Is it Necessary for Adults to Continue a Phenylalanine Strict Diet After Diagnosis of Phenylketonuria During Childhood?

Corresponding Author:
Mr. Taufiq Khan,
Medical student, University of Liverpool - United Kingdom

Submitting Author:
Mr. Muhammed R Siddiqui,
Registrar, Mayday Hospital, 23 Malvern Road, TN24 8HX - United Kingdom

Article ID: WMC00613
Article Type: Review articles
Submitted on: 10-Apr-2012, 09:04:57 PM GMT  Published on: 16-Apr-2012, 12:44:38 PM GMT
Article URL: http://www.webmedcentral.com/article_view/613
Subject Categories: GENERAL MEDICINE
Keywords: Phenylalanine, Phenylketonuria, Childhood

How to cite the article: Khan T, Siddiqui M. Is it Necessary for Adults to Continue a Phenylalanine Strict Diet After Diagnosis of Phenylketonuria During Childhood? . WebmedCentral GENERAL MEDICINE 2012;3(4):WMC00613

Copyright: This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Source(s) of Funding: None

Competing Interests: None
Is it Necessary for Adults to Continue a Phenylalanine Strict Diet After Diagnosis of Phenylketonuria During Childhood?

Author(s): Khan T, Siddiqui M

Abstract

Phenylketonuria is an inherited metabolic disorder whereby the sufferers are unable to produce phenylalanine hydroxylase, an enzyme that is required to metabolise the amino acid phenylalanine. If there is a deficiency of this enzyme, phenylalanine levels rise to potentially serious levels which can lead to mental retardation and other problems. In most developed countries, babies are screened for the disease within a few days of birth. If diagnosed, the common treatment for Phenylketonuria is a phenylalanine restricted diet which the sufferer must follow for at least a number of years. Beyond childhood, the diet is maintained, relaxed or discontinued. This review involved the critical appraisal of four studies regarding the risk of discontinuing the special diet. The studies offered varying views; some argued diet discontinuation had no significant effect on cognition and mental capacity, whilst one view was that the diet should be maintained into adulthood. It was concluded that the safest thing to do would be to continue the diet but at a higher phenylalanine intake. However, it must be stressed that this particular topic is one that requires further research.

Introduction

Phenylketonuria (PKU), an inborn error of metabolism which can lead to mental problems, was first discovered in 1934 by the Norwegian physician Ivar Asbjørn Følling. From the urine samples of ten mentally retarded patients, Følling discovered that there was an increased concentration of the amino acid phenylalanine. This was a revolutionary moment in medicine because it was the first time a biochemical abnormality was shown to be associated with mental retardation.

Under normal conditions, phenylalanine is metabolised to tyrosine by the enzyme phenylalanine hydroxylase. Amongst PKU sufferers, there is a defect in the enzyme which subsequently leads to the accumulation of phenylalanine to levels that are higher than normal (Hyperphenylalaninemia), the most common form of which is referred to as classic PKU where the sufferer is completely deficient in the phenylalanine hydroxylase enzyme. Due to the defect in the enzyme, phenylalanine concentrations can reach dangerous levels, which left untreated can ultimately lead to mental retardation, brain damage, seizures or epilepsy. Phenylalanine levels are said to be dangerous when the concentration exceeds 20mg/dL. However, with early diagnosis, appropriate action can be taken; a restricted phenylalanine diet being the most common form of treatment. The continuation of this diet into adulthood is a much disputed topic amongst doctors and scientists.

Phenylalanine

Phenylalanine is one of several large neutral amino acids (LNAAs). LNNAs compete for transport across the blood-brain barrier via the L-type amino acid carrier. Thus, if the body is unable to break down phenylalanine, elevated levels of the amino acid impair the uptake of other LNNAs. Restricted brain development amongst PKU sufferers is largely down to the reduction of other LNNAs as well as the abnormal levels of phenylalanine.

Tyrosine

Phenylalanine is one of the ten essential amino acids and as such it must be obtained from the diet. The importance of this amino acid lies in the fact that it is the precursor for tyrosine, the monoamine signalling dopamine, norepinephrine and epinephrine. The requirement of tyrosine is suggested to be 30 mg/kg/BW. The PAH enzyme converts phenylalanine to tyrosine in the presence of molecular oxygen and catalytic amounts of tetrahydrobiopterin (BH4), its nonprotein cofactor. Since PKU sufferers don’t posses the functional PAH enzyme, tyrosine becomes an essential amino acid which must be part of the diet.

The PAH gene

PKU results from a mutation of the phenylalanine
hydroxylase gene (PAH) on chromosome 12, region 12q23.2, which encodes for the phenylalanine hydroxylase enzyme. A mutation in this region leads to a variant form of the enzyme which subsequently results in the accumulation of phenylalanine to potentially dangerous levels.

Screening

If left untreated, symptoms of PKU may only be noticed until irreversible mental retardation has occurred. Thus, newborn screening is essential in preventing harmful effects. The original test for PKU was proposed in 1963 by the American microbiologist Robert Guthrie. The Guthrie Test as it became known was a simple but ingenious method of determining phenylalanine levels in blood. The test involves taking drops of blood from the baby’s heel using a special device. The blood is allowed to dry on a special filter paper disk. The disk is placed onto a tray with an agar culture and a bacterium which requires phenylalanine for growth. After being placed overnight in an incubator, the sample trays are analysed. Wherever there are regions of abnormally high levels of phenylalanine, bacterial growth ensues, giving the agar a whitish appearance. Normally, the blood phenylalanine concentration in newborns is 0.5 mg to 1 mg per dL. Some newborns who don’t have PKU may have phenylalanine levels in excess of 6 mg per dL. This is often related to delayed maturation of enzymes required for amino acid metabolism. Thus, further tests may be carried out, especially if initial results are out of the ordinary. In the UK, screening is not compulsory but strongly recommended. In the United States, all states currently have laws mandating that every newborn be screened for inborn errors of metabolism, including Phenylketonuria. Indeed, most developed countries screen for Phenylketonuria, either on a compulsory or voluntary basis. Since the early 1990’s, the Guthrie Test has progressively been replaced by tandem mass spectrometry and high performance liquid chromatography (HPLC) in screening for Phenylketonuria. A tandem mass spectrometer can detect various inborn errors of metabolism at the same time, something that wasn’t possible before. This technique is quicker and relatively inexpensive, despite the increase in the number of conditions being screened at the same time.

Incidence

In the UK and US, Phenylketonuria affects about 1 in 10,000 new born babies. The incidence varies amongst different ethnic groups. For example, it is one per 2,500 live births in Turkey and one per 4,000 live births in Ireland.

Diet/treatment

The best way to manage Phenylketonuria is to have a strict phenylalanine diet, with regular tests to monitor blood phenylalanine levels and cognitive function. Since phenylalanine is present in almost all foods, PKU sufferers often have to follow a low protein and synthetic diet. This diet has proven hard to adhere to, the food is often dry and hard which leads to under usage and boredom. The PKU diet includes fruit, vegetables, pasta and cereals, all low in protein. Foods such as meat, eggs and nuts are avoided as they have high phenylalanine content. However, the diet must contain some phenylalanine as it is required for normal development. The daily recommended amount of phenylalanine is 25mg/kg and the recommended amounts of other essential amino acids are given in table three of the appendix. Patients may also take supplements which include various amino acids, vitamins and minerals that may have been lacking in their synthetic diet. There are opposing views as to whether this diet should be continued into adulthood. One argument is that continuation of the diet is not necessary as the brain has developed and high phenylalanine levels will no longer have a detrimental effect. Other studies suggest that the low phenylalanine diet must be continued. It is this dispute that forms the basis of this SSM.

Aim

The aim of this Study is to determine the effects of discontinuing a phenylalanine restricted diet on early treated adults who suffer from Phenylketonuria. This task will largely be undertaken by looking at a number of studies on this particular topic.

Methods

Initially, various books were issued from the library which centred on inherited metabolic diseases. These books were largely used for background reading but they also provided important and useful information on Phenylketonuria, much of which was mentioned in the
Results

The results are summarised in tables 1-6. The studies selected were critically appraised using the Critical Appraisal Skills Programme (CASP).

**Study One:** Phenylketonuria in Adulthood: A Collaborative Study

This study involved the follow up of early treated phenylketonurics, who had either discontinued or continued the diet. The results of the study showed that subjects who maintained a phenylalanine restricted diet suffered from fewer problems compared to those who suspended the diet. Discontinuers showed an increased rate of eczema, asthma and mental disorders as well as poorer outcomes in intellectual ability.

The study can be seen as a useful and reliable one. It originally involved 211 newborn infants, a remarkable number considering the low incidence of Phenylketonuria. Several subjects dropped out of the study but this doesn’t hinder massively on the study since the reduction in numbers is unlikely to have significantly changed the outcome. The study also involved numerous psychological and medical tests which meant confident conclusions could be made regarding the precise effects of discontinuing dietary treatment.

However, the study did have its limitations. Ideally, the researchers would have preferred to have an equal number of subjects who either continued or discontinued the diet. This would always be difficult as the parents of the children would, out of concern for their child, decide that their child be on the special diet instead of a normal one. The lack of complete randomisation, which is inevitable from such studies, slightly reduces the reliability of the study. Another limitation of the study design was the failure to control certain confounding factors. For example, it was understandably difficult to measure intellectual ability reliably if the subjects received varying quality and quantity of education and support from parents.

Overall, the study design is strong due to the number of subjects that participated; a high number reduces the risk of random chance. Appropriate tests were used to determine the medical and cognitive effects of discontinuing the diet and a strong enough case was made that subjects should continue dietary treatment into adulthood.

**Study Two:** Phenylketonuric patients decades after diet

The aim of this study was to assess whether there was deterioration in intellectual ability amongst Phenylketonuria sufferers years after diet discontinuation. The study saw nineteen early treated phenylketonurics, between 4 and 13 years of age who had been off the phenylalanine restricted diet for 12-28 years. The subjects were assessed at the termination of the special diet and in a follow up period. Results showed that there was less that one IQ point on average difference between the mean IQ in the first assessment and the mean IQ obtained in the follow up assessment. The researchers thus suggested that diet discontinuation had little to no effect on cognitive ability but that a phenylalanine restricted diet through adulthood was advisable due to the unknown effects of high phenylalanine concentrations.

The study design was appropriate to meet the aim of the study, which was to compare cognitive changes just at the end of diet discontinuation and a number of years after. Testing the subjects IQ scores can be seen as a suitable way to assess cognitive changes. However, it must be acknowledged that IQ scores alone are not a highly reliable indicator of intellectual ability. The researchers could have introduced other tests alongside the IQ tests to assess cognition.

There were also a number of other limitations in the study. For example, the absence of a control group means the study isn’t as reliable as it could have been. If the authors also carried out IQ tests on phenylketonurics who maintained their diet or even on individuals who were perfectly healthy then a point of comparison could have been made.

Another weakness in the study was the number of participants. Patients were lost from the study due to various reasons such as migration or parent concern. This meant that the final analysis was based on only nineteen patients. Although Phenylketonuria is a disease with a low incidence, nineteen is too small of a number to draw reliable conclusions from as a small sample increases the risk of random chance. Moreover, the results are prone to confounding errors as no efforts seem to have been made to control any confounding factors. The age of the participants and parents education are identified as confounding factors but since no effort is made to control these, the reliability of the results is reduced.
Overall, the weaknesses of the study design perhaps don’t warrant the authors coming to the firm conclusion that discontinuation of the diet doesn’t lead to intellectual deterioration. However, it must be noted that the authors do advise the continuation of the diet on the basis that high phenylalanine levels may have unknown effects.

**Study Three:** Neuropsychologic Functions of Early Treated Patients with Phenylketonuria, on and off Diet: Results of a Cross-National and Cross-Sectional Study

This study spanned across different countries and involved testing three different groups of patients. The first group consisted of 22 French phenylketonurics who suspended the phenylalanine restricted diet since the age of five years old. The second group consisted of 23 German patients who continued the diet. 21 healthy subjects composed the third group. All the patients were assessed from childhood to adulthood.

Tests were performed to determine: whether the three groups showed different reaction times as they progressed from childhood to adulthood; whether a phenylalanine concentration of 360 ?mol/L can be regarded as safe as recommendations had stated; whether there was a link between test performances and quality of dietary control and if this relationship was applicable across each of the age groups; and if long term phenylalanine levels of high concentrations would have an aggravating effect on phenylketonurics both on or off the diet and on healthy individuals.

The results showed that developmental trends regarding reaction times were similar in all three treatment groups. A phenylalanine concentration of 360 ?mol/L is perfectly safe and in fact, phenylketonurics with a mean phenylalanine level below 360 ?mol/L performed as well as control subjects in various tests. Moreover, the results showed that differences between treatment groups decreased as subjects reached adulthood, supporting the idea that the special diet can be eased or even terminated during adulthood.

The researchers came to the overall conclusion that it is advisable to maintain blood phenylalanine levels below 360 ?mol/L during the first ten years of life. This study has a number of strengths compared to other studies. Unlike the previous studies mentioned in this review, this study used a range of tests to assess the effects of elevated phenylalanine levels on mental capacity. The researchers tested for the subjects’ visuomotor reaction time, sustained attention and visual stimulus.

All three treatment groups were matched together with regards to age, sex and IQ to eliminate any confounding factors.

The fact that this was a cross national study means there was more subjects than they otherwise would have been. However, the results of the study may have been even more reliable if there was a bigger sample size.

**Study Four:** Phenylketonuria: diet for life or not?

The aim of this study was to determine whether a phenylalanine restricted diet was necessary to maintain into adulthood without impairing neurological and intellectual function. Sixteen early diagnosed phenylketonurics were taken off the diet after their eleventh birthday. IQ tests, neurophysiological tests and magnetic resonance imaging (MRI) were used to test neuro-function before and after discontinuation of the diet.

The results showed little or no change in IQ scores or electrophysiological tests but all patients revealed abnormal neurological signs. The researchers thus concluded that the diet should be maintained for life but that a slightly higher phenylalanine intake (around 600 µmol/L) was acceptable.

The study would have been more reliable had there been more subjects to test from. Moreover, there doesn’t seem to be a control group present in the study, meaning no point of comparison can be made to determine whether diet discontinuation is detrimental to intellect.

**Discussion**

The issue of the duration of dietary treatment is one that needs more research. In the majority of the studies available on the topic, sample size seems to be an issue. Perhaps with the exception of study one, all the studies mentioned in this review can be said to have a small sample size. It must be acknowledged that Phenylketonuria is a disease with a low incidence and even samples of thirty or so subjects represents a large geographic area. Perhaps one option for the future is communication and co-operation between Phenylketonuria centres and clinics worldwide, as shown in study three. Sharing data on a cross national basis will certainly increase the sample size.

It is apparent that the effect of diet discontinuation on cognition is largely assessed by the use of IQ tests. This is not an entirely reliable indicator of cognitive ability as it has been argued that IQ tests are not always the best indicator of intelligence. Perhaps a more reliable method to use would be the utilisation of several tests in conjunction, as displayed in study three. One review gathered information from numerous studies to identify the range of tests used on phenylketonurics. The study reported that motor
speed, speech, language, memory, and basic logic to be generally unaffected amongst PKU sufferers. Differences were largely found in abstract reasoning and information processing.

A longitudinal design with a larger sample size used in combination with results from longitudinal IQ studies as well as different types of tests would significantly contribute to the issue of diet discontinuation.

Study three concludes that the diet should be maintained for at least the ten first years of life. This is justified by the French patients who were off the diet performing lower than the German patients who maintained the diet. Other studies also argue that discontinuation of diet doesn’t lead to a significant change in adulthood. Practically, patients find it tough and burdensome to adhere to the diet as they get older. Eating from a normal diet becomes an important part of social interaction and phenylketonurics attached to a special diet often feel more socially isolated as they grow older.

Some studies argue that a strict phenylalanine diet should be maintained through adulthood. Studies one, two and four all conclude that the diet should be continued on the basis that to do otherwise could lead to neurological complications and intellectual deterioration. Numerous other studies also advocate a ‘diet-for-life’ policy. Some studies also affirm that diet discontinuation can lead to other complications. For example, dopamine and serotonin deficiency have been associated with diet discontinuation. These are important neurotransmitters that have an array of important functions and are reasons alone as to why a strict diet must be maintained.

Conclusion

Dietary treatment of PKU patients starts within the first few weeks of life after screening. The duration of the diet however, has become a much disputed topic. The British Medical Research Council Working Party on Phenylketonuria offers a reasonable approach; that the diet should be maintained for as long as possible but that this will inevitably prove hard to adhere to in adolescents and adults, older patients should then be responsible for their phenylalanine levels and be aware of the risks associated with the termination of the diet.

It does seem that the risks of discontinuing the diet outweigh the disadvantages of continuing the diet; adding weight to the idea of ‘diet-for-life’. Thus, the most plausible route for phenylketonurics seems to continue the diet but at a higher phenylalanine intake. This way, patients may be able to eat food that they previously weren’t able to and this may alleviate feelings of social exclusion and depression which are commonly associated with the diet.

There is fresh hope for the future regarding the treatment of Phenylketonuria. Much research is being done into the effectiveness of gene therapy, enzyme replacement therapy and LNAA supplementation. The pharmaceutical company BioMarin Pharmaceutical have produced a tablet called ‘Kuvan’ (sapropterin dihydrochloride). This drug has been approved by the US Food and Drug Association (FDA) in the treatment of some PKU sufferers. Kuvan lowers phenylalanine levels to recommended ranges by increasing phenylalanine hydroxylase enzyme activity which allows for increased metabolism of phenylalanine. However, Kuvan must be used in combination with the phenylalanine restricted diet and the patient must still have their blood phenylalanine levels monitored frequently.

Currently, there isn’t a way of completely eradicating the problems that arise with increased phenylalanine concentrations due to phenylalanine hydroxylase deficiency. Until a way is found, dietary treatment will continue to be used as the foremost way to tackle Phenylketonuria. Therefore, it seems that the debate regarding diet duration will continue. With the available evidence, it appears that the diet should be maintained through adulthood with a higher phenylalanine intake. But this is a topic which requires further research.

References

Illustrations

Illustration 1

Table 1

Results obtained from Discover on the University of Liverpool’s Website.

<table>
<thead>
<tr>
<th>Search Term</th>
<th>Number of Results Received</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylketonuria</td>
<td>15232</td>
</tr>
<tr>
<td>Phenylketonuria; diet</td>
<td>4099</td>
</tr>
<tr>
<td>Phenylketonuria; diet; discontinuation</td>
<td>78</td>
</tr>
<tr>
<td>Phenylketonuria; diet; discontinuation; adults</td>
<td>33</td>
</tr>
</tbody>
</table>
Illustration 2

Table 2

Results obtained from PubMed.

<table>
<thead>
<tr>
<th>Search Term</th>
<th>Number of Results Received</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylketonuria</td>
<td>140</td>
</tr>
<tr>
<td>Phenylketonuria, Diet</td>
<td>81</td>
</tr>
<tr>
<td>Phenylketonuria, Diet, discontinuation</td>
<td>3</td>
</tr>
</tbody>
</table>
Illustration 3

Table 3

Selection criteria used in choosing studies

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Article</td>
<td>Studies had to be cohort studies or Randomised Controlled Trials (RCT).</td>
</tr>
<tr>
<td></td>
<td>Clinical reviews were also acceptable.</td>
</tr>
<tr>
<td>Age of Subjects</td>
<td>Since this is a review of PKU and diet in adults, subjects had to be 18+ years of age.</td>
</tr>
<tr>
<td>Humans/Animals</td>
<td>Humans only.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assessment of Participants</th>
<th>One way in which the effect of discontinuation of phenylalanine restricted diet can be determined is by assessing intellect/cognitive function. Therefore, the studies had to involve cognitive tests in some capacity.</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of the Participants</td>
<td>This is a review of the discontinuation of the special diet on early treated PKU adults. Therefore, subjects had to have been diagnosed and treated from a young age.</td>
</tr>
<tr>
<td>Language of the Study</td>
<td>English language.</td>
</tr>
<tr>
<td>Comparison of Results</td>
<td>The test results of the subjects before and after termination of their diet. Alternatively, a control group could be used. This would have allowed for a point of comparison.</td>
</tr>
</tbody>
</table>
## Illustration 4

### Table 4

Critical Appraisal of Studies 2, 3 and 4

<table>
<thead>
<tr>
<th>Question</th>
<th>Study 2</th>
<th>Study 3</th>
<th>Study 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did the study address a clearly focused issue?</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Did the authors use an appropriate method to answer the question?</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Was the cohort recruited in an acceptable way?</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Was the exposure accurately measured to minimize bias?</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Was the outcome accurately measured to minimize bias?</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Have the authors identified all important confounding factors?</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Question</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Have the authors taken account of the confounding factors in the design and/or analysis?</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Was the follow up of subjects complete enough?</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Was the follow up of subjects long enough?</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Do you believe the results?</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Can the results be applied to the local population?</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Do the results of this study fit with other available evidence?</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>18</td>
<td>14</td>
</tr>
</tbody>
</table>

0 = No

1 = Can’t tell

2 = Yes
Illustration 5

Table 5

Critical Appraisal of Study 1 (Randomised Controlled Trial)

<table>
<thead>
<tr>
<th>Question</th>
<th>Study 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did the study ask a clearly focussed question?</td>
<td>1</td>
</tr>
<tr>
<td>Was this a randomised controlled trial and was it appropriately so?</td>
<td>2</td>
</tr>
<tr>
<td>Were participants appropriately allocated to intervention and control groups?</td>
<td>1</td>
</tr>
<tr>
<td>Were participants, staff and study personnel ‘blind’ to participants’ study group?</td>
<td>0</td>
</tr>
<tr>
<td>Were all of the participants who entered the trial accounted for at its conclusion?</td>
<td>0</td>
</tr>
<tr>
<td>Were the participants in all groups followed up and data collected in the same way?</td>
<td>2</td>
</tr>
<tr>
<td>Did the study have enough participants to minimise the play of chance?</td>
<td>2</td>
</tr>
<tr>
<td>Were all important outcomes considered so the results can be applied?</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10</strong></td>
</tr>
</tbody>
</table>
Disclaimer

This article has been downloaded from WebmedCentral. With our unique author driven post publication peer review, contents posted on this web portal do not undergo any prepublication peer or editorial review. It is completely the responsibility of the authors to ensure not only scientific and ethical standards of the manuscript but also its grammatical accuracy. Authors must ensure that they obtain all the necessary permissions before submitting any information that requires obtaining a consent or approval from a third party. Authors should also ensure not to submit any information which they do not have the copyright of or of which they have transferred the copyrights to a third party.

Contents on WebmedCentral are purely for biomedical researchers and scientists. They are not meant to cater to the needs of an individual patient. The web portal or any content(s) therein is neither designed to support, nor replace, the relationship that exists between a patient/site visitor and his/her physician. Your use of the WebmedCentral site and its contents is entirely at your own risk. We do not take any responsibility for any harm that you may suffer or inflict on a third person by following the contents of this website.