NEUROTOXIC MEDICATIONS

Before taking any medication, be sure to discuss it fully with your doctor or pharmacist for possible side effects. Ask them to look for the words "could cause peripheral neuropathy" in the drug description. In almost all the conditions in which these drugs are used, an alternative is available.

Drugs which are toxic to the peripheral nervous system and may be harmful to a person with CMT, but please note, with the exception on Vincristine and Taxols, there is little or no scientific data on the potential risk:

Further information can be found here: http://bit.ly/drugslist2015

Definite High Risk (including asymptomatic CMT)

- Vinca alkaloids (Vincristine)
- Taxols (paclitaxel, docetaxel, cabazitaxel)

Moderate to Significant Risk

- Amiodarone (Cordarone)
- Arsenic Trioxide (Trisenox)
- Bortezomib (Velcade)
- Brentuximab Vedotin(Adcetris)
- Cetuximab (Erbitux)
- Cisplatin & Oxaliplatin
- Colchicine (extended use)
- Dapsone
- Didanosine (ddI, Videx)
- Dichloroacetate
- Disulfiram (Antabuse)
- Eribulin (Halaven)
- Fluoroquinolones
- Gold salts
- Ipilimumab (Yervoy)
- Ixabepilone (Ixempra)
- Leflunomide (Arava)
- Lenalidomide (Revlimid)
- Metronidazole/Misonidazole (extended use)
- Nitrofurantoin (Macrodantin, Furadantin, Macrobid)
- Nitrous oxide (inhalation abuse or Vitamin B12 deficiency)
- Nivolumab (Opdivo)
- Pembrolizumab (Keytruda)

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- Perhexiline (not used in U.S.)
- Pertuzumab (Perjeta)
- Pomalidomide (Pomalyst)
- Pyridoxine (Although megadoses [10 times or more the RDA] of Vitamin B6 may be harmful, high intakes of vitamin B6 from food sources have not been reported to cause adverse effects.) NIH Fact Sheet
- Stavudine (d4T, Zerit)
- Suramin
- Thalidomide
- Zalcitabine (ddC, Hivid)

Uncertain or Minor Risk

- 5-Fluoracil
- Adriamycin
- Almitrine (not in U.S.)
- Chloroquine
- Cytarabine (high dose)
- Ethambutol
- Etoposide (VP-16)
- Gemcitabine
- Griseofulvin
- Hexamethylmelamine
- Hydralazine
- Ifosphamide
- Infliximab
- Isoniazid (INH)
- Lansoprazole (Prevacid)
- Mefloquine
- Omeprazole (Prilosec)
- Penicillamine
- Phenytoin (Dilantin)
- Podophyllin resin
- Sertraline (Zoloft)
- Statins
- Tacrolimus (FK506, ProGraf)
- Zimeldine (not in U.S.)
- a-Interferon

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Negligible or Doubtful Risk

- Allopurinol
- Amitriptyline
- Chloramphenicol
- Chlorprothixene
- Cimetidine
- Clioquinil
- Clofibrate
- Cyclosporin A
- Enalapril
- Gluthethimide
- Lithium
- Phenelzine
- Propafenone
- Sulfonamides
- Sulphasalzine

A Note about Alcohol

Alcohol was removed from the neurotoxic drug list in July 2004. While people with CMT generally suffer no ill effects from the moderate consumption of alcohol, they should be particularly mindful of the fact that alcohol affects balance and coordination, and that overconsumption of alcohol is generally not recommend under any circumstances. If you have questions about alcohol and your health, consult your doctor.

A Study on Neurotoxic Medications

Neurologists Louis H. Weimer of Columbia University and David Podwall of the Albert Einstein College of medicine note that while "existing peripheral neuropathy is a generally accepted risk factor for increased susceptibility to neurotoxic agents," there is some question whether CMT patients should avoid neurotoxic medications even when their use is clearly indicated. The extensive distribution of the list of neurotoxic medications raises the additional concern that, in some cases, an inordinate degree of perceived risk could deter the use of a preferred medication for a condition unrelated to CMT.

Weimer and Podwall conducted an extensive literature search and found that 22 of 26 reports of neurotoxicity in CMT patients concerned vincristine, a chemotherapeutic agent (listed on Medical Alert as "definite high risk"). The remainder concerned nucleoside analogs and taxoids (which fall in the "moderate to significant risk" category).

They also reviewed data from the CMT North American Database,* a computerized registry of clinical details of CMT patients in the U.S. and Canada. The database provided 996 drug entries of 209 persons from 190 families. Medications with multiple reported exposures and more than one claim of symptomatic worsening of neuropathy included metronidazole, nitrous oxide, statins, nitrofurantoin, phenytoin, and sertraline. Others (isoniazid, penicillin — high IV doses) had 1 or 2 adverse reports. Still other agents were notable for exposures without reported

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neuropathic effect. These included adriamycin, chloramphenicol, dapsone, disulfiram, hydralazine, lithium, and pyridoxine.

Overall, Weimer and Podwall conclude that treatment with vincristine poses an "unacceptable risk to patients with known or possible CMT1A." They further conclude that the use of other agents in the significant risk category of the list should be considered with caution, and "the probable lesser risk of agents in lower categories should also be weighed when prescribing these drugs for people with CMT."

At the same time, however, Weimer and Podwall are careful to point out that these conclusions are based on limited direct evidence, and that there are several possible explanations for the lack of documentation in the literature regarding adverse effects of many of the drugs on the CMTA neurotoxic drug list.

In particular, cases of worsening of neuropathy may by unreported or unrecognized, so it is still prudent to make your treating physician aware that drugs on the Medical Alert list may have the potential to adversely affect someone with CMT and to discuss alternative medications. More importantly, if you begin taking any of the medications on the list, or any other medication, and you notice a change in your condition, you should notify your physician immediately.

*The CMT North American Database was initiated at Wayne State University. Funded by the Charcot-Marie-Tooth Association and the Muscular Dystrophy Association, it is currently maintained in the Department of Medical and Molecular Genetics at Indiana University.

The study conducted by Weimer and Podwall demonstrates the potential of the database project to provide researchers with the information needed to answer important questions regarding the treatment and management of CMT. At the same time, the study points out the limitations of the current data, and the need for more people with CMT to contribute their information. Click here to read about the database and how you can help.

CMT United Kingdom asked our Neurological Advisor, Dr David Hilton-Jones, MD, FRCP, FRCPE, to review these for us and to give us his advice.

Dr Hilton-Jones says: "All of these drugs can cause nerve damage (ie. neuropathy). There is no evidence that having CMT makes you more susceptible to such damage, even if that may seem an obvious possibility. I suggest:

1. Avoiding these drugs if a safer alternative is available and equally effective.
2. Not to panic if you have taken one of them for a serious problem.

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