Canadian Collaborative HIV Pharmacists Network Winter Newsletter

Happy New Year Everyone!!!!!!!!!!

I will be signing off soon as your Madame Prez. It has been a great year serving you. I am off to another tour of duty as a new mommy. My new email that can be used until July 2000 is michael.a.tucker@sb.com This is my husband's which I can access at home!!!!!!!!!! & I would love to still network with everyone while I am off so please update your email lists. Best of luck to Christine who is now officially in charge!!!!!!

Our Next Network Meeting at the Retrovirus Conference

Details with regards to registration deadlines etc are in the summer newsletter. In discussion with Ginette, Merck is pleased to offer everyone a $500.00 travel grant (including you Debbie) and 2 night's hotel accommodation (you can book this yourself). Please note that registration for the meeting will not be paid for. Members are responsible for booking their own flights The preliminary agenda for the meeting is attached. Christine will be in touch with regards to the details of exactly where the meeting will be held. An item on the agenda will be location of future meetings ie 2001 and beyond. I think to make everyone's life a whole lot easier our annual meeting should be at CAHR. We are a Canadian group and we don't have to worry about registering and planning at the last minute and it is much cheaper. If people still want to go to the Retrovirus Conference, they can certainly still do this on their own. The group can have further discussion around this at the San Francisco meeting. CAHR may be in Halifax in 2001 so I would get to play hostess to you all!!!!!!!!!

International AIDS Conference

The XIII International AIDS Conference 2000 organizers have announced important deadline dates for the XIII International AIDS Conference in Durban, South Africa, July 9-14, 2000.
Please make note of the following important dates:
February 1, 2000 will be the deadline for:

* Abstract submission
* Early registration fee
* Cancellation of registration with full refund
* Satellite meetings requests

April 1, 2000 will be the deadline for:

* Accommodation requests

May 1, 2000 will be deadline for:
* Standard registration fee. (Please note that the late registration fees will apply after this date.)
June 1, 2000 will be deadline for:
* Late breakers
The conference website can be found at this link:
http://www.aids2000.com/projects/aidsonline/aidshomepage.nsf/-webFrameset?openform

Glenda is back!!!!!!!!

"I just wanted to let you know that I have returned from down under with more freckles, slightly improved surfing skills and no detectable accent. I am back, stress-relieved (although its amazing how quickly that can change), and here in the clinic Mon-Thurs. I would appreciate being put back on the HIV network mailing list, and getting a copy of the last couple of newsletters. Our new hospital email system appears to accept all kinds of attachments without problems. I have a new email address as well.

I hope that all is well with you and you had a great summer- you have no doubt been as busy as ever. Let me know if there is anything I can volunteer to help with."

Clinical Pearls

Amprenavir

Re: dose adjustment? amprenavir with efavirenz

Anyone who is using amprenavir in combination with nevirapine or Efavirenz are you increasing the dose of amprenavir to compensate for the hepatic induction by the NNRTIs? If so, what dose are you using? (I have Attempted to get recommendations from Glaxo and Dupont but no one has solid data to support a particular dose adjustment).

The interaction between amprenavir and nevirapine is unknown but likely to be significant based on PK data with amprenavir and efavirenz. Efavirenz reduces amprenavir AUC by 36%, Cmax by 39% and Cmin by 43%. Considering the pharmacodynamic data available for amprenavir (and other PIs) which suggests high trough concentrations are necessary for a good response, it would be prudent to adjust the dose of amprenavir with either nevirapine or efavirenz. Current thoughts are to change amprenavir to 1200mg TID, add ritonavir 200mg BID or add nelfinavir 1250mg BID. The PK data to support this will be presented at ICAAC, there is no clinical data that I know of.

Adefovir

Available compassionate access

Adefovir was now available compassionate access through Gilead Sciences 1-800 GILEAD

Ritonavir Capsules

As everyone may have heard Ritonavir Capsules are now available for patients who are intolerant of the liquid (Hmmm isn't that just about everybody). Anyhow a Doc in your clinic needs to call the Abbott Access line at 1-888-832-7755 and ask for an enrollment form, then you can photocopy the form & fill it out for all of your patients who fit the criteria. You can apparently only order a 1 month supply at a time & for now it is free of charge.

More on Liquid Amprenavir

Here is some interesting information on the Amprenavir oral capsules/liquid interchangeability.

There are some theoretical concerns raised by substituting liquid for capsule formulation of Amprenavir, in addition to the practical issues queried. The approved label information indicates that "Amprenavir is 14% less bioavailable from the liquid formulation than from the capsules; therefore AGENERASE Capsules and AGENERASE Oral Solution are not interchangeable on a milligram per milligram basis."

With adjustments for reduced bioavailability (as appears to have been considered in the manufacturer's suggestion for 90mL bid), the total daily dose of Vitamin E would approach 8400 IU (several hundred times the adult Vitamin E reference daily intake of 30 IU). Each 1 mL oral solution contains 46 IU vitamin E as d-alpha TPGS (tocopheryl polyethylene glycol 1000 succinate). This compares with a total daily Vitamin E dose of 1744 IU associated with the recommended adult dose of the capsule formulation (109 IU vitamin E as d-alpha TGPS per150-mg amprenavir capsule).

The approved label information further indicates that "the effects of long-term, high-dose vitamin E administration in humans is not well characterized and has not been specifically studied in HIV-infected individuals. High vitamin E doses may exacerbate the blood coagulation defect of vitamin K deficiency caused by anticoagulant therapy or malabsorption."

FASEB's nutrient guide indicates that Vitamin E is relatively safe compared to the fat-soluble vitamins. Few side effects from high intakes of this vitamin have been reported, even at doses as high as 3200 mg daily (for practical purposes, 1 mg of the synthetic form, racemic a-tocopherol acetate, is equivalent to international unit (IU) of vitamin E). However, high vitamin E supplementation may be contraindicated when a coagulation defect is present due to vitamin K deficiency or in individuals receiving anticoagulant drugs.

In addition to other issues posed by the high Vitamin E content of this medication, some have noted also that associated PEG absorption presents the potential for hyperosmolality in patients with renal insufficiency.

International Teaching Materials

(Nikola) I just wanted to check if anyone has any medication teaching materials to share that are in a pictograph format, or in Swahili, Mandarin, Cantonese, First Nations languages and/or in the various dialects from the Sudan? (any others?)

ATIS is pleased to bring you information about our new Spanish website and Spanish publications, as well as HIV/AIDS conferences and Special Topics. We hope you find this information helpful. As always, we are interested in your comments. We can be contacted at atis@hivatis.org or 1-800-448-0440, TTY 1-888-480-3739, or our International number 1-301-519-0459.

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SPANISH WEBSITE and PUBLICATIONS
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ATIS Health Information Specialists are pleased to announce that a new Spanish section is available on the ATIS website,
http://www.hivatis.org/spanish/publications.html?list.

The often requested publication, "HIV and Its Treatment: What You Should Know", is now available in Spanish.

"VIH y su Tratamiento: Lo Que Usted Debe Saber", is available on the ATIS website, at http://www.hivatis.org/spanish/publications/consumer.html?list.

The publication is also available in PDF format,
http://www.hivatis.org/spanish/publications/consumer.pdf. To view the

publication in PDF format, you will need the Adobe Acrobat Reader, http://www.adobe.com/products/acrobat/readstep.html

ATIS plans to have hard copies of "VIH y su Tratamiento: Lo Que Usted Debe Saber" available by the end of the year and will notify you via e-mail when it is available in hardcopy.

ATIS will continue to add publications and other treatment information to the Spanish section, so refresh your browser frequently when visiting our Spanish website, http://www.hivatis.org/spanish/publications.html?list.

DRUG INTERACTIONS

Fortovase with Nevirapine?

I am aware of the drug interaction (approx. 25% SQV AUC reduction) but it seems that the significance of that drug interaction with an "absorbable formulation" of SQV is unknown.

I'd like to have your output on this matter in regards with dosage adjustment or other valuable information (clinical studies, etc) (Pierre)

(Christine)
We don't use very much Fortovase alone, mostly due to the pill burden but also less experience/studies. I can't say that I can offer much further information other than I would be a bit hesitant to use nevirapine and saquinavir sgc (i.e. without ritonavir). Even though the sgc has better bioavailability, I would be concerned about efficacy particularly with an enzyme inducer on board.

(Alice)
Yes, I would probably feel better with a "splash" of ritonavir on board. I wouldn't use keto as an inhibiting agent (even though it also increases SQV), because of the significant decrease in antifungal levels in conjunction with nevirapine.

Lipitor

Lipitor Lowers Blood Levels of Invirase and Norvir

A widely discussed adverse side effect of treatment with protease inhibitors is their potential to cause increased levels of cholesterol. This condition may place patients at increased risk for coronary heart disease. High levels of cholesterol, however, can be significantly reduced by treatment with lipid-lowering drugs, such as Lipitor (atorvastatin), according to David Zucman, MD, of Hospital Foch,

in Suresnes, France. At the 3rd International Conference on HIV Infection and Nutrition in Cannes, France (April 22-25, 1999), Zucman reported successful treatment with Lipitor of 12 patients whose cholesterol levels put them at risk for heart disease. "When the protease inhibitor was discontinued, cholesterol levels returned to normal," said Zucman.

Zucman then decided to evaluate how protease inhibitors and Lipitor interact, because both drugs are metabolized in the liver by the hepatic cytochrome p450. Three of Zucman's patients were taking Crixivan (indinavir), and he found no particular interaction between the two drugs. However, nine patients were taking the double combination of Norvir (ritonavir) plus Invirase (saquinavir). In these patients, there was a significant fall in protease inhibitor levels in the blood, which required halting treatment with Lipitor in these patients. Zucman recommends that patients with high cholesterol levels take lipid-lowering drugs to reduce the risk for heart disease, but he also recommends that the patients' blood levels of protease inhibitors need to be closely monitored. He added that use of Pravachol (pravastatin) might be better tolerated than Lipitor. Source: Zucman D. Hypercholesterolemia during protease inhibitor treatment: effect of atorvastatin. 3rd International Conference on HIV Infection and Nutrition. April 22-25. Cannes, France.

DI with AED's(Debbie)

How are people managing the DI b/w the antiepileptics and PIs and NNRTI's?

I have had 3 patients in the last 6 weeks who have been on either phenytoin or CBZ, and required ARV therapy to include PI or NNRTI. In two patients, they were receiving the antiepileptic for seizures secondary to toxo. Both pts are in the process of being switched from their current AED to lamotrigine or gabapentin. The third pt has been on phenytoin for over 15 years for epilepsy with good control, and does not wish to change AED's. Therefore we are starting her on triple nukes for now, but she will eventually need PI or NNRTI.

The lack of info on managing this interaction is frustrating! Are people empirically increasing the dose of PI/NNRTI? If so, by how much?

(Alice)
We are basically doing the same thing here - trying to avoid CBZ, phenytoin, and phenobarbital at all costs. If you do ever need to consider ARV other than triple RTIs, one potential option might be to go with double PI (e.g., SQV/RTV) where the levels of at least 1 PI (e.g., SQV) are so significantly increased by RTV that having a moderate enzyme inducer on board might not make that much of a difference. Of course, having RTV on board will probably mean readjustment of the anticonvulsant dosage, but at least there we can do levels pretty easily. In

terms of the valproic acid & viral replication issue, I'm not sure how clinically relevant it is in this day of HAART. Also, I think there were some issues with the study design of the older abstracts on this, although I'm not completely up to speed on all the details. Michelle and I had to write a letter to Ann Pharmacother in response to someone's inquiry on this matter (see below):

Authors' Reply to:
"Risk of Drug-Disease and Disease-Drug Interactions with Anticonvulsants in Human Immunodeficiency Virus (HIV+) Patients" (file 8240b)

In response to the letter written by Jennings and Romanelli, we agree with the authors' insights on the need to carefully assess for drug-disease interactions. Since this topic was discussed in greater detail in a prior review,1 we limited the focus of our most recent article to pertinent HIV drug-drug interactions.2 While we appreciate the information provided on the theoretical risk of valproate increasing viral replication, we are uncertain of its clinical relevance in an era of highly active antiretroviral therapy (HAART). The results of the in vitro studies referred to by Jennings and Romanelli may also not be directly applicable to clinical practice since plasma protein binding was not taken into consideration.3 When faced with the decision of selecting an anticonvulsant for a patient on HAART, we feel that agents which are not inducers of the hepatic cytochrome P450 isoenzymes (i.e. valproic acid, lamotrigine, and gabapentin) are safer choices since they are less likely to negatively affect the metabolism of antiretrovirals that are also CYP450 substrates. Potent inducers such as phenytoin, carbamazepine, and phenobarbital have the potential to significantly decrease protease inhibitor and non-nucleoside reverse transcriptase inhibitor (NNRTI) serum concentrations, and concomitant therapy may subsequently result in potential virologic breakthrough. These agents should be avoided or used with extreme caution when given concurrently with standard doses of HAART. In addition, agents such as valproic acid or gabapentin may be useful for other indications in HIV. For instance, valproic acid is widely prescribed for the management of HIV-related mania,4 while gabapentin may be useful for relieving symptoms associated with HIV peripheral neuropathy.5 Therefore, it is important to consider all aspects of a patient's health, including current virologic suppression and immune response, concomitant disease states, symptoms, medications, and quality of life when contemplating changes or additions to an individual's complex medication profile. Careful monitoring of toxicity and efficacy parameters (including viral RNA) remains appropriate whenever modifications in therapy are required.

References:
1. Tseng AL, Foisy MM. Management of drug interactions in patients with HIV. Ann Pharmacother 1997;31:1040-58.

2. Tseng AL, Foisy MM. Significant interactions with new antiretrovirals and psychotropic drugs. Ann Pharmacother 1999;33(4):461-73.
3. Jefferson JW. Possible risks associated with valproate treatment of AIDS-related mania [letter]. J Clin Psychiatry 1998;59(6):317.
4. RachBeisel JA, Weintraub E. Valproic acid treatment of AIDS-related mania [letter]. J Clin Psychiatry 1997;58(9):406-7.
5. Newshan G. HIV neuropathy treated with gabapentin. AIDS 1998;12:219-21.
Alice Lin-in Tseng, Pharm.D.

(Pierre)
I have personally avoided CMZ and phenytoin and have educated the ID physicians to do so as well. Since there is no information regarding the significance of the interaction, I have a hard time suggesting a dosage increase as the dose is unknown. It has been interesting because sometimes patients have been on these drugs for either seizures or neuropathic pain and not reassessed for many years. Occasionally we have been able to stop them altogether with no adverse outcome for the patient. In other patients, we have switched to agents that you have mentioned. It is frustrating that there is no information. I would really like to do a PK study with either CMZ or phenytoin. How about it fellow research group members? Is anybody interested? We have a pharmacist working at the UAH who just finished his PhD in kinetics and I am sure would be willing to help out. The logistics of such a study is always difficult (i.e. HIV patients vs healthy volunteers). In addition, I doubt single dose studies would be very useful due to the nature of enzyme inducers (i.e. takes a little while to synthesize more enzymes).

While we are on the topic, has anyone seen the article in Ann Pharmacotherap (1999;33:1113-6) regarding the use of valproic acid in HIV patients. I have not had a chance to get the original article (only the abstract), but it talks about the potential for VA to increase viral replication. What does everyone think?

(Tom)
Usually I've switched the patients from CBZ/Phenytoin to Valproate. In Ont, Garbapentin is only covered for tx of seizures if the others failed. One thing that makes me nervous is don't know what is the optimal dose for preventing seizures. So far have been using 500 mg BID Epival & no problems (knock on wood). Has anyone used higher doses or are you just titrating to response?

Calcium for Nelfinavir Related Diarrhea

(Kathy) From ICAAC - abstract 1308

Subjects were given 500 mg of calcium bid for nelfinavir induced diarrhrea. N=24 All subjects reported improvement, with 67 % reporting normal stools and 33 % mild diarrhea. Before taking part in the study, 50 % of the pts reported diarrhea as mild, 42 % moderate & 8 % severe. All patients had been taking at least one antidiarrheal agent prior to using calcium. Not sure of the mechanism. Has anyone tried this yet??

(Pierre)
We have started to recommend calcium carbonate {TUMS} (personal info from company) for nelfinavir-induced diarrhea. I have not received any feedback from the patients so far. Mechanism of action ??? no idea. But there is a concern with a possible interaction leading to a decrease absorption of NLV (NLV needs an acidic environment to be absorbed). CaC03 at doses of 5 tablets (of 500mg ????) with NLV 50 mg/kg led to 2-3 fold reduction of NLV AUC in preclinical drug interaction study (refer to page 3-3 of the expanded access program document). We should instruct our patients NOT to titrate up the dose as needed (such as loperamide for instance).

I will keep you posted on the clinical effect of CaCO3 in Ottawa....

Metamucil & PIs

(Christine)
I have had a couple of patients recently wanting to use Metamucil to control PI related diarrhea (i.e. NFV and IDV). I cannot find any information which is not unexpected, however I thought I would check with all of you to see if you have had any experience or thoughts on this matter.

(Nikola)
I have been suggesting psyllium to many patients and have had a number try it with moderate success (including decrease in use of other antidiarrheals). Considering the potential benefit and the great tolerability, I usually recommend that patients give it a try. There were also two abstracts presented at ICAAC describing psyllium's benefit (I don't have the exact reference here).

(Alice)
We've used it occasionally, and have had varying results. In addition to the calcium carbonate (500 mg BID) abstract that Kathy mentioned earlier, there was another ICAAC abstract that looked at using psyllium husk fiber bars (see below). Apparently these are available in most drugstores and are supposedly much easier to take and more palatable than loose Metamucil powder.

Abstract number: 1307

Citation: Abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, September 1999, page 502

Psyllium Husk Fiber Bars are Efficacious in the Treatment of Protease Inhibitor (PI)-Induced Diarrhea.

T. RONAGH, D. SCHROEDER

UMC Wellness Ctr., Las Vegas, NV.

Background: Previous data has reported that psyllium husk fiber is effective in eliminating or improving PI-induced diarrhea in HIV patients. Adherence to psyllium husk powder has presented problems for some patients due to taste and consistency concerns.
Objective: To assess efficacy and patient adherence of psyllium husk fiber bars (PHFBs) in the management of PI-induced diarrhea.
Methods: Open label, prospective trial. Sixteen patients with a history of persistent diarrhea associated with PI use were asked to complete pre- and post-study surveys regarding symptoms. Upon completion of the initial survey, patients received nutritional counseling and a 2 week supply of PHFBs with recommendations to take 2 bars one hour before bedtime. At the end of the 2 week study period patients were asked to complete a second survey evaluating the efficacy and taste of the bars.
Results: Fourteen of sixteen (86%) enrollees completed the 2 week study and both surveys. One patient d/c due to complications from gastric carcinoma and one for psychiatric reasons. At baseline, (N=14) 71% were male, mean age was 38 (range 26-53), mean viral load was 69,025 copies (range <50 - 357,000) and mean CD4 count was 275 (range 29-738). Prior to the use of PHFBs, 29% of patients self reported diarrhea as Grade 1 (mild), 64% as Grade 2 (moderate) and 7% as Grade 3 (severe). Mean grade for all patients was 1.78. After 2 weeks use, 93% (13/14) reported their diarrhea symptoms as improved. Fifty percent of patients reported normal stools, 29% reported Grade 1 and 21% Grade 2 diarrhea. Mean grade of diarrhea improved from 1.75 to 0.93 after 2 weeks of PHFB use. All patients (14/14) responded they liked the taste of the PHFBs and found them easy to adhere to.
Conclusion: In this prospective trial, 93% of study participants reported that psyllium husk fiber bars improved their diarrhea symptoms and were convenient to take. Majority (86%) of patients continued to use the fiber bars after completion of the study. Approximate cost for 2 weeks of PHFBs was $5. These findings support the use of psyllium husk fiber bars as a low-cost option for treating PI-induced diarrhea.

(Tom)

Haven't used this for quite a while, back when PIs became available. Did get good results probably because of the greater severity of diarrhea w/Ritonavir, plus pt tend not like it as much. Generally use Loperamide as 1st line as we want to get diarrhea under control ASAP, hopefully avoid pt d/c therapy. The psyllium husk bar & CaCO3 are worth a try in pt with mild-moderate diarrhea & if they're willing to pay. As you know there're many pt who wants everyone thing covered for free! Loperamide is covered by gov't in ON.

Nevirapine in pregnancy

(Linda)
I am wondering if anyone is using this regimen for any of their pregnant patients at delivery. We have a 38wk old +ve pt who has declined any ARV therapy (first saw her at 34wk) -- VL = 76,000. She has elected to go the "natural" medicine route since she's been in this area x13years. We are still trying to convince her to take something at delivery & for the baby. (She will likely also insist on breastfeeding). If we give the 1x 200mg dose to the Mom at delivery, how do we give the 2mg/kg dose to the babe if only tablets commercially avail in Canada? -- I had thought there were granules for susp, or can we make a suspension for a one time dose which must be given within 1st 72h? HELP! Thanks.

(Pierre)
We plan to use it for one of our pregnant woman in Ottawa. Here is the information I got from HPB:
There is a 10 mg/ml suspension formulation available through Special Access Program. You have to call Chris Daly at Boehringer Ingelheim (? not Glaxo) 905 631-4595 It comes in a 240 ml bottle (a little big for one 2 mg/kg dose.....)

(Natalie)
We have been using the 10mg/ml suspension of nevirapine since the beginning of 1998. As of September 27, 1999 Suzanne Soman at 905-631-4759 or fax 905-333-4464 or email ssolman@boehringer-ingelheim.ca is handling the Special Access Program for nevirapine. The neonatal dose (through to 3 months) PACTS protocol 365 is 5 mg/kg/day divided once daily for 15 days then 120 mg/m^2/dose q12h x 14 days then 200mg/m^2/dose q12h. Why nevirapine for the baby?? Not my first choice. I love answering pediatric questions (that's want I do for a living) but you have to wait until my working days for a reply (Tuesday, Thursday, Friday). Natalie

Reference:
1. Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV infection. 15 April 1999. http://www.hivatis.org. [Accessed 22 Oct 1999].

FDA warning to BMS re: hydroxyurea

The FDA issued a warning letter to Bristol-Myers Squibb Company (BMS) concerning a presentation by BMS entitled "Hydroxyurea and its Role in Treating HIV Disease" at the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in September. The FDA concluded that BMS promoted Hydrea and Droxia for an unapproved use and failed to disclose important safety information.

The letter asserts that, although BMS was aware of reports of serious adverse effects and fatalities and knew that this information was not yet widely publicized, it did not disclose this information.

The FDA has requested corrective action by BMS, including the immediate cessation of disseminating the promotional materials and the notification of conference attendees of ICAAC and other healthcare providers correcting the misleading information. The warning letter in its entirety can be found at http://www.fda.gov/cder/warn/oct99/8409.pdf.

Final Thoughts

Subject: What I've Learned

I've learned that I like my teacher because she
cries when we sing "Silent
Night". Age 6

I've learned that our dog doesn't want to eat my
broccoli either. Age 7

I've learned that when I wave to people in the
country, they stop what they
are doing and wave back. Age 9

I've learned that just when I get my room the way I
like it, mom makes me
clean it up again. Age 12

I've learned that if you want to cheer yourself up,
you should try cheering
someone else up. Age 14

I've learned that although it's hard to admit it,
I'm secretly glad my
parents are strict with me. Age 15

I've learned that silent company is offers more
healing than words of
advice. Age 24

I've learned that brushing my child's hair is one of
life's great pleasures.
Age 26

I've learned that wherever I go, the world's worst
drivers have followed me
there. Age 29

I've learned that if someone says something unkind
about me, I must live so
that no one will believe it. Age 39

I've learned that there are people who love you
dearly but just don't know
how to show it. Age 42

I've learned that you can make some one's day by
simply sending them a
little note. Age 44

I've learned that the greater a person's sense of
guilt, the greater his or
her need to cast blame on others. Age 46

I've learned that children and grandparents are
natural allies. Age 47

I've learned that no matter what happens, or how bad
it seems today, life
does go on, and it will be better tomorrow. Age 48

I've learned that singing "Amazing Grace" can lift
my spirits for hours.
Age 49

I've learned that motel mattresses are better on the side away from the
phone. Age 50

I've learned that you can tell a lot about a man by the way he handles these
three things: a rainy day, lost luggage, and tangled Christmas tree lights.
Age 52

I've learned that keeping a vegetable garden is worth a medicine cabinet
full of pills. Age 52

I've learned that regardless of your relationship with your parents, you
miss them terribly after they die. Age 53

I've learned that making a living is not the same thing as making a life.
Age 58

I've learned that if you want to do something positive for your children,
work to improve your marriage. Age 61

I've learned that life sometimes gives you a second chance. Age 62

I've learned that you shouldn't go through life with a catchers mitt on both
hands. You need to be able to throw something back.
Age 64

I've learned that if you pursue happiness, it will elude you. But if you
focus on your family, the needs of others, your work, meeting new people,
and doing the very best you can, happiness will find you. Age 65

I've learned that whenever I decide something with kindness, I usually make
the right decision. Age 66

I've learned that everyone can use a prayer. Age 72

I've learned that it pays to believe in miracles.
And to tell the truth,
I've seen several. Age 75

I've learned that even when I have pains, I don't have to be one. Age 82

I've learned that every day you should reach out and touch someone. People
love that human touch holding hands, a warm hug, or just a friendly pat on
the back. Age 85

I've learned that I still have a lot to learn.
Age 92

I've learned that you should pass this on to someone you care about.
Sometimes we all just need a little something to make us smile. It's ageless