Pathophysiology of Obstetrics VTE

Carol KK Lim
MFM, HoSHAS
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HoSHAS

Key Message

Pregnancy

is an independent risk factor for

VTE

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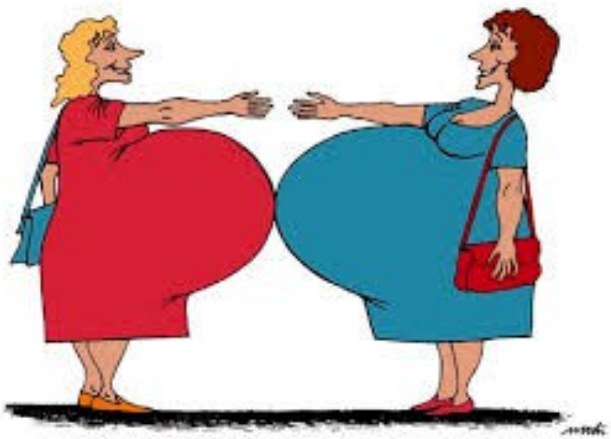


When pregnant, think VTE!!

Outline

What	VTE in Pregnancy
Why	Why VTE in Pregnancy?
Who	Women at risk (risk factors)
Where	Site
When	Which phase of pregnancy
How	Thromboprophylaxis

Kipling Method

I keep six honest serving-men,
They taught me all I knew;
*Their names are **What** and **Why** and **When***
*And **How** and **Where** and **Who**.*

Venous thromboembolism

- Venous thromboembolism (VTE) is a major health problem
- It is the 3rd most common cardiovascular disease after myocardial infarction and stroke
- 3 million VTE-related deaths per year worldwide
- 10% of hospital deaths are due to pulmonary embolism

Naess IA, JTH 2007
VTE CPG 2013
Cohen AT, Thromb Haemost 2007

VTE in Pregnancy

VTE incidence 1-2/1000 pregnancies

Pregnancy : 10x risk

Any stage of pregnancy

Highest during puerperium :

→ 5x risk vs pregnancy

→ 50x risk vs non-pregnant

Elective CS 2x risk vs Vaginal delivery

Emergency CS 2x risk vs Elective CS

Emergency CS ≅4x risk vs Vaginal delivery

**75-80% pregnancy-associated VTE is DVT and 20-25% PE *(≠ HoSHAS data)*

RCOG Green-top Guideline No.37a, Nov 2009

James. Hematology Am Soc Hematol Educ Program 2009

HoSHAS Obstetric VTE

(July 2013-April 2017)

	Antepartum	Postpartum	Total
DVT	5	7	12
PE	3	7	10
*DVT+ PE	0	3	3
Total	**8**	**17**	**25**

Overall incidence of Obst VTE: **0.85/1000 deliveries**
Prior to Sept 2015: 1.0/1000 deliveries
After Sept 2015: **0.61/1000 deliveries**

*Possible under-diagnosis

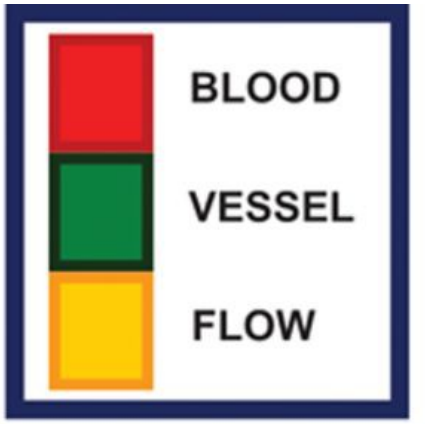
Obstetric VTE : Facts

- Pregnant women are 4-5x more likely to suffer from VTE
- 75-80% pregnancy-associated VTE is DVT and 20-25% PE

Obstetric VTE : Facts

- PE occurs in 15-24% of untreated DVTs with a mortality rate of 15-30%
- PE occurs in 4.5% of treated DVTs with a mortality rate of 1%

Virchow's Triad



HYPERCOAGULABILITY

- Major surgery / trauma
- Malignancy
- Pregnancy (post-partum)
- Inherited thrombophilia
- Infection and sepsis
- Inflammatory Bowel Disease
- Autoimmune condition
- Estrogen therapy
- Inflammation
- Dehydration

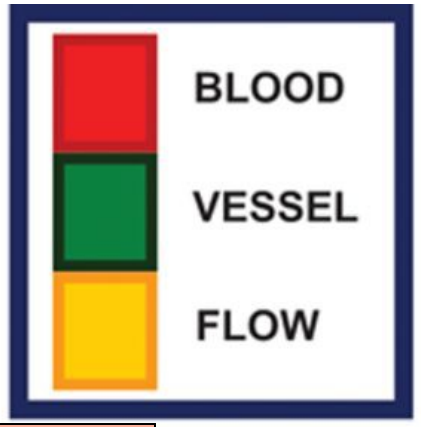
VASCULAR DAMAGE

- Thrombophlebitis
- Cellulitis
- Atherosclerosis
- Indwelling catheter / heart valve
- Venepuncture
- Physical trauma, strain or injury
- Microtrauma to vessel wall

CIRCULATORY STASIS

- Immobility
- Venous obstruction (obesity, tumour, pregnancy)
- Varicose veins
- Atrial fibrillation or left ventricular dysfunction
- Congenital abnormalities affecting venous anatomy (e.g., May-Thurner and Paget-Schroëtter syndrome)
- Low heart rate (bradycardia) and low blood pressure

Virchow's Triad during Pregnancy



HYPERCOAGULABILITY

Hypercoagulobility in pregnancy
-increase clotting factors (VIII, IX, X) & fibrinogen
-reduced levels of anti-coagulators (protein S, antithrombin)

VASCULAR DAMAGE

Vascular compression at delivery
Assisted / operative Delivery

CIRCULATORY STASIS

Compression of left iliac vein (by gravid uterus, right iliac art & left infundibulopelvic vessels); Immobilisation; Hormonally mediated venous dilatation

Pathophysiology of thrombosis

- Thrombosis occurs when there is disruption of Virchow's triad.
- Modifications of haemostasis by pregnancy renders blood hypercoagulable.
- Hyperemesis and pre-eclampsia further contribute to thrombogenesis.
- Excessive fluid loss in hyperemesis concentrates blood and the resultant bed rest further promotes stasis of blood flow.

(1) Hypercoagulability

- Hypercoagulability in pregnancy, in preparation for parturition.

a) **Increased** concentration of clotting factors VIII, IX and X. Fibrinogen level increase by 50% while fibrynolytic activity is decreased.

b) Levels in anticoagulators such as antithrombin and protein S **fall**.

c) Levels in PAI-1 & PAI-2 (placenta) increase 5-fold →Hypofibrinolytics

(1) Hypercoagulability (cont')

- These changes are observed from 1st trimester to 6 weeks after delivery.

- Peak in coagulation in immediate postpartum which tails off after 3 weeks postpartum.

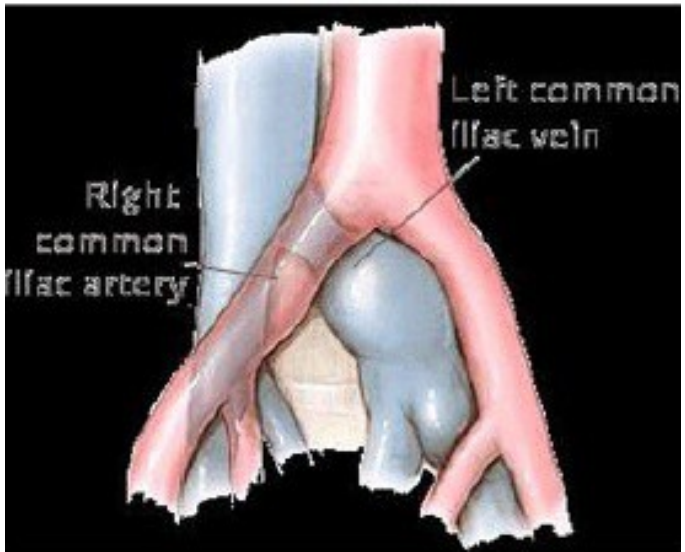
→ Pregnancy: blood is in **procoagulant state**

(2) Venous stasis

a) Venous dilatation (hormonal effect)

b) Compression of the gravid uterus on the IVC

c) Compression of the Lt iliac vein by left infundibulopelvic vessels & Rt Iliac Artery



(3) Endothelial injury

a) Vascular compression at delivery

b) Assisted / operative delivery

Pregnancy…..

….an **independent risk factor**

for VTE

Direct Causes of maternal deaths in Malays 2008-2014

CAUSES OF MATERNAL DEATHS (MALAYSIA)	2009		2010		2011		2012		2013		2014	
	n	MMR	N	MMR	n	MMR	n	MMR	n	MMR	n	MMR
Pulmonary Embolism	**13**	**2.6**	**15**	**3.1**	**10**	**2.0**	**14**	**2.7**	**13**	**2.6**	**15**	**2.9**
Amniotic fluid embolism	10	2.0	15	3.1	6	1.2	9	1.7	9	1.8	9	1.8
PPH	20	10.5	13	2.6	19	3.7	15	2.9	14	2.8	15	2.9
Hypertensive Disorders in Pregnancy	18	13.7	25	5.1	25	4.9	19	3.6	11	2.2	12	2.3
Obstetric Trauma	4	5.4	10	2.0	12	2.3	4	0.8	5	1.0	6	1.2

Family Health Division, MOH Malaysia

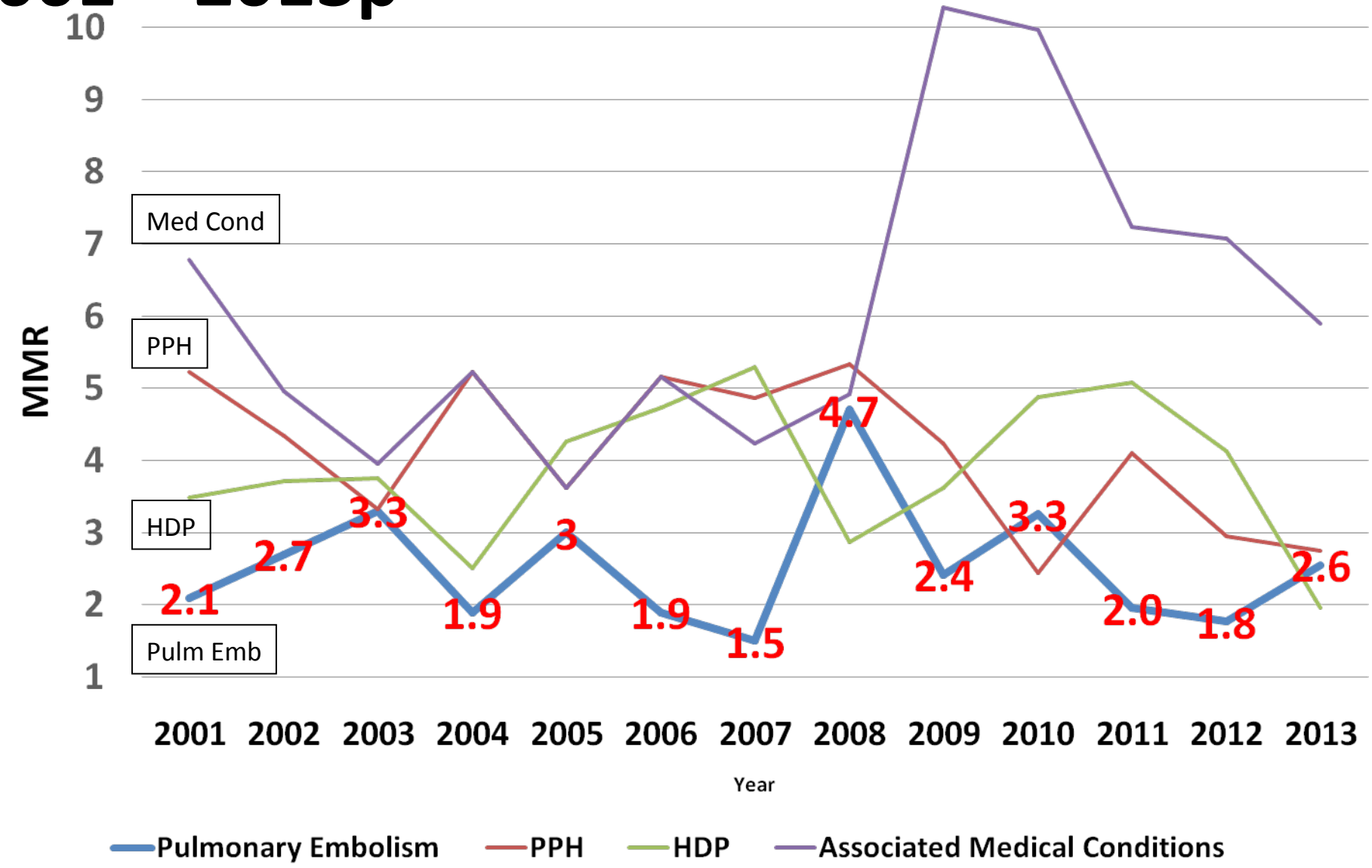
Direct Causes of maternal deaths in Malays 2008-2014

CAUSES OF	2009		2010		2011		2012		2013		2014	
Hypertensive Disorders in Pregnancy	18	13.7	25	5.1	25	4.9	19	3.6	11	2.2	12	2.3
Obstetric Trauma	4	5.4	10	2.0	12	2.3	4	0.8	5	1.0	6	1.2

An average of 13-14 deaths from pulmonary embolism per year!

Family Health Division, MOH Malaysia

Maternal Deaths Cause-Specific MMR 2001 – 2013p



Source: Family Health Development Division & Health Informatics Centre

Malaysia : VTE MMR

Pulm Embolism 2.5/100K LB in 2009-2011p

12.3% of Direct Mat Deaths in 2009-2011p

Sabah: 1.6/100K LB in 2012 (1 PE)
4.61/100K LB 2013 (both cerebral vein thrombosis)
1.6/100K LB in 2014 (1PE)

Pahang: 8.3/100K LB in 2012 (2 PE)
4.1/100K LB in 2013 (1 PE)
7.9/100K LB in 2014 (2 PE)
3.92/100K LB in 2015 (1 PE)
3.92/100K LB in 2016 (1 CVT)

Temerloh: 7.4/100K LB in 2004-2016 (7 PE)

Pahang State Health Department
Sabah State Health Department

Pahang VTE Maternal Deaths

Analysis of pattern of Pahang MMR

? Temerloh women are more thrombogenic

- Lacking in thromboprophylaxis – not systematic, not using the recommended agent, inadequate
- Failure to diagnose, delay in treatment

→Essentially …….

<u>NOT</u> thinking VTE!

Obstetric VTE in Malaysia

- No local publication on Obstetric VTE incidence
- ?poor understanding by HCP
- Lack thromboprophylaxis program
- ?Fragmented care in current system
- ?Issue of LMWH (sourced from porcine)
- Costly thromboprophylaxis program

VTE in Malaysian women?

- Not that uncommon (It is as common as in the West!)
- Under-diagnosed, unsuspected
- Lack of awareness, does not believe (in denial?!)
- Similar risk factors

The eyes do not see what the mind does not know!!

Blind Mind = Blind Eye

Some of the Risk Factors for Obstetric VTE:

Obesity

Medical Co-Morbidities

LSCS

IVF / ART pregnancy

Frequent factors we encounter nowadays

VTE risk in pregnancy & puerperium exist not only during admission but also as out patient.

Walking VTE Risks!

Risk Factor for VTE

- Pre-existing risk factors

Eg: Previous VTE
High risk thrombophilia
Medical co-morbidities
Obesity
Smoker, etc

- Obstetric risk factors

Eg: LSCS – EMLSCS, ELLSCS
Pre-eclampsia
ART/IVF
Mid-cavity or rotational operative delivery

- Transient risk factors

Eg: OHSS (T1 only)
Any surgical procedure in pregnancy or puerperium except immediate repair of perimeum
Hyperemesis
Current systemic infection
Immobility
Dehydration

sion, etc

Risk factors are scored accordingly from 1-4.

RCOG 2015

RCOG 2009 vs 2015 guidelines

<u>Risk factors:</u>

- Readmission (new 2015)
- Surgical procedure in puerperium (except immediate repair of the perineum) → intermediate risk (low risk in 2009)
- T1DM with nephropathy (new 2015)
- Preterm delivery in this pregnancy (new 2015)
- Stillbirth in this pregnancy (new 2015)
- Transient risk factors (dehydration, hyperemesis, current systemic infection, long-distance travel)

RCOG 2009 vs 2015 guidelines

<u>Scoring:</u>

- New system
- May start from 28weeks (score 3)
- Postpartum thromboprophylaxis now extends from 7 to 10days

Training Manual – Prevention & Treatment of Thromboembolism in Pregnancy & Puerperium, 2nd Ed (2017)

Pre-existing risk factors

Risk factors	Score
Previous VTE	4
High-risk thrombophilia (anti-thrombin, protein C, protein S deficiency)	3
Medical comorbidities e.g. cancer, heart failure, active SLE, nephritic syndrome, Type 1 DM with nephropathy, current IV drug user, TB, thalassemia major or intermedia, post splenectomy	3
Obesity BMI≥40kg/m2	2
Obesity BMI 30-39kg/m2	1
Family history of VTE	1
Low-risk thrombophilia (Factor V Leiden, High Factor VIII)	1
Current smoker (≥10/day)	1

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Obstetric risk factors

Risk factors	Score
All caesarean sections (both Emergency & Elective)	2
Pre-eclampsia	1
IVF (1st trimester only)	1
Mid-cavity or rotational operative delivery	1
Prolonged labour >24hr	1
PPH of>1L or requiring blood transfusion	1
Stillbirth (current)	1

Transient risk factors

Risk factors	Score
Surgical procedures (excluding episiotomy, 1st & 2nd degree perineal repair, ERPOC)*	4
Hyperemesis gravidarum/OHSS*	4
Systemic infection / infection requiring IV antibiotics	1
Immobility, dehydration	1
Admission beyond 3 days	1
Non-stop long distance travel (>4 hrs)	1

* thromboprophylaxis cover is advised until the patient has sufficiently recovered from surgery or her signs and symptoms of hyperemesis gravidarum or OHSS

Score summary

Period	Score	Duration of thromboprophylaxis
Antenatal	≥4	Consider giving from 1st trimester up to 6 weeks postnatal (up to 6 weeks postnatal if there is a single risk with a score of 4. If a combination score of≥4, then give up to 3 weeks postnatal then to be reviewed by an O&G specialist to decide if a further 3 weeks of prophylaxis is warranted)
Antenatal	3	Consider prophylaxis from 28 weeks till 3 weeks postnatal
Postnatal	2	Consider prophylaxis for 10 days
Postnatal	>2	Consider prophylaxis for 10 days or longer, specialist to decide

All antenatal and postnatal patients, even those considered low risk should be counselled on VTE prevention and recognition of VTE signs & symptoms

New MOH Obst VTE Checklist

- Training Manual Prevention & Treatment of Thromboembolism in Pregnancy & Puerperium, 2nd Edition (2017)

- The difference:

1) Weightage / Risk score
2) Risk factors – some were taken off
3) Duration of postnatal thromboprophylaxis

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Risk Factors - removed

- Age
- Parity
- Varicose vein
- Multiple pregnancy
- Preterm delivery

Risk Factors - modified

- Smoker - ≥10/day

- All LSCS – same score of 2*

**start thromboprophylaxis the evening before scheduled ELLSCS (at least 12hr from LSCS)*

Cadangan Penambahbaikan Dalam Pengendalian Kes Berisiko dan VTE/PE:

- Beri pilihan kepada pesakit semasa kaunseling: antara UFH & LMWH
- Memurnikan SOPs
- Senarai semak faktor risiko disimpan di dalam *smart phone*
- Bertanya tentang faktor risiko dan simptom DVT / Pulm Embolism semasa membuat postnatal ward rounds
- Bekerjasama dengan kakitangan kesihatan primer dan komuniti.
- Perancang keluarga perlu diberi perhatian – tawarkan penggunaan kaedah yang sesuai, contoh: implan.
- Latihan – fokus kepada penjagaan kesihatan di peringkat primer

→ **VTE boleh dicegah!**

Ringkasan

- Kehamilan merupakan risiko untuk mendapat VTE.

  LSCS; puerperium – risiko lebih tinggi
- Semua unit obstetrik mesti mempunyai SOP untuk thromboprophylaxis
- Semua wanita (antenatal & postnatal) mesti dinilai untuk risiko VTE (semasa booking, admission, selepas kelahiran)
- Penilaian perlu direkodkan.
- Latihan berterusan perlu dijalanakn untuk meningkatkan kesedaran dan pengetahuan
- Berhati-hati dalam mengendalikan pesakit yang mengambil anticoagulant semasa antenatal.

Mesej Penting: (5Ws1H)

APA (what)	Kehamilan ialah risiko untuk mendapat VTE
KENAPA (why)	Kehamilan memenuhi ketiga-tiga ciri dalam Virchow's Triad
BILA (when)	Boleh berlaku pada mana-mana fasa kehamilan dan pueperium
DI MANA (where)	Pulmonary Embolism, DVT
SIAPA (who)	Warga emas, obes, kadar LSCS yang tinggi, ↑ART pregnancy (senarai semak)
BAGAIMANA (how)	Kenalpasti risiko, latihan, SOP, tingkatkan kesedaran.

… JANGAN LUPA PERANCANG KELUARGA!

Thank You for your attention!

The task of science is to stake
out the limits of the knowable,
and to center consciousness
within them.

- Rudolf Virchow

carolkklim@yahoo.com