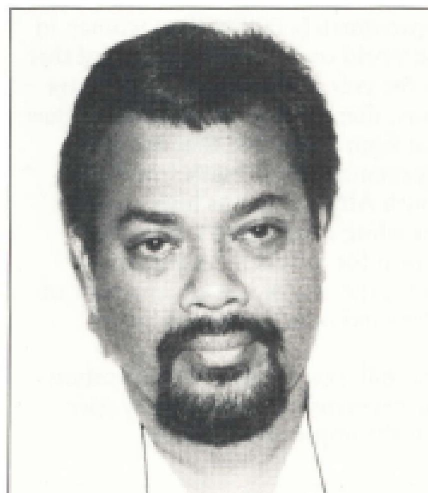
Hormone Replacement Therapy versus Nature

The Case for Hormonal Replacement Therapy

— Jimi la Rose



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Curriculum vitae

Jimi was born in Georgetown, Guyana, and graduated from the University of the West Indies, Jamaica, in 1974. After completing his internship, he studied Acupuncture in Beijing (PROC) and later spent a year researching the effectiveness of Acupuncture in a multi-ethnic population in Guyana. From 1977 to 1987, he worked with USAID, in association with the MEDEX Group, University of Hawaii, as an International Health Manpower consultant on training of trainers of mid-level and other PHC workers in Guyana, Pakistan, Lesotho and Liberia. In 1987, he worked with Howard University as an advisor on Medical Education to the Government of Malawi. In 1988, he completed his MA in Education at Columbia Pacific (USA). He joined the Department of Family Medicine at Medunsa in 1989 and is currently the Coordinator for Undergraduate training in Family Medicine, while completing his MPrax Med studies. He is married and has three children. Jimi has a special interest in Medical Education and in particular Student-centered learning.

Summary

The medical history of a black woman treated with Hormonal Replacement Therapy, is presented as a court case before a Judge and a jury. It is argued that although one should and could not treat all menopausal women with hormones, it was the best thing to do for this particular patient in these circumstances, and it was not interfering with nature to do so. Other issues dealt with, are: the prevention of osteoporosis by HRT, the long term side-effects versus its usefulness, the vasomotor and psychological symptoms associated with menopause and the financial costs involved.

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KEYWORDS:
Case Report; Drug Therapy; Hormones; Menopause

"There is a season for everything under the sun"

Ecclesiastes 3:1

Your Honour, members of the jury, ladies and gentlemen. With the court's permission, I would like to respond to my learned opponent's arguments and the evidence presented so far, both for and against the use of Hormonal Replacement Therapy for my client's patient.

My client has been brought before this court on the charge of *"deliberately interfering with the course of Nature"*, by prescribing Hormonal Replacement Therapy for a patient. The prosecution argues that to do this, is contrary to the wishes and intent of Nature. Unfortunately Nature was not put on the stand to agree with this statement or not. On this stand is my client, a respected family doctor, and central to this trial is his patient. I would like to take the opportunity to refresh your memories as to the data pertinent to my client's patient.

Sandra is a black 40 year old female nurse practitioner from a nearby township. She is unmarried, without children and has two younger sisters. Both of her parents are alive and well. She qualified as a nurse in 1978 and then as a nurse practitioner in 1987. She had been in practice for the past 4 years. It was during this time, in fact, November 1989 to be precise, that she reported to her family doctor, my client, with the complaint of severe lower abdominal cramps and irregular menstrual bleeding. Because of his findings on a gynaecological examination, he referred Sandra to a competent gynaecologist at the nearby tertiary care centre. She was advised to have a total hysterectomy because she had large fibroids and one of them was undergoing red degeneration. She was informed prior to the operation that she could go into artificial menopause and of all its consequences, as the operating surgeon could not guarantee that her ovaries will be preserved. After discussing it with her family doctor, she opted for the operation. She had an uneventful postoperative period. She later in 1990 presented to my client complaining of hot flushes and insomnia. She was advised that this was normal and to be expected of a woman after menopause. She claimed that she understood and opted to see if she could live with it. She again presented to my client three months

later still complaining of severe hot flushes and now she was becoming irritable and extremely tired. My client opted to prescribe Clonidine and a small nocturnal dose of Imipramine. Sandra reported a month later that although she was sleeping much better, the hot flushes were the same and she was just as irritable and tired. She then requested my client to prescribe some of Oestrogen/Progesterone tablets that are scheduled only for women in their reproductive years, and to be used only for contraceptive purposes. My client after excluding contraindications, and finding nothing on physical examination, prescribed Prempak. He was reported by an overzealous colleague for an infringement of the HRT Act 89, paragraph 2, promulgated in 1989. Your honour, ladies and gentlemen of the jury, it is not my intention to deny that my client did wilfully contravene the regulations, nor is it my intention to persuade you that the regulations are inappropriate when generally applied.

Deliberately interfering with the course of nature?

It is my intention however, to ask you to look at my client and in particular the circumstances under which the medication was prescribed and judge for yourself, given who Sandra was, and is and perhaps could never be, whether my client while contravening the law, might not have been following the dictates of a higher law, that of Nature itself, the very law he is charged of transgressing.

Let me first start off by looking at the evidence presented by my learned counsel, representing the Establishment. He stated, quite correctly, I may add, that the average age of the menopause has not changed over the centuries. He presented evidence led by two expert witnesses, Brincat and Studd,[1] to the fact that in the 6th century AD, Aristotle reported that the average age of the menopause was 50 years, the same as Paulus Aegineta one century later, the same as Hildegard in the 12th and Gilbertus Anglicus in the 13th century. These same experts testified under oath, that the age of the menarche, socio-economic factors, race, poverty, weight or height do not appear to be related to the age of the menopause. What my learned colleague failed to mention, also reported by the same experts, was the little known fact that the average life expectancy of the woman has increased tremendously since the last century. At the time of the Roman Empire, the average life expectancy of women was only 23 years. From the Middle Ages until the late nineteenth century, fewer than 30% of women reached the menopause. Today with the average life expectancy of women being 78 years, there are just under 10 million post-menopausal women in the UK and over 40 million in the USA. Silman writing in the BMJ[2] states that in 1980, there were approximately 600 million women in the world over the age of 65, and that by the year 2000, a mere eight years away, there will be at least three times that figure. Granted that the life expectancy of our black women in South Africa is not as high as with her white counterparts, this is no reason for my client's patient to spend the rest of her life in a state of profound oestrogen deprivation.

600 million women older than 65 years (in 1980) – and there will be 1 800 million in the year 2000!

Secondly, on a point of clarification, the prosecution inadvertently gave you the impression that the menopause was the period of life after menstruation ceased. The term menopause only refers to the one fixed event in a woman's life and is the last menstrual bleed in the same way that the menarche refers to the first menstrual bleed.[3] To be precise, that period of time around the cessation of menstruation is called the climacteric after the greek word-*klimakter* meaning critical age or rung of the ladder. The climacteric is indeed to many women a "critical age"-physiologically, socially, sexually and psychologically. The extent of the climacteric changes varies from person to person, community to community and country to country. Professor Denis Davey from UCT,[4] stated in this court, that in the "western world" on the average, probably 75 out of every 100 post-menopausal women will experience some climacteric symptoms, and nearly one quarter of them will seek help from their family doctors. This means that on the average 15 to 20% of all our

At 70, a woman could lose 50% of her bone mass.

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climacteric women, our sisters and mothers, will present themselves to their doctors for attention.

The climacteric can thus truly lay claim to being one of the commonest medical conditions known to women and its management must concern most medical practitioners. Oblivious to reality, my colleague from the Establishment, belittles Sandra's symptoms. He argues, quite amazingly, seeing that he is a man, that Sandra's symptoms were minor.

I have provided you with the opportunity to judge for yourself as to how severe her symptoms were, by having Dr MacLennan, the Director of the Royal Adelaide Hospital's Menopause clinic,[5] testify that her condition was serious. He presented an Oestrogen Deficiency Symptom Scoring System, as an objective method of having the patient quantify the severity of her symptoms. We offered the court the opportunity of cross-examining Sandra in order to

HRT most useful for relief of hot flushes.

have her respond to the questions on the scoring system. You heard with your own ears, how she felt as a person and saw how she scored on that system. I ask you to take a moment and review her score on the Oestrogen Deficiency Symptom Scoring system - exhibit A. I remind you that according to Dr MacLennan, a score of 15 and over, correlates strongly with objective measurements of oestrogen deficiency.

Exhibit A. Oestrogen Deficient Symptom Scoring System[5]

NAME: Sandra Sithole
Age: 40 yrs

Symptom	Score
Hot flushes	2
Light Headed feelings	1
Headaches	1
Irritability	2
Depression	1
Unloved Feelings	2
Anxious	1
Sleeplessness	3
Unusual tiredness	2
Backache	0
Joint pains	0
Muscle pains	0
New facial hair	0
Unusually dry skin	0
Less sexual desire	1
Less sexual feeling	1
Dry vagina	2
Dyspareunia	2
Total Score	21
Treatment on/off	off

0 = absence
1 = mild
2 = moderate
3 = severe

Furthermore, ladies and gentlemen of the jury, my colleague from the Establishment was allowed to introduce evidence, (which I objected to, but the Honourable Judge deemed as admissible), to tell you of a truly unfortunate occurrence with the use of Hormonal Replacement Therapy, before the ban by the Establishment. He related to you the sad story of a 44 year old shop assistant presenting to her doctor requesting long-term use of Hormonal Replacement Therapy.[6] She had been to a community talk by a local gynaecologist on the subject. He had recommended it to all women in order to prevent osteoporosis. Although she was not

In 1987 in Australia, 1/6 of the drug budget spent on oestrogen related diseases.

troubled with any menopausal symptoms, she decided that she would like to try it.

She had an unremarkable menstrual history. Her blood pressure was normal and her last Pap smear done recently, was normal. She was started on Prempak - 0,625mg daily. For the first year, things went well. Then she started to have intermittent, irregular vaginal bleeding, which she attributed to her missing some tablets. Over the next few weeks, the bleeding became heavier and more prolonged.

She became listless and even lost some weight. On returning to her doctor, she was advised to stop the Prempak. However the symptoms continued and she was advised to go to a gynaecologist for a diagnostic dilatation and curettage. Curettings revealed endometrial carcinoma. A hysterectomy confirmed an invasive, poorly differentiated adenocarcinoma, with local spread into nearby lymph nodes. She was treated with post-operative

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radiotherapy and progesterone for sometime, but died within nine months. I agree, a terrible case, but my client's patient, apart from being female and in her forties, has nothing in common with this unfortunate patient. Was this case relevant to the situation with my client and his patient? Certainly. The prosecution presented this case to raise certain issues germane to the whole issue of HRT in general. Some of the issues raised in this courtroom were as follows:

The patient is the final expert on her own body, feelings, concerns.

a. Should long term HRT be recommended to all women as a prevention against osteoporosis?

b. Don't the long term side effects outweigh its usefulness?

c. Should HRT be advisable for all menopausal women, wouldn't the cost be astronomical?

d. What real evidence is there to support the use of HRT in treating the vasomotor and psychological symptoms supposedly associated with menopause?

Prevention of Osteoporosis

The prosecution has presented evidence in support of an age related bone loss in both sexes[1] and that there is an acceleration of the rate of loss in women after menopause. It is estimated that by the age of 70, a woman could lose 50% of her bone mass, while a man would only lose 25% by the age of 90. This loss of bone mass makes the woman more prone to develop hip and forearm fractures. However, the expert continued to state that these statistics only apply to white (Caucasian) women, because they start off with a lesser peak bone mass and lose bone faster than black women. I will concede that this factor may affect if and when Sandra develops osteoporosis. He also correctly states that underweight women, (and Sandra certainly does not fit in this category, as her weight was 78kg and her height was 1,6m,) or women with a small build are at greater risk due to a reduction of peripheral conversion of adrenal androgens to oestrogen. Sandra does not live a sedentary life-style. She walks at least 3 kilometres every day to work and seems to be always on the move. Sandra does not smoke or drink alcohol, factors known to increase bone loss. The only risk factors for osteoporosis[7] that Sandra has, is that she has never been pregnant and she lost ovarian function before the age of 45. Apparently Nulliparity is a risk factor. It is possible that during pregnancy, some of the age related bone loss is arrested so that a woman who has had repeated pregnancies will end up having a greater peak bone mass at the time of her menopause. What am I trying to say? I am trying to say that if I were to argue that my client used HRT under the guise of preventing osteoporosis, then, it would be false. My client was well aware of the lowered risks of osteoporosis in the black female population.

To answer my learned colleague's original question - should HRT be given to all women, and especially black women in South Africa, to prevent the development of osteoporosis? The answer is no. It should only be given to those at high risk of developing osteoporosis and Sandra, fortunately does not fall into that category. Neither was HRT prescribed to Sandra for this reason.

Usefulness versus side effects

Another question was raised. Don't the side effects, especially the long term ones, outweigh any so-called usefulness of HRT? I agree that the use of unopposed oestrogen replacement therapy in post-menopausal woman with intact uteri, has been shown to be associated with an approximately doubling of the incidence of endometrial carcinoma. This is not the case with my client's patient. Sandra is without her uterus. She will never, I repeat, never ever run the risk of developing a cancer in her womb because she has none.

My learned colleague also raised the possible association of HRT with an increased incidence of breast cancer especially with prolonged use of oestrogens. Recent evidence mentioned by Prof Davey[4] during my cross-examination, in fact, shows the opposite. If I may quote the respected professor, "Recent evidence from a study by Gambell in 1982, suggests that in women receiving combined cyclical oestrogen/progesterone therapy, the incidence of breast cancer is not only *not increased* but it is *reduced* to one sixth of the naturally occurring incidence. I

Not all women want or need HRT.

...Hormone Replacement Therapy

suggest therefore, that HRT especially the oestrogen/progesterone form, may not only be regarded as safe, but that there is the distinct possibility that it might also help to prevent Sandra from developing breast cancer.

Finally the last possible side effect my client has exposed his patient to, is the possibility of an increased risk of developing clots in her blood vessels.

Life should be measured not so much in the number of years, but in the quality of those years.

This is seen more commonly with the synthetic rather than the natural oestrogens. My client prescribed Prempak, which has natural oestrogens plus progesterone. It is unlikely that Sandra will develop a stroke because of HRT.

Costs concerns

If HRT were to be recommended to all menopausal women, wouldn't the costs be prohibitive?

Without a doubt, if the medical establishment were to recommend the blanket use of HRT in all post-menopausal women, it would be a tremendous burden on the health budget. In fact in Australia, in 1987,[5] nearly one sixth of its drug budget was spent on oestrogen deficiency related diseases. This is an expensive proposition. However the improved quality of life rather than cost is likely to be the prime motivating factor when the public becomes more aware of the distinct advantages of HRT. However, that is not the question before this court. I am not asking this court to sit in judgment of the appropriateness of HRT for this nation. I am asking you to decide whether it was inappropriate for my client to prescribe HRT for one person, Sandra.

The treatment of hot flushes

Is there any real evidence to support that hot flushes can be better treated with HRT rather than other drugs?

The prosecution presented evidence that I did not contest, stating that Clonidine[1] is an effective drug to treat the symptoms of vasomotor instability common to some post-menopausal women. Although flushes are the most characteristic symptoms of the climacteric, not much is known about their aetiology. The precise role that oestrogens play has yet to be established. Explanations such as the one offered by Prof Davey,[4] suggesting that each hot flush is associated with the release of Luteinizing Hormone Releasing Factor and Luteinizing Hormone, are certainly wrong, because the flushes occur with greater severity in women who have been hypophysetomised.[1]

Brincat and Studd[1] suggest that all the major sex steroids seem to play a part. Clonidine, a midazoline derivative and a central alpha-adrenergic stimulant, has been used in the past with some success. However in carefully controlled trials, it has not been shown to be better than a placebo. It however does appear to be of value as supplementary therapy in patients with vasomotor symptoms not relieved by oestrogens.[4] Prof Llewellyn-Jones[3] added his voice in support of the relief offered by oestrogen to patients with uncomfortable hot flushes. My answer to the prosecutor's question is Yes. There is evidence that drugs other than HRT are useful, but none as yet to suggest, more useful than HRT in the relief of hot flushes.

Psychological benefits

Finally, is there any real evidence that the psychological changes experienced by a menopausal woman, respond better to HRT as opposed to psychotherapy?

My colleague argues that the depression, irritability, feeling of being unloved, that some climacteric women experience, has no direct relation to the loss of ovarian function per se. I do acknowledge that there are many problems associated with women around the age of 50, that may have nothing to do with oestrogen deprivation. The older woman may be stressed by her elderly parents, pressures from adolescent children. Her role may be undergoing a change[5] from being a busy mother to the feeling that she is unneeded, unappreciated and aging. The prosecution stated that unlike the situation with hot flushes and vaginal dryness, in which there is strong evidence to support their association with the climacteric,[8] there is no such strong evidence to associate depression and other

Nature was messed up by degenerating fibroids and a hysterectomy.

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psychological experiences with it. It is a well known fact the highest incidence of Depression in the middle life years does not occur after the menopause but in the few years preceding menopause,[1] suggesting therefore, that it is not the low oestrogens, but the change in hormonal concentration, much like the cyclical depression of the Premenstrual Syndrome. Women who are prone to depression, are more likely to be anxious about menopause and attribute their low moods to it. Myra Hunter from King's College Hospital in London,[10] testified that in her prospective study of 47 women, 31 were peri-menopausal, 10 were post-menopausal and 6 were pre-menopausal, she could find no strong association between the menopause and their mood changes. She stated that while biological explanations could not be ruled out, psychological and social factors such as previous depression, negative beliefs and socio-economic status, appear adequate to explain a reasonable proportion (51%) of the mood variations reported by the menopausal women. I think that this study which only included 10 post-menopausal women, was too small, for that conclusion to be valid.

You have heard all what the experts have to say. The one expert that the prosecution failed to call to the stand was my client's patient. After all, isn't she an expert on her own body, her own feelings and her own concerns. We brought her to the stand. You have all heard what Sandra had to say. How did she respond to the Clonidine? It did not help her. She still had the hot flushes. What happened when she was put on HRT?

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It is Sandra's belief that HRT was helping her with her hot flushes and her feelings of irritability and unusual tiredness. She was concerned about what would happen if HRT was not made available at least for another year or so. The hot flushes she can live with. It is the painful sex with her boyfriend that is really bothering her right now. This was not a concern identified by my client, but then again, you cannot expect doctors to be too concerned about the motives behind client requests. We lawyers have been indoctrinated in what our medical colleagues are now calling patient centredness. Be that as it may, Sandra testified in this court, that she would like to get married to her new boyfriend. She is concerned that if she could not enjoy sex with the boyfriend, she does not see a future in this relationship. She expected her family doctor to be sensitive to these needs and to be willing to help her.

What does my client think? What were his motives? My client, Sandra's family doctor, testified under oath that he believes that not all women want and do need HRT.[11] However he is convinced that Sandra, at age 40, with no uterus and no functioning ovarian tissue, is doomed to a life of profound oestrogen deprivation, possible early osteoporosis, fluctuating psyche, vaginal atrophy and dyspareunia, unless this court would find that she is a suitable case. My client is not asking for permission to keep Sandra on HRT indefinitely. He will review her situation from year to year. He does not expect for Sandra to be on HRT for more than 5 to 10 years as recommended by Dr Garnett and Studd.[9] I will concede that my client, prior to being involved in this client

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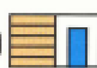

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related exercise, might not have been fully aware of all the pros and cons of HRT, as a good family doctor should have been. However, the one important thing that he has learnt, is that his gut instinct, based on a desire to help Sandra, helped him to make the right decision. He has come out of this ordeal, a more well informed physician, and this can only serve for the good of his patients in the future. He expects that in the future, he will be in a better position to help such patients make the right decision.

As for me, seeing that I am not a woman, and not a medical person, just an ordinary lawyer, whose sole responsibility to this court, is to help sort out facts from fiction, my personal beliefs should not be used in deciding who is right or not. I am married and my wife is not yet 40 years. She has been experiencing irregular and heavy menstruation recently and in contemplating asking her family doctor about a possible hysterectomy. If it is recommended, she too could be in a similar situation like Sandra. Perhaps, she too will have to face the rest of her life starved of vital hormones. I would want her family doctor to weigh her situation based on her own needs and decide on merit whether she needs HRT. Use the facts presented, discard the fiction and make the right choice for my client and his patient.

In summary, Your Honour, ladies and gentlemen of the jury, my client, in prescribing HRT for Sandra, was not acting against Nature. He was in fact, assisting Nature, messed up by degenerating fibroids and a hysterectomy, in doing what Nature intended to do in the first place. It is Nature's intention and desire, that life should be measured not so much in the amount of years, but in the quality of those years. Nature had originally intended that Sandra would be menopausal around 50 years plus or minus 5, and then with the grace of God, be gone by 60 or the most 70. Preventing Sandra from continued access to HRT, is dooming her to a life of misery for the next 20 to 30 years.

Will you sentence her to spend the next 15 years of her life not knowing what good sex feels like, or what true companionship with a real friend is? Sandra is not another black statistic. Just because most black women do not complain of climacteric symptoms, that is no reason to negate Sandra's symptoms. Treat her like the person she is.

Indeed, *there is a season for everything under the sun* and I say it is time for us to take off the blindfolds from the Lady of Justice and let her see clearly what she and all her sisters could experience if they too become post-menopausal before Nature intended, and suffer like my client's patient, Sandra.

Your Honour, ladies, gentlemen of the jury, the defense rests.

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