SERUM CARNITINE LEVELS in POST POLIO

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ABSTRACT: Results to date of an on-going study on the effects of supplemental carnitine as an effective treatment of fatigue and muscle pain occurring as post polio symptoms in Western Australian polio survivors. This study documents serum levels prior to and during carnitine supplementation on 222 female polios, 142 male polios, 70 female children of polios, 37 male children of polios and 30 grandchildren of polios (10 female, 20 male). Since 1996, serum carnitine levels have been the basis of clinical treatment for fatigue in around 400 polio survivors and 137 descendants of polio survivors attending the WA Polio Clinic. Optimal individual dosage has been determined by using diarrhoea as the sign of overdose and alleviation of fatigue and muscle pain as the goal. Dose has varied between 250mg - 2500mg mané. It has been found more beneficial taken as a single dose, with top up later in the day if necessary prior to extra physical exertion eg hydrotherapy, golf, shopping etc. Participants have successfully self adjusted their carnitine dosage according to individual daily physical requirements. A surprising finding made by the Polio Clinic, is that increasing numbers of children and even grandchildren of polio survivors are presenting to the Clinic, experiencing similar symptoms of fatigue and muscle pain, test low with serum levels and also respond well to the use of supplemental carnitine.

The WA Polio Clinic run by the Post Polio Network of WA (PPNWA) has been investigating supplemental carnitine as a possible treatment for the fatigue and muscle pain experienced as the Late Effects of Polio since 1994. Following an initial small pilot study (200 self reporting 1994-96), then a double blind trial (21 in 1996-97), it was resolved that the use of serum carnitine levels was sufficient to monitor clinical usage of carnitine in polio survivors by the WA Polio Clinic.

Since 1996 serum carnitine levels have been obtained on around 400 polio survivors and 137 children and grandchildren. A number of other members are known to be successfully using carnitine without reference to the Clinic and without first obtaining serum levels. Despite attempts to obtain pre- carnitine and current carnitine levels on all participants, many have continued to use carnitine for problem solving without obtaining further blood levels to confirm dosage, relying on resolution of symptoms alone.

POST POLIO

PPNWA has 1750 WA polio survivors on its register, including 90 deceased over the last 12 years. Currently the PPNWA Newsletter is sent to 1170 of these people and a number of others inter-state. Serum levels are available on about 400 of the 1170 WA polios.

Statistics drawn from 1160 questionnaires returned between 1992 - 2002 show 96% of polio survivors in WA considered they were experiencing further problems now due to prior polio. Of these there has been a drop in undue fatigue from 71% in 1993 to 58% in 2002. Increasing muscle weakness has dropped from 77% in 1993 to 66% in 2002. Pain was down slightly from 77% in 1993 to 75% in 2002 but this includes skeletal pain as well as muscular.

CARNITINE

The main symptoms of carnitine deficiency were found to replicate Post Polio Syndrome - ie fatigue, muscle pain, muscle weakness and lack of endurance. Carnitine is the essential co-factor in the transfer of long chain fatty acids across the mitochondrial membrane in Type 1 muscle cells for energy production via the Krebs cycle. Two carnitine enzymes are also manufactured by the body as part of the mitochondrial transport system, carnitine palmitoyl-transferase 1 & 2 and also acyl-carnitine translocase. These all assist in the breakdown of acyl-Co A to acyl-carnitine and Co A and reversal again inside the mitochondria.

Although carnitine deficiency is rare and generally only recognised as a potentially fatal genetic condition occurring mainly in children, certain **recognised trigger factors that lower carnitine** levels are of **relevance to polio survivors.**

1. reduced dietary intake of carnitine rich foods
2. vegetarian style diet
3. exhaustion
4. infection
5. surgery
6. anaesthesia
7. fasting
8. pregnancy & breastfeeding
9. antibiotics use - particularly ampicillins
10. organic disease - diabetes, thyroid, liver, etc

25% of the body's carnitine requirements are manufactured in the liver and kidneys, provided the other ingredients are available ie lysine, methionine iron, B3, B6, B12, Vit C. The remaining 75% comes from dietary sources. Mutton and avocado are the best sources, followed by lamb and beef. Pork contains half of that in beef, and chicken has only one tenth of the carnitine in beef. All other foods have negligible amounts.

WHY CARNITINE NEEDED FOR POST POLIO

There seems to be a need for blood levels to be at the top of the given normal range or even above this, **for polio survivors to function adequately.** ie **free carnitine 45 umol/L or more.** Many are finding that free carnitine **levels in the 60's to 80's** are **needed** for **relief of symptoms**.

1. It is likely that polios function better with higher serum levels to enable faster replenishment of cell levels, particularly during exercise to forestall the "hitting the wall' symptoms common in post polio.. (NB Just walking and regular daily activities can be fatiguing for some polios.)

2. The main storage of carnitine in the body is in muscle cells and polio survivors have lost muscle due to polio, so, in fact, are likely to have reduced storage capacity on a daily basis.

3. Research by K Borg MD and G Grimby MD in Sweden, show reinervation changes following polio, that have increased the number of Type 1 muscles in polio survivors. Their research has also found that former Type 2 changed to Type 1 work less efficiently than a normal Type 1 muscle. Muscle type change results in corresponding change of fuel preference to run these muscles, thus increasing the amount of carnitine required by a polio survivor.

4. As a result of muscle loss due to polio, remaining muscles work at a faster rate to achieve normal muscle function, so carnitine supplies will become depleted more quickly leading to fatigue and loss of function and endurance. This can be overcome to a degree by higher serum levels giving ready access to more carnitine for the cell.

5. Chronic Fatigue (CFS) researchers using the polio virus to gain clues on CFS, have revealed that the polio virus not only affects the anterior horn cells in the spinal column but also the mitochondria of the muscle cell. As this is the site of carnitine action, it is possible that damage here is affecting the transfer mechanism of carnitine enzymes as well. Higher serum levels seems to result in improved function due to osmotic effect.

6. It is possible that initial low levels in male and/ or female parents that have had polio, is having an effect genetically on the programming that determines life time optimal levels in their descendants. Our research has shown progressively lower serum levels in successive generations of some polio survivors.

CARNITINE TRIAL

As polio people have been seen through the WA Polio Clinic, where fatigue has been a problem, they have been encouraged to have a pre-carnitine level done before commencing the supplement. There has been less success unfortunately in getting people to have the test repeated when they are feeling better on the carnitine. Where possible this has been taken a month after achieving a therapeutic dose.

Therapeutic dose can be found by instructing the patient to increase the dose by 250mg every 2-3 days until bowel tolerance is reached (diarrhoea or gastric upset is the sign of overdose, so reduce by 250mg when overdose symptoms appear.) There may be little noticeable improvement in symptoms until therapeutic dose is achieved.
(eg one patient reports - on 5 capsules still tired, on 6 feels great, on 7 gets diarrhoea.)

It is useful to get the comparative result as there have been instances where this has signalled that the patient has stopped at an insufficient dose or is taking the supplement at the wrong time of the day, thus allowing correction and better results.

Males require higher levels than females as carnitine is also used in sperm production. Although the given normal levels for free carnitine are 30-60umol/L, **optimal levels in post polio** have been found to be **45+ in females and 50+ in males.** Generally they will do better if levels are in the 60-80 range. Bowel tolerance with improved energy levels remain the best determinant of optimal dose although it is handy to know around what serum level this is achieved.

FINDINGS

As this has been grass-root research with high input from the people achieving the results and who have been willing to experiment, a number of interesting points have emerged.

1. Best results are from taking carnitine as one daily dose on rising first thing in the morning.

2. Top up through the day if needed for greater than normal physical activity.

3. At least one red meat meal a day is desirable. (alternatively have an avocado with other proteins)

4. If activity levels increase because of increased available energy, an increase in carnitine dose may also be required to maintain new level of physical and mental activity.

5. If carnitine is taken too late in the day it can interfere with sleep patterns as it provides energy (handy though for night time commitments).

6. The people most likely to benefit from carnitine are those with the most muscle power. (People in wheelchairs don't have a lot of muscle left for carnitine to assist with.) Often people walking around and/or still working feel they are frauds and are less likely to seek help, as they feel those with more disability need more help. **In actual fact, the more muscles they are still using, the more carnitine is likely to help them keep going.**

7. If carnitine supplementation ceases, users will usually return to previous levels of fatigue. The time taken for this to occur varies with the individual. Some go downhill within a few days. Others may take weeks or months.

8. Some people have had serum levels done and elected not to take carnitine or stopped after some time. They often return some years later as they have deteriorated further and repeat serum levels shows the same low levels or even lower.

9. Sometimes the free and total carnitine levels come back with the same reading giving a 0% for acyl over total percentage (ie used portion over total in blood. Free level is what is available to use, difference between total and free gives acyl or used portion. Good usage is 17%-25%).
If the test is repeated there may then be a difference between the 2 readings next time but the free level is still usually around the first reading. In either case, low percentage or low free level, supplemental carnitine improves the usage.

10. It is advisable to leave a month between pre- and on-carnitine levels. Some people have had the blood test too close by mistake and there is often little difference reflected before 3-4 weeks.

11. If there is a problem with the test result, check on time of day test done and relationship to time carnitine taken, doses missed lately, run out of carnitine supplement or increased activity levels.

12. Other factors for lowering carnitine levels. Other medical conditions, drugs, treatments can affect available carnitine. Levels monitored on a patient undergoing radiation therapy showed a rapid decline over 2-4 weeks resulting in increased supplement requirement. Penicillin drugs, epileptic drugs, haemodialysis, anaesthetics, surgery, stress, infection can lower levels.

13. Betablockers - given for hypertension or migraines inhibits the action of carnitine enzyme CPT-1, thus explaining why polios have problems with taking betablockers. An alternative hypertensive acting drug needs to be used.

14. Kidney Disease - one patient who reportedly has diminished kidney function, has experienced pain in the kidneys when taking a higher dose of carnitine. Acyl Carnitine (used carnitine) is normally excreted through the kidneys. If the filtration process is under stress, increasing the amount of carnitine requiring excretion can put strain on the kidneys so supplement with caution.

15. Pregnancy - for both polios still having children and descendants becoming pregnant, this is becoming important. By the 14th week of gestation the developing foetus has reduced the mother's available carnitine by half. By the end of the pregnancy this can be down to a quarter. If the mother was already low in carnitine, neither she nor the developing infant will be getting enough. If she breastfeeds they will both remain in this situation. The long term effects may be a floppy baby, delayed milestones and a life time need for extra carnitine for the child.

16. Children and grandchildren of polios - Serum levels can reveal increasingly lower levels of carnitine in successive generations. Warnings need to be given prior to conception to both male and female descendants of polios planning to have children. Supplementation to optimal levels should be achieved for 6 months prior to conception to avoid perpetuating carnitine deficiency in families of polio survivors. Surveillance for many decades will be required on this familial tendency. Not all families will be affected. It is more likely where polio was contracted early in life or where children were conceived within a few years of the original polio. Signs in descendants include delayed milestones, laziness, fatigue, muscles aches, growing pains, slouched posture, herniation, chronic fatigue.
It is more likely in the subsequent children when the gap between siblings is less than 4-5 years.

17. Trigger factors for children - As with polio survivors deteriorating following episodes that can lead to a depression of carnitine levels, so these same factors may precipitate a carnitine deficiency in children and grandchildren that had seemed unaffected , after - illness, surgery, accidents, stressful times, pregnancy etc. It is likely they may not realise that they have a problem as they have become used to feeling like this and think this is normal. It may be necessary to ask descendants if they get tired easily, run out of energy, have aches and pains. On enquiry often un-noticed signs emerge that demonstrate they have a long standing low energy level that has never been recognised, have a measurable deficiency and are easily fixed with supplemental carnitine and some extra magnesium for muscle relaxation and pain.

18. Older polios - It has been found that a lot of the older age group of polios (70-90 years) are not experiencing the same problems of fatigue and muscle pain that is apparent in the 40-70 age group. This may be in part due to the lack of intensive therapy in the recovery process after polio that became common practice in epidemic years. But a more likely factor is that this group of people is less likely to have changed their diet due to advertising pressure over the last 20-30 years and probably still have their red meat and 3 veg for tea every night, thus maintaining their carnitine levels. The other group falling into this category are farmers eating red meat 2-3 times a day On retiring and moving to the city, polio farmers, now eating less red meat, start to run into polio problems after about 6 months. On suggesting they resume eating red meat daily, the pain and fatigue quickly resolves and they can maintain their levels with diet alone without needing any supplementation.

19. CAUTIONS - in addition to those with kidney failure, anyone who is known to react badly to certain drugs, foods or other vitamin supplements, should approach any new exposure, including carnitine, with caution. This has occurred on 2 occasions with WA polios over the last 8 years. Symptoms can include oedema of digits and extremities, bloating, constipation, pharyngeal oedema, vomiting, gastric upset. Others taking too much carnitine may develop a fishy body odour. This usually disappears when the dose is reduced slightly.

Carnitine powders are synthetically made so there is no danger of mad cow disease occurring due to carnitine ingestion.

20. Quality of carnitine powders. It has been found that the best quality carnitine is light and fluffy like icing sugar. Poorest quality is crystalline like sugar and shines in sunlight. A medium grade is like caster sugar, but still sparkles. Participants have found they need to take as much as double the quantity of the medium grade to get the same results. It is surmised that there is poorer gut absorption despite dissolving the powder in liquid prior to ingestion. It has been established that the manufacturers are not grinding the finished product to as fine a powder as has been done previously, thus compromising the quality. Carnitine is extremely sensitive to moisture, so users should be warned to replace the cap firmly and quickly when using. Do not keep in fridge or expose to high temperatures (over 30º C). Fine powder can be measured at 1ml scoop (flat) = 500mg. Medium quality - 1ml scoop = 250mg.

BLOOD GROUPS

There appears to be a correlation between serum levels and blood groups. It has been noted that O and A2 blood groups particularly (the high meat eating blood groups) are more likely to record lower levels and need more supplement to get their carnitine levels up. A1 and AB blood groups tend to have higher serum levels and need to take less carnitine supplement to achieve a good level. It is suspected that O and A2 naturally have more type 1 muscles which require carnitine, whilst A1 and AB have a greater dominance of type 2, using the insulin cycle more for energy production. Loss and change of muscle due to polio further complicates this picture, increasing the amount of carnitine needed compared to a non polio person.

CONCLUSION

Polio survivors can gain some control over the symptoms of fatigue, muscle pain and to some degree muscle weakness due to PPS, by taking more care to consume dietary foods high in carnitine on a daily basis and supplementing as necessary. The ability to use carnitine supplementation to increase energy levels doesn't give polio people license to undertake prolonged activities that further stress polio weakened bodies. Common sense needs to be used to find the happy medium between what people want to be able to do and their physical limitations. Carnitine is a useful addition to the range of options available to take better care for polio survivors and to support body function and the demands we make on the body in order to live a useful and fulfilling life.

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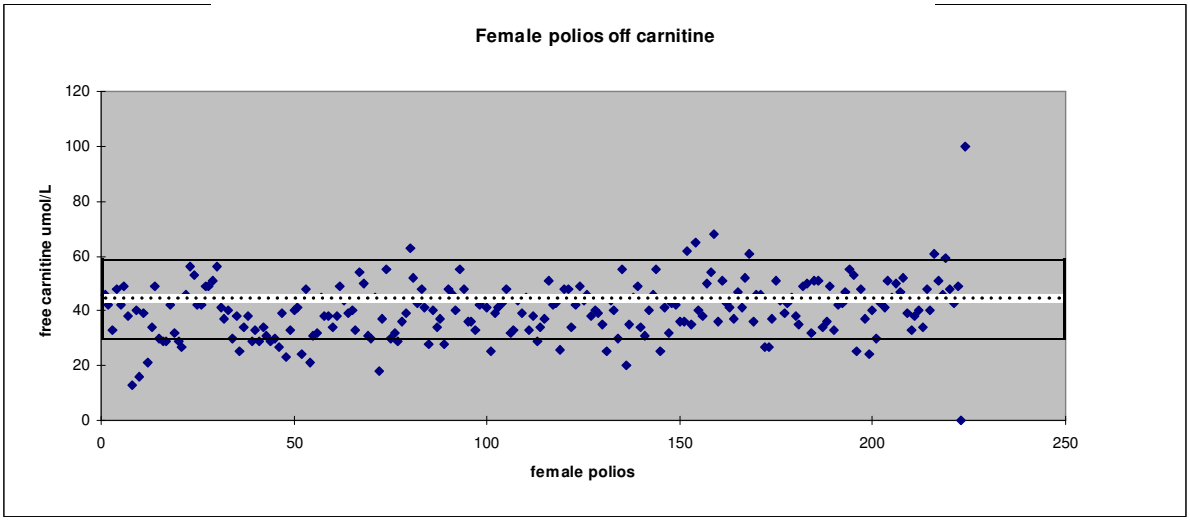
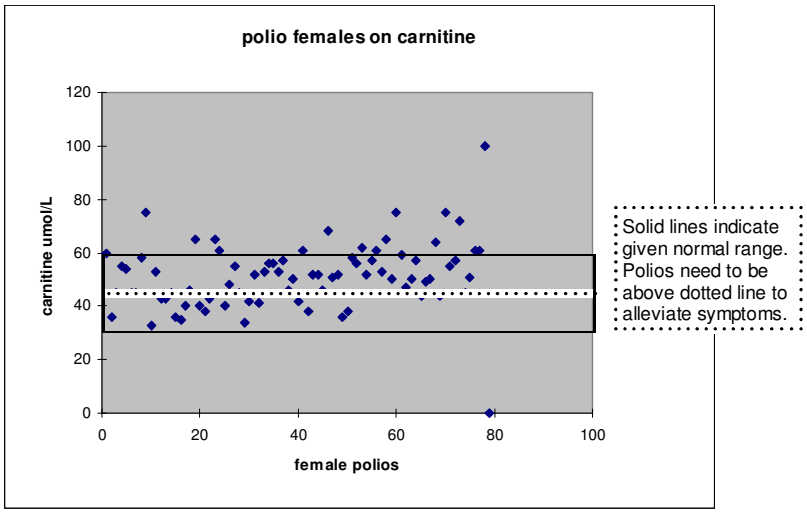


Serum carnitine levels on 222 female polio survivors obtained 1996-2002.
Chart arranged in ascending age order from 15 - 83 years of age at time of test.
The majority fall below the Free carnitine level of 45 found to be the minimum required to alleviate post polio symptoms of fatigue and muscle pain.



Serum carnitine levels on 77 female polio survivors obtained 1996-2002.
Chart arranged in ascending age order from 37 - 79 years of age at time of test.
Less people have returned for their follow-up on carnitine blood test. Chart shows improved free carnitine levels with corresponding improvement in symptoms.
Participants have found resolution of fatigue symptoms only when in the top half or above of given normal range of 30 - 60. Those falling below 45 on their repeat test were advised to increase their supplemental dosage to obtain better results. Some had increased their activity levels or were not taking dose correctly at time of test.

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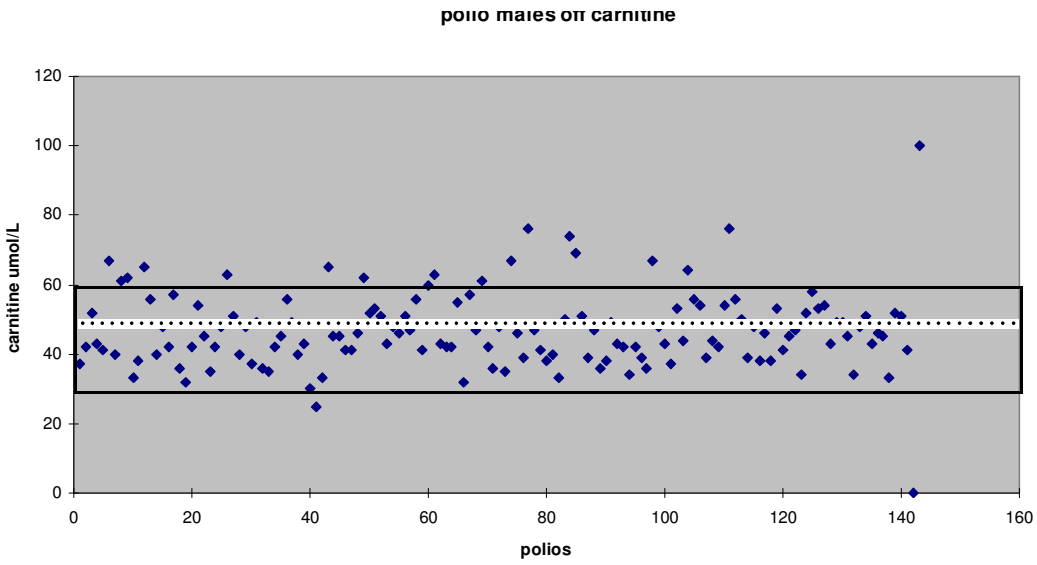
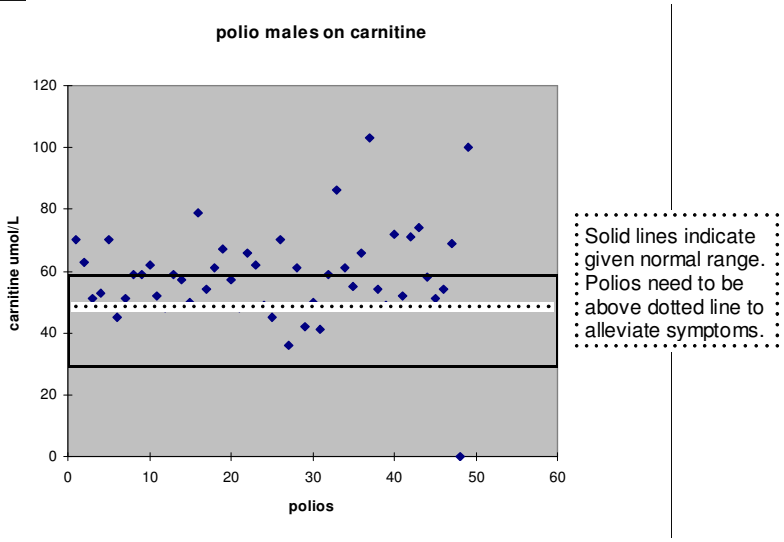


Serum carnitine levels on 142 male polio survivors obtained 1996-2002.
Chart arranged in ascending age order from 27 - 80 years of age at time of test.
The majority fall below the Free carnitine level of 50 found to be the minimum required to alleviate post polio symptoms of fatigue and muscle pain.



Serum carnitine levels on 47 male polio survivors obtained 1996-2002.
Chart arranged in ascending age order from 43 - 78 years of age at time of test.
Less people have returned for their follow-up on carnitine blood test. Chart shows improved free carnitine levels with corresponding improvement in symptoms. Participants have found resolution of fatigue symptoms only when at the top of or above given normal range of 30 - 60. Those falling below 50 on their repeat test were advised to increase their supplemental dosage to obtain better results. Some had increased their activity levels or were not taking dose correctly at time of test.

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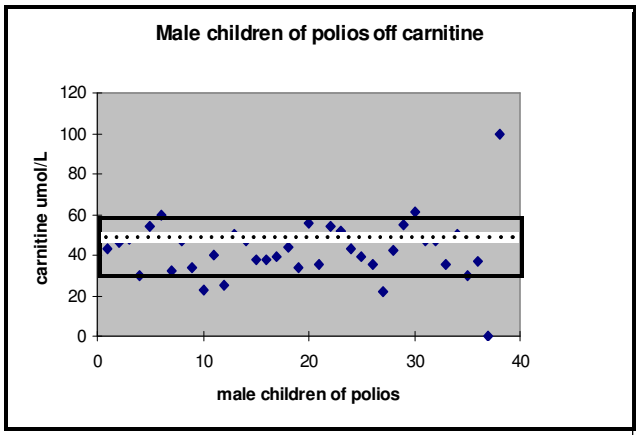
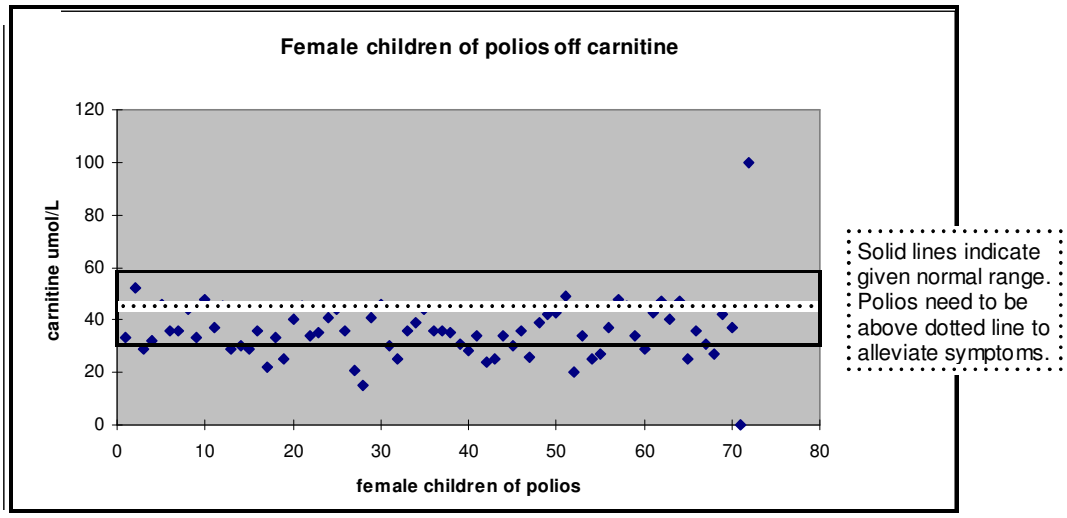
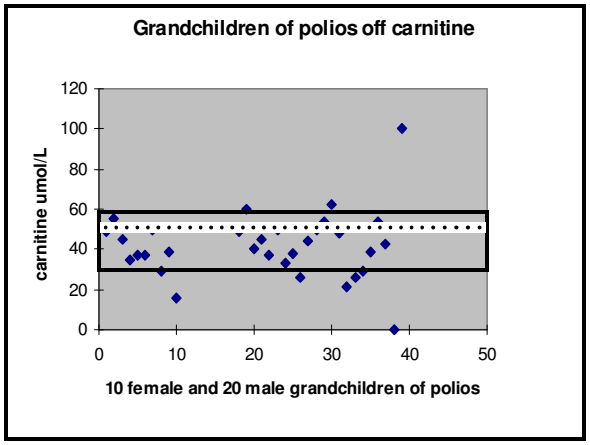


Results of free carnitine levels on 36 male children of polio survivors aged 4 to 52. On carnitine supplementation they have found reduction in fatigue, increased energy for work and household commitments. Other family members note change in family dynamics.



Results of free carnitine levels on 70 female children of polio survivors. Ages range from 3 to 56 years. Note the number that fall below 30 umol/L in this group. They are particularly vulnerable during and following pregnancy although only 2 of these readings are during pregnancy.



Results of free carnitne levels on 10 female and 20 male grandchildren. Ages range from 6 months to 25 years.

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