 for italics, 3 for bold type and 4 for bold and underlined. In standard repertorisation the shortcomings of each repertory-rubric are added to each other, even when a modern computerised repertory with all kinds of additions is used. See Table 2.

Many repertorisations (like Table 2) will emphasise frequently used medicines more than seldom-used medicines. This problem increases when we use more and larger rubrics. In this repertorisation three of the four symptoms (1, 2 and 4) are derived from the materia medica of *Latrodectus mactans* and this medicine should be strongly considered, even though it does not appear in the 'top 10' on repertorisation.

Repertorisation with LR

We cannot discard all existing information in the repertory, but gradually the information of LR assessment of an increasing number of symptoms should be added. LR assessment is most efficient for symptoms which occur rather frequently and are regarded as keynotes for certain medicines. Larger symp-

Table 2 A hypothetical repertorisation, using a traditional repertory

1	MIND—FEAR—death, of	146
2	CHEST—PAIN—Heart	139
3	GENERALS—FOOD and DRINKS—fruit—desire	39
4	STOMACH—VOMITING; TYPE OF—black	58

	<i>ars.</i> 4	<i>lach.</i> 4	<i>phos.</i> 4	<i>puls.</i> 4	<i>verat.</i> 4	<i>acon.</i> 3	<i>alum.</i> 3	<i>ant-t.</i> 3	<i>arg-n.</i> 3	<i>arn.</i> 3	<i>ars-s-f.</i> 3
1	4	2	3	2	2	4	1	1	2	2	2
2	3	3	2	3	1	3	—	—	3	2	—
3	1	1	1	1	3	—	2	2	—	—	1
4	3	2	3	1	3	1	1	1	2	1	1

tom-rubrics will benefit the most. In Table 3, we show how a repertorisation based on LR could look like.

The total LR is the product of the LR of all symptoms, provided that the symptoms are mutually independent. In this hypothetical repertorisation an asterisk is placed after the symptom number to indicate that the symptom has been assessed by LR, the question mark after *Lachesis* for symptom 2 indicates that it is the original entry of the repertory but not (yet) confirmed by LR assessment (Table 3). In this repertorisation numbers are different from the original repertory to synchronise type with LR. LR = 6 stands for bold and underlined type, LR = 3 for italics and LR = 2 for plain type. The one-step differential diagnosis is different from the step-by-step approach. One-step differential diagnosis you take the symptoms together without prior ideas about possible medicines. Prior-chance in this stage is probably 1–10%. Table 4 shows posterior-chance for different medicines with 1% and 10% prior probability of being the correct medicine.

Handling small rubrics

Small symptom-rubrics will be difficult to assess in prospective studies, because they relate to infrequently occurring symptoms. Translation of existing rubrics into LR-rubrics does not yet consider the influence of the prevalence of the symptom. In moderate sized rubrics this will be no problem, but with small unassessed rubrics repertorisations will give a totally different picture compared to assessed rubrics. This can be demonstrated by two 2 × 2 tables. (Tables 5 and 6)

Suppose that the prevalence of the symptom ‘fear of death’ is about 5% in the general population and in the *Aconitum*-population 30%, so LR + = 6:

The symptom ‘fear of death, predicts time’ has a much lower prevalence, say 0.004 (0.4 %). In this case for *Aconitum* LR + = 100:

When we use small rubrics (rare symptoms) the proposed translation of type into LR is not adequate, because the prevalence of a symptom also influences LR. Current computer-repertories the greater importance of small rubrics (symptoms with low prevalence) can be represented by ponderation factors. The

Table 3 The same repertorisation as in Table 2, using a hypothetical LR-based repertory

A hypothetical repertorisation based on LR could look like this

1	MIND—FEAR—death, of	6
2	CHEST—PAIN—Heart	5
3	GENERALS—FOOD and DRINKS—fruit—desire	1
4	STOMACH—VOMITING; TYPE OF—black	6

	<i>lat-m.</i>	<i>ars.</i>	<i>lach.</i>	<i>acon.</i>	<i>etc.</i>
1*	6	5	3.5	4	
2*	5	5	2?	2	
3	1	1	2	2	
4	6	6	3	2	
Total LR	180	150	42	32	

Table 4 Posterior-chances with different LR+ and different prior-chances

	LR+	Posterior-chance (%)	
		With prior-chance=1%	With prior-chance=10%
lat-m	180	65	95
ars.	150	60	94
lach.	42	30	82
acon.	32	24	78

Table 5 Importance of a fairly common symptom; LR+=6

	Cure by <i>Aconitum</i>	No cure by <i>Aconitum</i>	
Fear of death	a = 3	b = 50	53
No fear of death	c = 7	d = 950	957
	10	1000	1010

Table 6 Importance of a rare symptom; LR+=100

	Cure by <i>Aconitum</i>	No cure by <i>Aconitum</i>	
Fear of death, predicts time	a = 2	b = 2	4
No fear of death, predicts	c = 8	d = 998	1006
	10	1000	1010

correction for rubric-size depends on the number of medicines in the rubric.⁵ This correction might also be used to upgrade the estimated LR of small rubrics. When we assess LR, its value depends on two factors. The first is the relevance of the symptom for the

remedy (represented by groups a and c of the 2×2 table); the second is the prevalence of the symptom (mainly represented by groups b and d of the 2×2 table). Therefore, it must be possible to estimate LR for not yet assessed rubrics by a combination of translating type into prevalence in the remedy population and translating rubric size into prevalence of the rest of the population.

Discussion

At the moment, we handle the repertory as if all symptoms are independent items, in this paper we do the same with the addition of LR. Frequently however, the symptoms in one case are interrelated. There are medicines where the combination of symptoms has more meaning than the sum of the separate symptoms (eg the combination of eye and heart symptoms with *Spigelia*). On the other hand, if two symptoms are semantically comparable they will not add up. Eventually we must investigate the influence of relatedness of symptoms, but this will only be possible if we know the LR of single symptoms. We must beware, however, not to assess LR of possibly related symptoms in one prospective study. This kind of problem might be expected if we assess two keynote symptoms for one remedy in one study.

The use of LR leaves less room for speculation. In the present repertory the absence of a medicine in a rubric might be interpreted as an indication that the remedy is not likely if the symptom is present, but this often disregarded. In a rubric that is properly adjusted for LR the absence of a medicine (or $LR = \pm 1$) means that the occurrence of the symptom is average; the symptom is nor a positive nor a negative indication for that medicine.

LR investigation is most suited for symptoms that are regarded as keynotes for certain medicines with a not too infrequent occurrence in the population, say 2–15%. This is a relatively small number of the total proportion of symptoms in the repertory. So most rubrics will still be based on the faulty system of occurrence of the symptom in cure or proving. For proper use of the LR-repertory it seems necessary to introduce estimates of LR in the rubrics that are not yet assessed. These estimations could be based on a combined translation of type and rubric size. Type should be based on materia medica, so keynote symptoms should be in bold type.

What about LR—?

So far, we have avoided the subject of LR—, the indication of how much our expectation for effectiveness decreases if the symptom is absent. We are still uncertain about the value of LR—. The main reason is

that we use a threshold value for our symptoms, also considering all circumstances. If, say, we assess ‘fear of dark’ there will be many patients where this fear is slight and below the threshold value at which we would include it in a repertorisation, but that does not exclude those patients from a medicine like *Stramonium*. Our materia medica validation showed that only 42% of the *Stramonium* patients have the fear of dark above our threshold value.⁶ It is possible, though, that these patients have a slight fear of dark. Therefore it might be useful to use a scale instead of a dichotomous value, eg a three point scale like: 0 = ‘symptom absent’, 1 = ‘symptom moderate’ and 2 = ‘symptom strong (constitutional)’. The same problem occurs with specifications of symptoms. If the patient does not have the symptom ‘fear of death, predicts the time’, but does have ‘fear of death’ without specification, it might be useful to apply intensity 2 for ‘fear of death, predicts time’ and intensity 1 for ‘fear of death’. Determining two threshold values will be more complicated than one, but it might give better opportunities to use LR—. This problem has to be investigated further.

Conclusion

Introducing LR to the repertory will not only change its content but also its use. Because of the altered use we should consider structural updating. Entries of medicines in the repertory must reflect the importance of the symptom in relation to the remedy, not the occurrence of the symptom in provings and casuistry. This new repertory will increase usefulness and reliability, especially of large rubrics. It will enable us to make more reliable predictions about the number of symptoms we need in one case and the curative potential of a medicine.

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