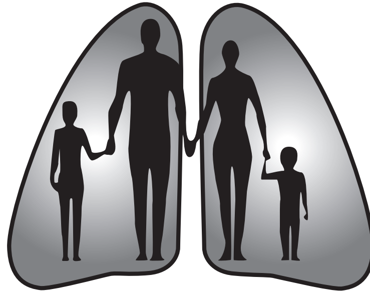
FPACG NEWSLETTER



FPAGC

FAMILY PHYSICIAN AIRWAYS GROUP OF CANADA
l'Association canadienne des médecoms de famille contre l'asthme

Chairman's Report March 2002

Hope springs eternal for the warm weather of spring. Welcome to another FPAGC Newsletter. It has been another busy year for the group and the Executive. I will review the activities of the group and share with you some future activities that I hope will excite some of you.

We continue to be active in providing educational initiatives across Canada. Mainpro C workshops have been provided in October 2001 in Vancouver at the conjoint meeting of the British Columbia and Canadian Colleges of Family Practice meeting. In November 2001, we provided two different workshops for the Ontario College of Family Physicians in Toronto. ASED 5 was held also in Toronto in later November 2001 and the FPAGC presented there also. Workshops on Asthma management have been held in a couple of other Ontario locations as well.

What is coming? There are a couple of very interesting conferences in exciting locations in the near future, both of which the FPAGC are involved in. April 21-23, 2002 will find an FPAGC Mainpro C produced Spirometry workshop at the Alberta Respiratory Disease Symposium in Banff. For those of you interested in details about this conference email docrob@telusplanet.net.

The second International Primary Care Respiratory Group Meeting will be taking place in Amsterdam June 7-9, 2002. I will give more details about this inside the newsletter.

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Chairmans Report (*Continued From Cover Page)*

We are working out all of the wrinkles in our Action Plan which you can download at www.AsthmaActionPlan .com .We are excited that our work is hopefully going to be used with National initiatives. Please see the current version, it is a little simpler and easier to use.

Our website address is www.fpagc.com . Dr. Cheah is working on getting all of our past newsletters scanned on to the site. There are some excellent resource articles available in those old newsletters!

In the coming year we are planning to do a bit of research! Primary care research is often thought to be too much trouble, but after being exposed to my international colleagues (see IPCRG), the value is clear. We will be sending you a survey regarding your interest in some research, some funded, some not; as well as some initial primary care research questions that we feel need answering. Please take the time to answer the survey. I promise it will not take long!! It will make a difference and maybe peak your interest into new directions for your practices.

This is an exciting year. We have seen the launch of a new drug for Asthma, Symbicort and hopefully we will see the launch of Spiriva (for COPD) before this year is over. A detailed review of Symbicort is found in this issue, we will review Spiriva in the future as well. In addition a new class of oral antibiotics called Ketalides will be released likely this year; this will add to our armamentarium for the treatment of respiratory infections. Keep watching......

Alan Kaplan MD CCFP(EM)
Chair, FPAGC

IPCRG

June 2000 took me to England to participate in the First International Primary Care Group meeting. It was an outstanding success. Meeting primary care physicians with an interest in airway diseases inspired me to continue working with the Canadian group to optimize our care here at home. It was refreshing to see that some of these physicians are similarly taking lead positions in the management of these conditions in their countries. The medications are similar and the issues are legion, but new ideas always facilitate changing initiatives.

The second International Primary Care Respiratory Group meeting will be held in beautiful Amsterdam on June 7-9, 2002. There will be the overall theme of the international flavour of the treatment of respiratory diseases. There will be clinical seminars, workshops and research abstracts presented. Themes include infectious respiratory diseases, lung cancer (current diagnosis, treatment and prognosis), allergy & rhinitis (current diagnosis, new treatment modalities and consequences for general practice), COPD: treatment & monitoring, current insights, Asthma: new treatment

modalities, Asthma in Children: current insights.

Workshop topics will include spirometric diagnosis of asthma & COPD, inhalation technique, acute pulmonary dyspnea (diagnosis, treatment and referral according to current standards in children and adults), PC based monitoring of asthma & COPD & Telemedicine: Demonstration of available systems, skin prick and allergy.

More information can be found at the website: www.ipcrg.org

Have a look, I guarantee a conference worth attending, and the location is pretty special also!

Alan Kaplan MD CCFP(EM)
Chair, FPAGC

Asthma in Pregnancy

At ASED 5, I presented a workshop on the management of Asthma in Pregnancy. For those of you who were there, you can read the next article, as this will be a review!

Pregnancy has many effects on the respiratory system. These begin in the upper respiratory system where it is common to see capillary engorgement of all of the mucosa. This can produce symptoms of an URI with nasal congestion, voice change and laryngitis. The diaphragm elevates 4 cm. during the pregnancy but surprisingly it does not cause a restrictive patter. This is because hormonal effects loosen the ligaments in the chest and the anteroposterior and transverse diameters of the lungs increase. Because of this the lung volumes do not significantly change in pregnancy. However, the minute ventilation does increase, and this causes a respiratory alkalosis and a shift to the left of the oxygen disassociation curve. This causes placental vasoconstriction and will release the ability of the hemoglobin molecule to release oxygen.

Dyspnea is very common in pregnancy. Most women (50% by end of 19 weeks and 75% by end of 35 weeks) feel the increased minute ventilation and experience it as shortness of breath. It can be separated out from disease processes by the normal lung function, and the fact that it does not really interfere with daily activities and it does not progressively worsen. The diagnosis of asthma is made the same way during pregnancy as when not pregnant ,with the exception of some challenge tests.

The rule of 1/3s is handy during pregnancy; ie., 1/3 get better, 1/3 get worse, and 1/3 stay the same. It is usually the more severe asthmatics that worsen. The deterioration usually occurs at 20-36 weeks and usually improves from then on.

Usually labor is tolerated well, with only about 10% of asthmatics deteriorating. This is a good thing! The hyperventilation that occurs (remember that hee-hee-hee) worsens the alkalosis and hypocarbia. This also shifts the oxygen disassociation curve further to the left, making it more difficult for the hemoglobin molecule to release oxygen. This could lead to worsening maternal and subsequently

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Asthma in Pregnancy (*Continued From Page 3)*

fetal oxygenation. But remember, a little maternal hypoxemia means a LOT of fetal hypoxia! Be aggressive with maternal support of oxygenation during labor.

About 3 months after pregnancy, the asthma will revert (all other things remaining stable) to the pre-pregnant state. Remember also that about 2/3 of subsequent pregnancies will follow the same pattern as the first with respect to their asthma.

Asthma morbidity is well studied in pregnancy and poor outcomes are directly related to poor control of the asthma. Maternal outcomes include increased incidence of hyperemesis, premature labor, pre-eclampsia, toxemia, gestational hypertension, increased prenatal mortality. Fetal outcomes include abortion, preterm births low birth weight, IUGR, perinatal morbidity (eg.TTN) and mortality.

Treatment of asthma in pregnancy is more or less the same as when not pregnant. First ensure that environmental precautions are being made. Secondly, remember GERD, which complicates many (as much as 1/3) pregnancies. Therefore continue the usual advice of smaller meals, not lying down after meals, and perhaps Sulcrate, H2 blockers, or even PPIs.

Of course we all worry about the potential teratogenicity of medications, but this is mostly unfounded for asthma drugs. B2 agonists have been shown to inhibit labor. Inhaled steroids are a little more topical in that there are animal studies showing teratogenicity for budesonide and fluticasone, but of course no human studies. There have been no reported teratogenicity of these drugs. We have the most experience with beclomethasone and the animal studies are negative and again, no reported human cases of teratogenicity. I believe that they are safe as per the following:

"Recent studies have not demonstrated an increase in the risk for congenital malformations, stillbirths or fetal mortality with the use of inhaled or systemic corticosteroids."

Page 501, Tuffaha and Busse,
Asthma in Pregnancy and Menses

Chapter 38, Manual of Asthma Management,
2nd Edition, O'Byrne and Thompson

For oral steroids it is clear that there are differences between them. Dexamethasone and betametha-sone cross placenta rapidly and in high concentrations, whereas methylprednisolone and prednisone cross poorly. Therefore, at doses <25mg/day, Prednisone does not cross due to placental metabolism (this is not true of dexamethasone or betamethasone). This allows a low incidence of adrenal suppression in infants with prednisone.

There is currently no human data reported for Leukotriene Receptor Antagonists and so they are not recommended for use in pregnancy. There have been no reported cases of teratogenicity with them; occasionally the risk benefit ratio may rationalize their use in pregnancy. This must be established on an individual case setting.

Long-acting B2s have also not been studied in pregnancy but seem to have already been readily used. Again, the risk benefit ration must be measured.

We do know that Adrenalin is bad. Its use has been associated with possible malformation and it is associated with reduced utero-placental blood flow in animals. For this reason, it is felt wisest to not introduce immunotherapy during pregnancy, but it is felt to be safe to continue immunotherapy in a stable patient on stable dosing.

Remember that poorly controlled asthma is potentially more dangerous for the fetus than medication. The GOAL of medication in the management of asthma during pregnancy is the control of asthma!!

Alan Kaplan MD CCFP(EM)
Chair FPAGC

SYMBICORT

Symbicort was officially released in Canada by AstraZeneca in February 2001. It is a combination of an inhaled corticosteroid budesonide (Pulmicort) and a long acting B2 agonist formoterol (Oxeze). It has been long available in the United Kingdom and elsewhere.

We have learned from studies such as FACET and OPTIMA B that the combination of ICS and LABA (Long Acting Beta Agonist) is often superior to doubling the steroid alone. We also are learning that the combination of an inhaled steroid with the LABA in one molecule is superior to the two agents separately. This has also been shown with Advair. It is felt that the LABA facilitates the entrance of the ICS to the cell nucleus where it works, and that the ICS increases B2 receptors on the cell membranes to increase the sensitivity to the medication. The two in a single molecule do it even better.

Many of us have had tremendous success with the use of Advair. It is efficacious and definitely improves compliance. The addition of a dose counter to 60 has helped allow maintenance of compliance. How is Symbicort different? The differences are twofold. The inhaled steroids are not the same; budesonide vs. fluticasone. Much has been postulated as to the difference of these two inhaled steroids. I will avoid this controversy, and only say that we are indeed fortunate to have two such efficacious medications at our disposal.

There is a difference in the LABAs. Salmeterol (Serevent) is the first LABA. It has been proven to be an excellent bronchodilator for 12 hours. It also has been shown to prevent exercise induced asthma for that long. It does seem to have a relative ceiling effect at 50 ug. Formoterol (Oxeze) was first released by another company in the form of Foradil. This was a capsule in a rotahaler type of device that never caught on very well. Formoterol has similar properties to salmeterol but is more lipophillic. This allows 12 hour bronchodilation but a more rapid onset of 5 minutes which approximates that of salbutamol. In addition,

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SYMBICORT (*Continued From Page 5*)

there is a dose response ratio for formoterol with the highest current recommended doses of 72 ug per day recommended. This difference allows Symbicort to have a faster onset of action. This was proven in "Onset of bronchodilation of Budesonide/Formoterol vs. Salmeterol/Fluticasone in single inhalers" Pulmonary Pharmacology and Therapeutics, (2001) 14, 29-34.

This allows the postulation that only one inhaler would be needed. A medication that could be used for relief of symptoms which also would provide 12 hour relief of those symptoms and also treat the underlying process of inflammation at the same time! This would decrease the need of having two or three different inhalers and would also likely improve compliance. A study called the SMART study is currently underway to see if this is a viable idea.

Symbicort is released in a Turbuhaler format and it has a dose counter of 120 doses. Currently Advair has a discus formulation with a counter and an MDI formulation (non-CFC) without a counter. It will come in two doses, a 200 ug budesonide and 6ug formoterol equivalent and a 100ug budesonide and 6 ug. formoterol equivalent. Much discussion of the dosing schedule will be had. There have been suggestions of two puff BID tapering down to one puff BID to even one puff daily (for maintenance of mild asthma as it has been studied that once daily Budesonide is effective in mild asthma).

It is exciting to have more choic-es for the management of obstructive airways diseases.

I will update this in future newsletters as Symbicort's use becomes more widespread.

Alan Kaplan MD CCFP(EM)
Chair, FPAGC

Research Initiatives

Are you interested in becoming part of clinical research?

The FPAGC in partnership with GlaxoSmith Klein will be asking you this question in the near future. GSK is currently developing a database of interested clinicians to take part in their clinical trials. This of course includes a number of studies focusing on respiratory-based issues.

I personally have been involved in a number of clinical trials, and have found the experience to be most rewarding. Furthermore, getting involved and running a trial in your office is easier than you might think.

Watch out for the GSK research survey to the FPAGC members, which should be in the mail shortly.

Robert Hauptman
Secretary-Treasurer FPAGC

CME Initiatives

How are your Mainpro C credits? Are they up to date? If you are like many CCFP members, you still need a number of Mainpro C credits. However, don't despair! The FPAGC offers a number of Mainpro C accredited programs for FPAGC members and other family physicians.

The FPAGC currently runs a Mainpro C program on asthma and a Mainpro C program on spirometry. The FPAGC is also presently developing a Mainpro C program on COPD, which should be completed by the end of 2002.

For more information on these programs, or if you are interested in running one of these programs in your area, please contact Dr. Alan Kaplan or myself (our contact numbers are at the back of this newsletter).

Robert Hauptman
Secretary-Treasurer FPAGC

Systemic Steroids in Asthma: How long is enough?

One of the common dilemmas in asthma management is how long a course of systemic steroids should be administered to a patient with acute asthma. A recent study presented at the Fifth International Congress on Pediatric Pulmonology tries to address this issue.

Senja Kannisto and associates of the Department of Pediatrics at Kuopio University Hospital in Finland compared the efficacy of three versus seven day courses of prednisilone administered to 40 asthmatic children aged 3 - 15 years with acute asthma. The children received 1.5 mg/kg/day with a maximum dose of 30 mg. The dose of prednisilone was administered as a single morning dose. All of the children were hospitalized for at least one day reflecting the severity of their acute asthma exacerbation.

Both groups of patients had initial FEV1 levels of 76 percent and 78 percent of predicted (for the 3 and 7 day treatment groups respectively). After 4 weeks of follow-up both groups' FEV1 levels had increased to 97 percent and 95 percent respectively. Asthma symptoms and need for breakthrough bronchodilators were equally improved in both steroid treatment groups. More importantly, adrenocortical suppression as measured by low-dose ACTH tests was present in only 56 percent of the 3-day treatment group as opposed to 76 percent in the 7-day group.

Although this is a rather small study, the results are intriguing and seem to suggest that one could achieve the same efficacy with a three day course of systemic steroids as

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Systemic Steroids in Asthma: How long is enough?

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compared with a seven day course, and with the possibility of less side effects.

"ICPP: Three Days of Prednisilone Better than Seven for children with Acute Asthma."

Senja Kannisto and associates.

Submitted by
Robert Hauptman MD
Secretary Treasurer FPAGC

The Treatment of Mild Asthma

The OPTIMA Study: O'Byrne et al, Am J Respir Crit Care Med, vol 164,2001,1392-97

This mainly Canadian,(17 countries total) double blind, randomized, parallel group study, was designed to examine the benefits of LOW DOSE ICS (budesimide-Pulmicort) with or with out the addition of a LAB2 (formoterol- Oxeze) in patients with MILD asthma.

Two groups of mild asthmatics over age 12 were studied for one year. Grp A (ICS free) had not used ICS for at least 3 months and had a FEV1 >80% predicted after SAB2 (terbutaline 1 mg.) Grp B were on low to moderate dose ICS (less than 400 ug / d bud. or equivalent) for at least 3 months and had a FEV1 > 70% predicted after terbutaline.

During a 4 month run in period Grp A took placebo bid while Grp B took bud. 100 ug bid. Poorly controlled pts during the last 2 wks of the run in were randomized (defined by one of rescue use 2 or more times, a > 12% increase in FEV1 or a > 15% increased variability in PEF after terbutaline) Grp A took placebo, bud 100 ug bid, or bud 100 ug/ formoterl 4.5 ug bid. Grp B took bud 100 ug bid or bud 100 ug / formoterol 4.5 ug bid or bud 200 ug bid or bud 200 ug/ formoterol 4.5 ug. Bid. All meds were delivered by a single Turbuhaler device.

Primary outcome measures were, time to first severe asthma exacerbation (need for oral steroids, visit to ER or admission or a decrease in am PEF > 25% for 2 consecutive mornings) Secondary outcomes were changes in am PEF, FEV1 % predicted, % of days with symptoms, % of asthma wakenings, number of rescue inhalations, and rate per pt per year of severe exacerbations.

In Grp A 33% of the placebo grp had a severe exacerbation and asthma was poorly controlled for 14.4% of days. With bud 100 bid there was a 60% reduction in the risk for the first severe exacerbation and a 48% reduction in the rate of poorly controlled asthma days. There was also a reduction in the rate of exacerbations, asthma symptoms, nocturnal awakenings, an increase in FEV1 , and less use of rescue medication. The addi-

tion of formoterol did not provide any benefit except improved FEV1 and am PEF.

In Grp B 33% of patients taking bud 100 bid had a severe exacerbation and asthma was poorly controlled on 13% of days. The use of bud 200 bid showed a trend to improvement in all outcome measurements but none reached statistical significance. Adding formoterol to BOTH bud groups reduced the risk of first asthma exacerbation by 43% and the rate of poorly controlled asthma days by 30%. All other endpoints were improved in both formoterol groups as well.

The authors concluded;

1) In mild steroid-free patients, low doses of ICS (bud 200 ug / d) improves asthma control and reduces exacerbations. These patients do not obtain important clinical benefit from the addition of formoterol as part of their maintenance treatment.

2) Some patients will not obtain optimal control on low dose ICS (bud 200 ug/d). In these patients maintenance therapy with formoterol 4.5 ug bid combined with bud improves asthma control and reduces exacerbations. However doubling the ICS dose (to 400 ug / d) while showing trends to better control and less exacerbations did not do so significantly.

COMMENT: This is an important study in patients with mild asthma. These patients make up the majority of asthmatics especially in primary care. Optimal management of these patients has not been studied in detail prior to this paper. Canadian Consensus Guidelines suggest lowest dose ICS to obtain asthma control as the first choice for maintenance therapy. The Optima study shows that VERY LOW dose treatment (bud 200 ug/ d) is adequate for most patients. Additional treatment with formoterol is not beneficial for most of these patients. However in patients taking low dose ICS there is greater benefit in using bud combined with formoterol for maintenance therapy. Doubling the dose of ICS (to 400 ug/d) although showing a trend to improvement does not make the same statistically significant improvement.

The goal of asthma therapy is to maintain acceptable control using the least amount of ICS to avoid possible side effects of chronic ICS use. This study helps reach this goal for maintenance therapy for our patients with mild asthma.

John Rea M.D.
Executive Committee FPAGC

CFC Transition Strategy

This article updates my previous on this issue. Just to highlight, the Montreal Protocol in 1992 determined that all CFC products (Chlorinated Fluorocarbons) be discontinued due to their harmful effects on the ozone layer. The MDIs (metered dose inhalers) were held as an exception to the rule due to their medicinal need and the lack of alternatives. The timelines for discontinuation of the CFC MDIs has changed a few times, but have now been passed as law with its publishing in Gazette 2. You can expect some media attention to this issue in April or May this year. Here are the timelines:

JULY 1, 2002 no more production or importation of CFC Salbutamol in Canada

JANUARY 1, 2003 no more sales of CFC Salbutamol in Canada

JANUARY 1, 2004 no more production or importation of CFC ICS in Canada

JANUARY 1, 2005 no more sales of any CFC MDI in Canada

ICS= inhaled steroid

There are lots of alternatives now available. First of all, the dry powder products are all non-CFC. HFA (Hydroflouro-alkanes) Salbutamol is available as Airomir (3M) or Ventolin HFA (Glaxo). HFA Beclomethasone is available called Qvar (3M). HFA Fluticasone (Glaxo) is available, although not currently widely yet in pharmacies. Advair (Glaxo) has salmeterol and fluticasone in HFA formulations in its MDI.

It will be important to inform your patients about the changes. Their inhalers may be changed from CFC to HFA and there are some differences. Airomir has a slightly different delivery system, which provides a different force of jet stream at a different temperature. The net effect is the same, the sensation is different and therefore may lead patients to feel they are not getting their medicine. It is also more temperature stable and has more reliable dosing at the beginning and end of the life of the inhaler. Qvar again has a different system; it is in a solution rather than a suspension. This allows the particles to be smaller and get further into the lung. The issue of treating the "whole lung" will be a topic of interest in the future. In addition, as the dose gets further into the lung, the effective dose is twice as strong, allowing lower cumulative doses of ICS. We will be hearing much more about dosing adjustments in the future.

George Allen, coach of the Washington Redskins, used to say, "the future is now". Please consider our children's future health and the health of the ozone layer as you consider prescribing the more ozone friendly HFA or dry powder products.

Alan Kaplan,

Chair FPAGC

Member of CFC Transition Strategy Educational Group, Environment Canada

Member of Consultation Group for CFC Transition, Health Canada

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APPLICATION FOR MEMBERSHIP

If you are interested in a Membership to Family Physician Airways Group of Canada please complete this form and mail to:

Family Physician Airways Group of Canada
25 St. Michael Street, St. Albert, AB T8N 1C7

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Fax ______________________________

Special Interest:
(e.g. lecturing, research, writing, others)

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MISSION STATEMENT

The Family Physicians Airways Group of Canada is committed to helping those with airway diseases lead a full life. The group is dedicated to helping all family physicians maintain and increase their skill in assisting those with asthma and COPD. The strategy of the Group is to maintain a speaker bank, a data base, and practical tools to help physicians attain these skills.

"A group of family physicians with a special interest in asthma."

DÉCLARATION DE PRINCIPES.

L'Association canadienne des médecins de famille contre l'asthme. Un groupe de médecins de famille ayant un intérêt particulier pour le traitement de l'asthme. Les members de l'Association canadienne des médecins de famille contre l'asthme s'engagent à aider les personnes atteintes d'asthme à jour pleinement de leur vie. L'Association veut aider tous les médecins de famille à entretenir et améliorer leurs connaissances dans le traitement de L'asthme. L'Association se propose de maintenir une liste de conférenciers et une banque de références, et colliger des informations practiques pour permettre aux médecins d'accquérir ces connaissances.

The opinions expressed in this newsletter are those of the authors, and not necessaritly those of the Family Physician Airway Group of Canada.