

Seventh Blackie Memorial Lecture 1995

PROVING THE UNBELIEVEABLE

By

Dr Klaus Linde

Introduction by Dr Iain Chalmers, Director, UK Cochrane Centre, NHS & R & D Programme, Summertown Pavilion, Middle Way, Oxford OX2 7LG.

There is a certain irony in this lecture about homoeopathy being given here in the Barber-Surgeons' Hall. Ivy Compton Burnett's father (Dr Margery Blackie's Uncle by marriage) was an homoeopathic doctor, and is quoted as saying: "The social value of surgery is a baronetcy; the social value of homoeopathic remedies is slander and contempt!"

Three hundred and fifty years ago, in Flanders, a physician called van Helmont deplored the common practice of bloodletting. He proposed that he and his bloodletting colleagues should take 300 to 500 people with fevers, and cast lots, such that one half should be treated by him and the other half by them. The number of funerals in each group was the outcome measure he proposed to assess the relative merits of their respective approaches to treatment. In this proposal, van Helmont was describing a way of making a fair comparison between alternative treatments - casting lots (randomising) to generate two similar groups of people who were then offered the different types of treatment.

One hundred and fifty years ago, in Boston, in one of the earliest examples of medical audit, doctors who did not use blood letting to treat pneumonia were deemed to be practising negligently. Indeed during the nineteenth century more generally, some really horrible things were being done in orthodox medicine. One of the ways women having eclamptic convulsions during pregnancy were treated, for example, was by mastectomy. It is not surprising that the ways of orthodox medicine prompted some people to ask: "Are there not more gentle ways to help people recover from their illnesses?" I imagine that this may have been one of the most powerful incentives for those who developed the theory and practice of the homoeopathy at that time.

Fifty years ago it was beginning to be accepted that the randomisation which had been proposed by van Helmont 300 years earlier was a sound basis for making fair comparisons between alternative treatments. Even so, many people, like the bloodletters before them, still believed it was reasonable to base practice on theories about why certain forms of intervention must be helpful, than on less carefully controlled comparisons. For example, some people thought that pregnant women, who had low levels of oestrogens in their urine, should be 'topped up' with a synthetic oestrogen called diethylstilboestrol (DES). Doctors who had used van Helmont's approach to assessing the drug's effects were unable to find any evidence that it was useful. The much greater number of doctors who had used a less cautious approach to evaluation (comparing the experiences of women who happened to have had the drug with those who had not received it) concluded that it should be given to all pregnant women. As a consequence, it was prescribed to millions of pregnant women over the subsequent few decades. As a consequence of this lack of therapeutic caution, a tragedy occurred which might have been avoided had the more cautious approach been adopted generally. Some of the daughters of women who had taken the drug developed cancer in their late teens and early twenties, and they and some sons of women who had received the drug have experienced other health problems.

Fifty years ago, not only were people beginning to learn about the dangers of extrapolating from theory to practice without taking notice of the important intervening steps of evaluating practice by generating fair treatment comparison groups, they were also learning about other ways in which bias can be misleading. Dr Wolf, a respiratory physician, was doing a placebo-controlled trial of a new treatment for asthma. He gave the new active drug to one randomised group of his patients and placebo to the other group and he

knew which of his patients were receiving the active drug and which the placebo. The patients given the active drug felt better than those given placebo and their respiratory function tests improved. So it came as a surprise to Dr Wolf when the drug company wrote to him apologising that he had been sent two lots of placebo, and no supplies of the active drug. Dr Wolf's experience is a reminder of the extremely important role that the so-called placebo effect (suggestion) can play in helping people to cope with illness.

Because of the need to make fair comparisons between alternative treatments, and the need to be aware of the dangers of jumping from theory to practice, a thorough review of the controlled studies of homoeopathy is very welcome. When I once said to a critic of complementary medicine - Peter Skrabanek - that it was important to conduct and consider the results of properly controlled studies in homoeopathy if one wished to come to a fair judgement about its effects, he suggested, "that I was so prepared to be open minded that my brains were falling out". Peter was unable to make me ashamed to be so criticised!

It is against this background that I am particularly glad to have been asked to introduce Dr Klaus Linde, who I have known for nearly three years. In my view, Dr Linde has prepared the most thorough review of the controlled studies of homoeopathy currently available, and I am proud that he is centrally involved in the Cochrane Collaboration's Complementary Medicine Field. He and his colleagues will help to ensure that review of complementary as well as orthodox forms of health care are disseminated and kept up to date through the Cochrane Database of Systematic Reviews.

Dr Linde studied literature before studying medicine in Bologna and in München, and even before receiving his medical degree he had become associated with the Münchener Modell - a programme of research to evaluate complementary therapies and to integrate teaching about these within the medical curriculum in Germany. It is with pleasure that I invite him to speak to us about "Proving the Unbelievable?"

Dr Klaus Linde, Physician at the 'Münchener Modell Project' Ludwig Maximillians University, Munich.

Introduction

PROVING THE UNBELIEVEABLE ?

Ladies and Gentlemen, it is a great pleasure and honour for me to be allowed to deliver the 7th Blackie Memorial Lecture. I am happy and proud to be here, and also a bit nervous. I was surprised to receive the invitation and, obviously, I felt so flattered that I agreed immediately. In the following months I became concerned when I read phrases like 'the Blackie Memorial Lecture is usually delivered by an eminent physician. I would not recommend you to send your patients to me, since after finishing medical school - quite by chance - I became immersed in research and have rarely seen patients for the last five years. Furthermore, I have never done original research in homoeopathy such as a laboratory experiment or a randomised clinical trial whereas I have in phytomedicine. I am one of these insupportable people called in Germany 'Besserwisser' - those knowing everything better than others. That is those who look at what others have done, and then tell them what their works showed and what was wrong with it. But at least, on this level I try to do my best. I am a young 'green' researcher. So please, don't expect wisdom from me. Maybe, however, some of my thoughts will reflect some of the things going on in research in homoeopathy.

I don't want to bore you with a long introduction, but before proceeding with my subject I want to provide you briefly with some background information on the 'Münchener Modell' the university project I am working in, thus making it possible for you to 'classify' me a little.

The 'Münchener Modell', the project for 'Integration of Natural Healing Procedures into Research and Teaching' at the University of Munich, started in 1982 as an initiative from students, practitioners and researchers. It is funded by the Bavarian Parliament and by a foundation. In the years until 1991 its main emphasis was on teaching the basics of complementary medicine to medical students. After this became a regular part of all German medical education in 1992, the project's emphasis shifted towards research. Although we also do some randomised trials and basic research, the major research topic is observational studies on large numbers of patients treated in clinics using complementary medical methods. Homoeopathy is obviously one of the most important, but most of the time it is used in combination with other methods. My personal responsibility in our project - which now includes more than 10 staff - are (1) systematic reviews of research on complementary medicine and (2) the coordination of controlled clinical trials. As I have a long standing interest in homoeopathy since medical school, I have included it as a major topic for systematic reviews.

With this background let us start to prove the unbelievable, and reflect on how the discussion on 'proving homoeopathy' has developed over recent years.

REVIEWING THE EVIDENCE ON HOMOEOPATHY

Previous review of homoeopathy

I was always surprised and confused by the unscientific nature of the 'scientific' discussion of homoeopathy. In the main, it is not a discussion of the principles, characteristics and implications of homoeopathy, but of the question "do potencies and in particular, high potencies, have a specific effect?" The translation of this question into clinical research leads to the question posed by David Reilly in the title of his famous hay fever trial published in the Lancet in 1986: "Is homoeopathy a placebo response?" [1].

There are many experts - both homoeopaths and scientists - who have drawn their 'scientific' conclusions about the evidence for or against the existence of effects of high dilutions or high potencies. In the beginning,

I was completely confused by the fact that everyone seemed to draw a different conclusion. Consider the following two examples:

The first is taken from a joint statement by Prokop, Glowatzki, Binder, Posnansky and Hopff in a book by the pharmacologist Hopff[2], 'Homoeopathy - a critical view', published by a major German mainstream medical publishers (Thieme):

'It is important to mention that homoeopathy has often been tested by competent scientists of many disciplines in public institutions, as well as in special clinics at universities. It has, however, never been shown to be superior than non-treatment or placebo'.

The second example is taken from a review of the Austrian homoeopathy Müller [3]:

'Summarising, it can be concluded that numerous laboratory and clinical experimental studies, conducted in strictly scientific conditions, prove clearly the efficacy of homoeopathic remedies.'

After having read a number of such review papers on homoeopathy, I thought that the reason for these contradictory conclusions was that a small number of experts only cited results consistently with their previously held conclusions. A larger number, whilst preferring to cite results concurring with their 'conclusions' also tried to be as objective as possible, by discussing contradictory results. However, there were always weaknesses and deficiencies in these contradictory studies, and so, in the end, the original conclusion could be reached.

In 1991 a paper was published in the British Medical Journal [4], which - as I thought - had surmounted all the drawbacks of these other reviews. Jos Kleijnen, Gerben ter Riet and Paul Knipschild from the Department of Clinical Epidemiology at the University of Maastricht had collected all available controlled clinical trials of 'homoeopathy'. Controlled clinical trials are seen as the best type of evidence for showing that an intervention is effective. Kleijnen et al. not only collected every trial they could but, in addition had taken a very important further step: They had predefined their criteria to distinguish the 'good' from the 'bad' valid and invalid data. They used a system which gives points (a score) if certain methodologies criteria are fulfilled and came up with charts of the trials of homoeopathy. The best trials were at the top of the charts, the worst trials were at the bottom. They found that nearly 80% of the trials results favourable for homoeopathy, and among the better trials about two thirds had 'positive' results.

For convinced homoeopaths it was clear: 'Homoeopathy was proven scientifically'. For fully undecided people the conclusion was probably: 'Homoeopathy might work'. Kleijnen et al. who are open sceptics had a very interesting conclusion: they would be ready to accept that homoeopathy can be effective if only the mechanisms of action could be determined. Peter Götzsche, a well-known methodologist from Denmark, commented on the review of Kleijnen et al. in a letter to the Lancet, in a way that probably represents the opinion and conclusions of the group of people who I would call 'convinced sceptics': 'Rather than accepting the absurd idea that placebo can be better than itself, it seems more realistic to assume that the positive results in the homoeopathy trials were caused by bias.' [5]

There were two critical points in the review of Kleijnen and colleagues:

- The first was on the score for assessing the quality. In general, such scores are controversial as there is no gold standard to quantify quality. In particular, Kleijnen's score did not include a methodological key

issue, the question of bias induced by excluding patients from the analysis who originally entered in the trial.

The second critical point was the way they assessed the study results. Kleijnen et al. did a so-called vote-count: they separated the trials into 'positive' and 'negative', mainly based on the conclusion of the authors of the original trials. This method is extremely crude and has problems regarding sensitivity (high likelihood of missing small effects), reliability (different authors may come to different conclusions), and validity (does the "vote" really represent the study result). From a homoeopathic viewpoint a lot of criticisms could have been raised, but as the results of the Kleijnen's review were so favourable for them, homoeopaths were very reticent to speak out.

Our own systematic review.

As even this excellent review had relevant shortcomings and the controversy on homoeopathy was still not solved, we thought arrogantly, perhaps! We could do the definitive review of controlled clinical trials of homoeopathy, avoiding the shortcomings of the previous reviews and providing final answers. For more than three years we have worked on this review. It is a collaboration between a number of people in Munich (Nicola Clausius, Dieter Melchart, Florian Eitel), Wayne Jonas, the director of the NIH office of Alternative Medicine in Bethesda, Gil Ramirez, the co-director of the San Antonio Cochrane Center, Texas, and Larry Hedges, Professor of Statistics in Chicago. Our protocol versions were peer reviewed by a number of critical and helpful experts including Iain Chalmers, Andy Oxman and Peter Göttsche.

Some days ago, we did the first analyses of all our data and the answer seems to be clear; it is

'No'

or in numbers: the odds ratio is 1.34

What does this mean:

I don't know how many of you know Douglas Adams' comedy science fiction radio series 'The Hitchhiker's Guide to the Galaxy' which was later published as a novel. There is a chapter in which Adams is narrating the story of a very intelligent population who developed a huge computer whose only task was to find the final answer to all questions. The computer thought and calculated for several million years and finally gave out the information that he found the final answer. A number of scientists were elected to be the first to hear it. When the great moment had come the computer seemed to very nervous and did not want to come up with it. But finally he told the scientists that the answer was 37. the scientists were really struck. The computer then told them that they now had to find the exact question for that answer. It would be unable to resolve the problem but it could plan a new and better computer and after several billion years, it would get the question.

We had an explicit question in undertaking our review. However, I am not sure if our answer is meaningful. You may consider it for yourself. What exactly did we do?

The primary question was:

Is (there evidence that) all homoeopathy (is) a placebo response? Or put another way: what is the mean effect of homoeopathy compared with placebo, and is this compatible with the placebo hypothesis? From the beginning we were aware that this question was problematic (would you ask: is a drug therapy a placebo response?), but - as mentioned above - this is the crucial point in the academic discussion of homoeopathy.

We had several sub-questions, but even though they are still broad and crude, they may be difficult to understand for those knowing little about homoeopathy.

Is classical homoeopathy a placebo?

Is clinical homoeopathy a placebo?

Is complex homoeopathy a placebo?

Is isopathy a placebo?

Are high potencies placebos?

We decided to use two approaches to answer our questions. In the first, all studies were grouped together, regardless of comparability in a clinical sense.

In the second, we looked for subsets of independently replicated clinically comparable trials, using a similar homoeopathic interventions (e.g. the same remedy) in similar patients (e.g. pollinosis) measuring similar outcomes (e.g. severity of ocular symptoms).

Methods

We did an extensive literature search for prospective randomised, and/or double-blind, clinical trials comparing a homoeopathic intervention to a placebo. From the trials identified, we extracted information on the patients, the interventions, outcomes, methodological details and results. Methodological quality was rated using two different score systems, with a higher score designating 'better' quality.

Finally, the results of the clinical trials selected had to be summarised. We used a predefined strategy with preferences as to what, and how, to extract the results from the single studies. As a first preference we extracted data for predefined main outcome measures, second and third preferences were patient and physician global assessments, and if a study had no such data we chose the outcome which seemed clinically most relevant.

If results from several different studies are quantitatively summarised, it is called 'meta-analysis'. In doing this first the size of the effect of every study is estimated and then all the material is lumped together and an average effect size is calculated. Normally, this should be done with studies which are similar with regard to patients, interventions, outcome and quality. Even then, meta-analysis may be problematic. We had studies differing in all respects, but as our undifferentiated questions required such an approach, we lumped everything together.

Additionally, we globally categorised a study result as positive (homoeopathy better than placebo), no difference, or negative (placebo better from homoeopathy). This method is called a vote count.

Results

The results presented here are preliminary results from our first analysis; the final results will be published elsewhere.

We identified 184 controlled clinical trials of homoeopathy. 35 investigated an individualised intervention ('classical' homoeopathy), 101 the use of a single remedy for a certain condition ('clinical homoeopathy'), 35 complex preparations (fixed combinations of remedies for certain conditions), and 13 isopathy. 133 clinical trials included a placebo-control and 118 of those met all of our preset inclusion criteria. In 73% of these trials there was at least a trend in favour of homoeopathy, in 24% there was no difference, and in 3% placebo was better.

74 trials contained sufficient data for our preliminary meta-analysis. Overall, in the trials included, homoeopathy was statistically significantly

superior to placebo. The results were similar when classical homoeopathy, clinical homoeopathy, isopathy, complex preparations and high potencies were analysed separately. When we analysed the results of those studies which met our predefined criteria for 'better quality, the superiority of homoeopathy versus placebo was less marked but still significant for most subgroups.

Discussion

Please, be aware that this is not truth, this is just a systematic review. Our results might have been distorted by publication bias (failure to publish undesired negative results), by flaws in the trials as well as in our review. Furthermore, we found no independently replicated trials using the same remedy, in similar patients and measuring similar outcomes.

However, we tried to control for biases as much as possible, and performed several sensitivity analyses to check the robustness of our results. In conclusion, the trials available do not support the hypothesis that homoeopathy is a placebo.

But is that unbelievable, i.e. homoeopathy now proven? And, if not, do you think that if ten more positive trials were published it would then be proved?

THE AUTOGANZFELD DEBATE

Maybe the socio-scientific processes and complexity of proving controversial hypotheses will become a little clearer if we look on other controversial areas of research.

Experiments in the area of extra sensory perception (ESP), in the sphere of para-psychology, deal with things that are even more unbelievable than homoeopathy. Their trials have to be even more rigorous, and looking at the literature shows how intriguing their studies are. I want to show you that even with very good empirical evidence it is hard to convince anyone.

Maybe the most straightforward experimental evaluations of ESP are the Auto-Ganzfeld experiments. In a very simplified manner they can be described as follows: the human subject on the receiving end of this experiment is sitting in an acoustically isolated room wearing headphones through which he hears white noise. He is perfectly relaxed and his eyes are covered. In another room a distance away, is the sender, a person like you and me, with a computer which selects pictures at random, from a stock of two hundred. The sender is asked to concentrate and to 'transmit' the picture to the receiver for thirty minutes. At the end of 30 minutes the receiver is asked to identify the picture received which fits best his perceptions and feelings during the 'transmission' phase from a set of four (the 3 'wrong' pictures again chosen by the computer at random). By chance, you would expect in a large series of such experiments that the 'transmitted' picture is correctly identified 25% of the time. However, in several series of well-controlled studies up to 1985, the hit rate was about 35% and the statistical significance of the effect was 'astronomic'[6].

Was this the proof that ESP exists?

Obviously - and absolutely correctly according to my opinion - the results of these Ganzfeld experiments did not lead to an uncritical acceptance of ESP [7]. Science often has to face sensational claims supported by a certain body of evidence which are subsequently shown to be unjustified. And - also absolutely correctly in my opinion - you need more, and better evidence for 'proving' ESP or homoeopathy than for proving that aspirin is effective in decreasing headache. There is simply more background knowledge to make the effectiveness of aspirin plausible, than for effects of homoeopathic high potencies or for ESP.

What were the arguments of the sceptics?

The first argument was that the ESP results were not really positive, but mere fluctuations due to chance. This was due to the fact that originally the results were not presented in the easy and straightforward way above. However, when the analysis was restricted to the above-mentioned simple 'hit rate' it became clear that this argument could not invalidate the findings.

An obvious second argument was the existence of publication bias. Although this argument could not be invalidated totally by the ESP researchers, there were several points which made it unlikely. (1) the Parapsychological Association has had an official policy against selective reporting of 'positive' results since 1975. I don't know if any other scientific society has yet come so far! (2) Well-controlled Ganzfeld experiments need considerable financial and laboratory resources. Very few labs have the capacity to do such research in a reliable way; this fact - which is clearly a problem for independent replication - makes publication bias more unlikely. (3) The parapsychologists calculated the number of experimental sessions needed to nullify the findings by chance. Given the high degree of significance on the results, this number was so high that it was simply not reasonable to assume publication bias as the cause of the observed results.

Finally, sceptics suggested there were flaws in the experiments: sensory leakage, deception, fraud and so on. Compared with most clinical trials in conventional medicine or homoeopathy, the early Ganzfeld experiments were much more rigorous and straightforward. But as the results seemed so implausible, it was assumed that there simply had to be bias.

At this point something quite unique happened: The most prominent sceptics and proponents came together to make a joint communiqué on how future experiments should be done to be really convincing [8]. In 1994, the results of these experiments were published in a major psychological journal. Still the results were 'astronomically' significant with a hit rate of about 35% [9]. Again the discussion started. Again statistics and methodology were discussed but there was little reason for serious doubt. Finally, the argument was put forward that the assumption that ESP exists is absurd and incompatible with scientific knowledge, and therefore, the results could not be true.

Although such reasoning is not scientifically reasonable it is quite common. The lesson to be learned from the Auto-Ganzfeld debate for homoeopathy is that one should not expect that by accumulating more and better empirical evidence, the controversy will be automatically solved.

IF HOMOEOPATHY IS A PLACEBO.....

Let's come back to homoeopathy. The existing evidence to indicate that homoeopathy cannot be seen as a placebo in general. However, I want to raise the hypothesis: 'homoeopathy is negligible. In the end, it might be that the effect of the remedy itself is not, or not very often, the major cause of improvements or changes.

DISCUSSION AND CONCLUSION

I fear that you may be confused but, I hope, not only due to my presentation.

We have seen that the available controlled clinical trials seem to provide evidence that homoeopathy cannot be regarded only as placebo. The example of ESP research shows that by simply accumulating good evidence it is difficult to solve controversies concerning 'unbelievable' issues.

Finally, I tried to explain why the limitations in investigating the 'specific' effects of a therapy might lead to a rejection of beneficial therapies.

Clinical research on homoeopathy has been focussed up to now mainly on the placebo question. In recent years a number of excellent trials on this type have been performed. Although most of these trials showed at least a tendency in favour of homoeopathy, the superiority over placebo was often disappointingly small. In most areas of clinical research effects sizes become smaller, the more the quality of the trials improve. I predict this for clinical research on homoeopathy too, even if homoeopathic remedies should cause specific effects. Double-blind placebo-controlled trials are useful, but the limitations of that approach might result in misleading conclusions about clinical effectiveness.

Only a few trials have compared homoeopathic treatment strategies to standard therapies and very few of these trials used a pragmatic approach to testing homoeopathy in conditions similar to its actual practical use. There is a clear need for more pragmatic trials. However, there are a number of practical problems. (1) 'Conventional' physicians are often reluctant to randomise their patients to a treatment which they consider to be a placebo. (2) Pragmatic trials are more open to bias, and given the controversial character of homoeopathy, will be strongly criticised. (3) And most important, there is not enough information on the practical use (conditions, interventions) and results (response rates) of homoeopathic treatments, to systematically identify the most relevant areas for research and to develop conclusive protocols. Up to now, most study models were developed placebo. The homoeopathic medica is based on observations which are, at least in part, of a doubtful validity. Recent well controlled provings (e.g. [10]) provide convincing evidence that volunteers receiving a placebo develop as many and very similar symptoms as those getting the remedies. I haven't seen a rigorous proving which has shown convincingly that a remedy causes more or different symptoms to a placebo. This does not mean that provings have not provided useful information, but even for a critical component of homoeopathy - which I would consider myself to be - it is hard to imagine that all information in material medicae and repertories is reliable. Another critical point is the impression that different homoeopaths seem to treat patients very differently, even in the same country. Are there really so many correct 'similes' for a patient?

So, even if homoeopathy might work in principle, I hypothesise that in everyday practice it is often 'only' a placebo. But I speculate that - at least in the case of good standard of homoeopathy, taking seriously the patient as an individual - it can be effect.

How can this be?

Imagine a double blind controlled trial of an analgesic versus placebo for chronic pain. The analgesic might have improved the complaints in 50% of the patients, the placebo in 30%. In consequence the analgesic is 20% better than placebo. In a second hypothetical trial, a classic homoeopathic strategy is compared to placebo. In both groups 60% of patients might have improved; in consequence, it is no more effective than placebo. Imagine now that the results do not come from two separate but from one trial: patients would be randomised to the two double-blind studies. The 'homoeopathic placebo' would be more effective than the analgesic but 'only a placebo'. As a patient, which treatment would you prefer?

These trial results are pure speculation, but there is good evidence that response rates in placebo groups of similar trials vary greatly and have a relevant impact on results (see e.g. [11]). Individualised homoeopathic treatment involves a lot more than prescribing a pill and it might well be that a number of these processes (e.g. repeated intense anamneses, instructions regarding nutrition) cause specific and beneficial effects. All

of these are classified as 'placebo' or 'unspecific' effects, once the investigation begins to look at potentiation. All those who have experienced the atmosphere of a well done homoeopathic consultation, realise this possibility must not be regarded as on the basis of practicability and acceptability to methodologists. Furthermore, homoeopaths, overestimating at least the specific effects of their methods, agreed to study models which were far removed from their actual practice.

In conclusion, I think what is needed most at the moment is more descriptive information on the actual use of homoeopathy, on structures, processes and outcomes whether homoeopathy is 'scientifically proven' or not and it is widely used. Homoeopaths should learn the basics of methodology, to learn that double-blind placebo-controlled trials are not the only tools available, and the placebo question not the only relevant one. Various questions are relevant, and to answer these a number of different and valuable tools exist and should be developed. Research on homoeopathy should not only be seen as a cumbersome way to prove the unbelievable, but to describe, understand and improve actual performance.

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Mr Robin Holland Martin, Chairman of the Trustees of the Blackie Foundation Trust gave the vote of thanks.

It is very relevant that we are meeting in the City of London today, for two reasons. First of all, this lovely building is steeped in the history of medicine and in the history of the Worshipful Company of the Barber Surgeons. The best part of the Hall is behind the projector screen in the shape of a magnificent portrait of Henry VIII by Holbein. If there ever was a monarch who needed constitutional typing, it was Henry VIII! He certainly should be studied; there he was irascible, reddish haired, creative, decisively indecisive about marriage - all sorts of elements which our honourable research director, William Davey, could have easily tackled if he had been looking after that monarch as well as the current one.

The second reason for coming back to the City is that twenty five years ago in the Guildhall, just a stone's throw across London Wall, Dr Margery Blackie organised a rather majestic evening which the Queen attended. At that reception she managed to raise more than £10,000, which in today's currency is equivalent to about £80,000. This evening was a landmark for Homoeopathy in the United Kingdom, and it was with this capital that she set up the Blackie Foundation Trust the following year. She called me in as a trustee to watch over the investments purchased with the money raised.

We have moved on from there. The first ten years of the Trust's activities were concentrated on education. This was a great stimulus to the doctors of the day taking courses - Margery had an inimitable style when conducting these events. It was only the year she died in 1981 that we managed to attract William Davey to come in and lead us in the direction of research. He has succeeded in that, as has been illustrated today, and he has been responsible for the very high standards attached to the Trust's research activities. It has been a very interesting twenty-four years the Trust has enjoyed so far. There is no doubt that in this extraordinary world looking at homoeopathy there is a lot more that can be done and we have had a most interesting stimulus today.

I turn now to our Guest Speaker to thank him very much indeed for coming to speak to us today. It was quite an imposition to ask you and I wondered why you had accepted! The answer was that we caught you wondering what it was going to be like. We are delighted you have taken the time and trouble to come here from Munich. It has been a very provoking and stimulating event and we thank you enormously for your contribution today. You spoke with clarity, conducting us through a complex subject so that we all could begin to understand and grasp it.

Perhaps I could add a few more thanks. First of all to the Master of this august Company. It is through his kindness we are here today, and his staff have been very helpful in making the day a success. It is also very good to see all those who are involved in the Blackie Foundation Trust here this evening, starting with our President Sir Maurice Laing and his wife and some of the Trustees, and the members of that very active body, the Scientific and Ethical Committee, chaired by Dr Kim Jobst. We have shared out responsibilities, with Galen Ives chairing this morning's session and Michael Denman this afternoon's; and Iain Chalmers introduced our guest speaker. We are very grateful to you all for what you have done today and in the past. I would like to give one special thanks which is to our organiser, Penny Ephson, who has worked unstintingly over these last few weeks to make the meeting a success. She has a more important event ahead of her on Saturday, but that has not distracted her from concentrating on the details of today. Well done, and a warm thank-you also to all the volunteers. Finally, our thanks to all the participants and guests, who are now invited to retire for well-earned refreshments.