Postpartum Hemorrhage (PPH)

An Evidence Based View

Part I

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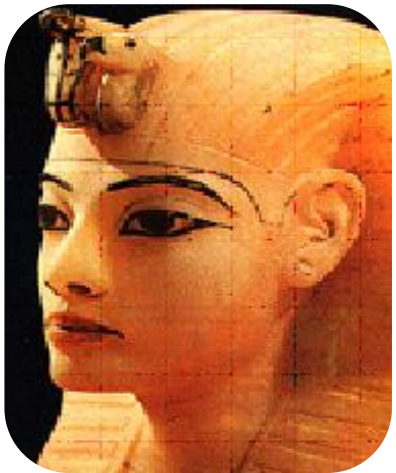
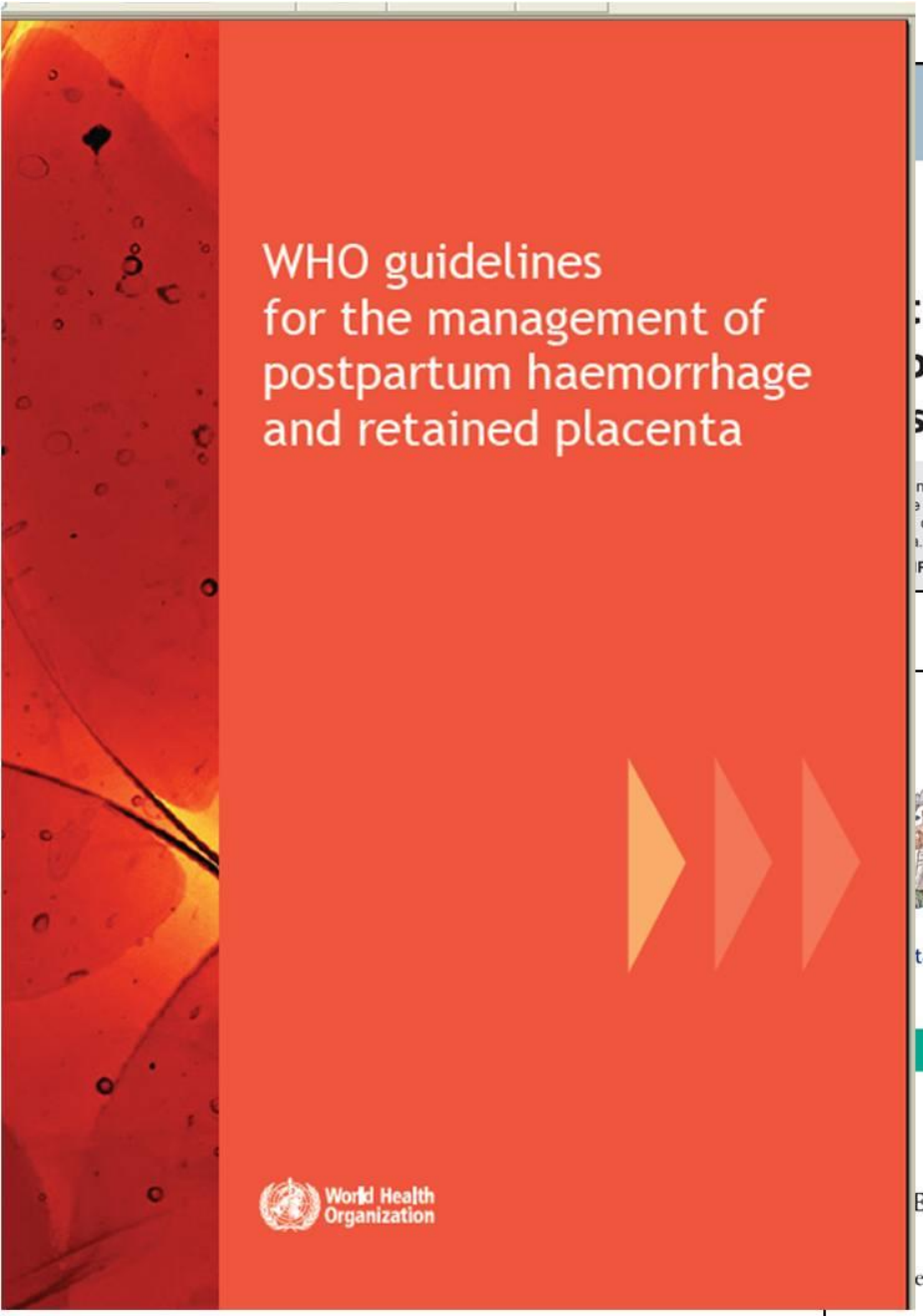


Sources of Evidence

- Pub Med.
- Cochrane library.
- SOGC Hemorrhagic Shock Guideline No 115 2002
- RCOG Guideline P.Previa No.27 *2005*
- Misoprostol Guidance WHO 2007&FIGO 2009
- RCOG Guideline PPH No.52 May 2009
- WHO Guidelines PPH 2009
- SOGC PPH Guideline No 235 Octob.2009



SOGC CLINICAL PRACTICE GUIDELINE

No. 235 October 2009 (Replaces No. 88, April 2000)

:ive Management of the Third Stage of
)our: Prevention and Treatment of
stpartum Hemorrhage

nical Practice Guideline has been prepared by the Clinical
e Obstetrics Committee and approved by the Executive and
of the Society of Obstetricians and Gynaecologists of
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PAL AUTHOR

be relevant. Each full-text article was critically appraised with use of the Jadad Scale and the levels of evidence definitions of the Canadian Task Force on Preventive Health Care.

Values: The quality of evidence was rated with use of the criteria described by the Canadian Task Force on Preventive Health Care.

Sponsor: The Society of Obstetricians and Gynaecologists of

Royal College of
Obstetricians and
Gynaecologists

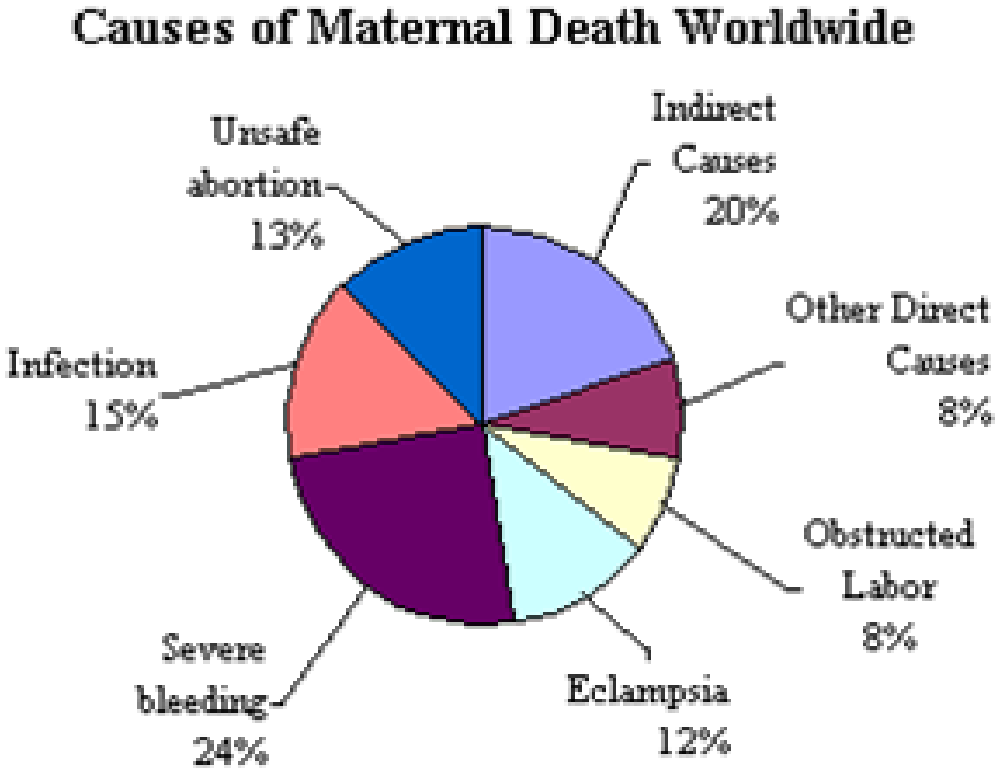
tandards to improve women's health

Green-top Guideline
No. 52
May 2009

EVENTION AND MANAGEMENT OF POSTPARTUM HAEMORRHAGE

e first edition of this guideline.

1. Purpose and scope



Worldwide postpartum hemorrhage is the commonest cause of maternal mortality. (Especially in developing countries)

Case 1

- A 21 years-old woman married for 3 years 1-0-0-1 “male child”.
- In this 2nd pregnancy she is :
  - 39 weeks gestation
  - At the 2nd stage of labour
  - Imminent to deliver her baby .

Case 1

- Weight :52 kg, Pulse :88/min.,

  Bp :110/80 mmHg, RR:18\min.

- Last HB (at 38w): 9.8 g/dl
- Previous delivery was vaginal delivery, but had received one set of blood transfusion due to atonic postpartum hemorrhage (PPH)

1- What Is The Best Line For Managing Her 3rd Stage ?

a- IM 10 u oxytocin

b- IV 5 U oxytocin

c- IM 10u Oxytocine + IM Methergin

d- Carbetocin (oxytocin analogue) 100µg IM

e- Misoprostol 1000 µg rectally

Management of 3rd Stage

Active management of the 3rd stage of labour lowers maternal blood loss and reduces the risk of PPH by about 60%.

It should be offered to all women

Grade A

Cochrane review Issue 3,2009

RCOG Guidelines 2009 &SOGC Guidelines2009

Management Of Third Stage

Low-risk Vaginal Deliveries:

Grade A

Oxytocin 10 iu (IM) or

Oxytocin 30 iu IV infusion in1000 mL,150 mL/h *

High risk V. Deliveries or CS :

Grade A

- **Oxytocin 5 iu IV over 5 minutes .*Or***
- **Carbetocin (Oxytocin analogue) 100 g IV bolus over 1 minute ***

Grade B

RCOG Guidelines 2009 &SOGC Guidelines2009*

Management Of Third Stage

Oxytocin 5-10 iu + Methergin 0.2mg (Syntometrine) may be used in the absence of hypertension (for instance, antenatal low haemoglobin) as it reduces the risk of minor PPH (500-1000 ml) but increases vomiting.

RCOG Guideline PPH No.52 May 2009 (Grade C)

A single 100 µg IV injection of carbetocin is as effective as a continuous 2-h infusion of oxytocin

Burrto et al,Arch Gynecol Obstet. 2009 Nov;280(5):707-12 RCT

Carbetocin Vs oxytocin for the prevention of PP following CS:

Carbetocin is associated with a reduced use of additional oxytocics

Attilakos et al, BJOG. 2010 Jul;117(8):929-36. Epub 2010 May 19 RCT

Oxytocics Comparison

	Methyle Ergometrine (Methergine		Oxytocin		Carbetocin Pabal	
	IV	IM	IV	IM	IV	IM
Onset of action	2-3 m	2-5m	< 1 m	3 m	< 1 m	< 2 m
Contraction Time	60m	3 H	1 6 m	30 m	67 m	120 m
Storage	< 25°C Dark storage		< 25°C		2-6°C (refrigerator)	

Management Of Third Stage

Carbetocin has an efficacy similar to syntometrine for prevention of postpartum haemorrhage, but is associated with less adverse effects.

Su LL et al BJOG. 2009 Oct;116(11):1461-6. Double Blind RCT

Management Of Third Stage

Misoprostol is not as effective as oxytocin but it may be used when oxytocin is not available, such as the home-birth setting.

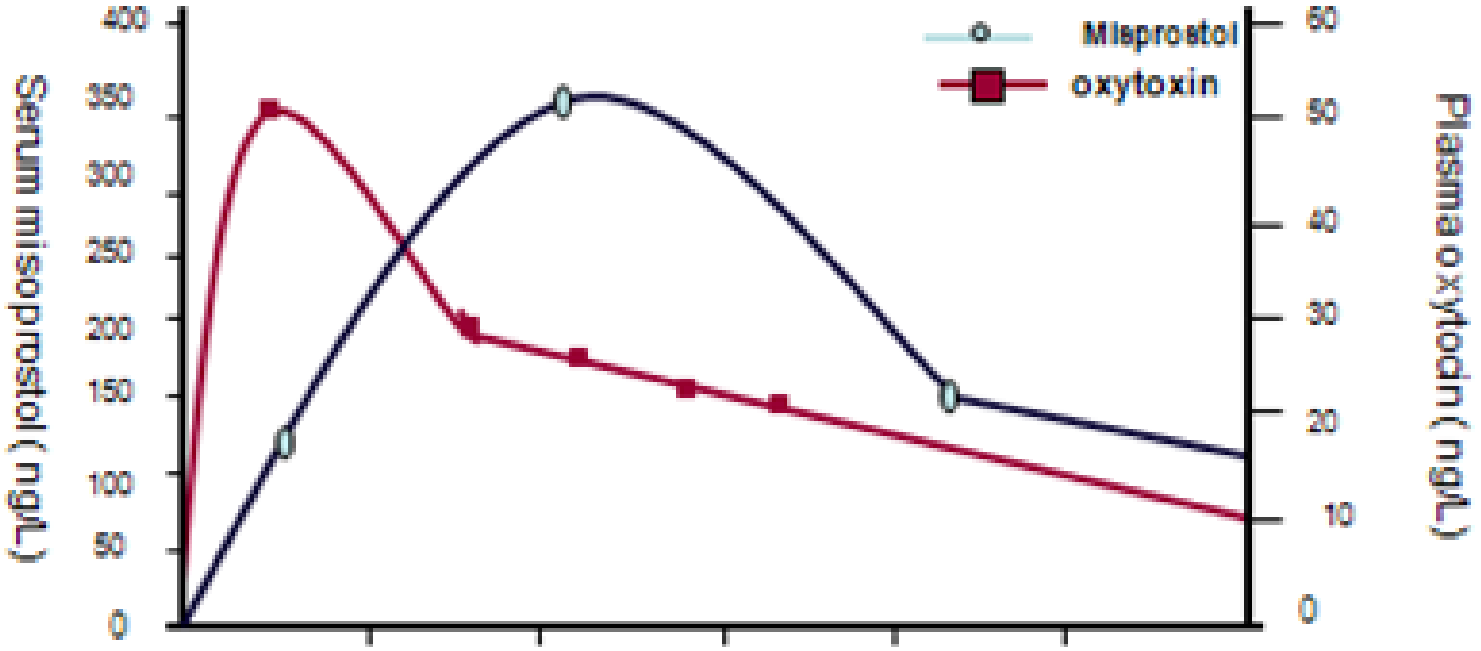
RCOG Guidelines 2009 &SOGC Guidelines2009 | Grade A

Recommended Dosages

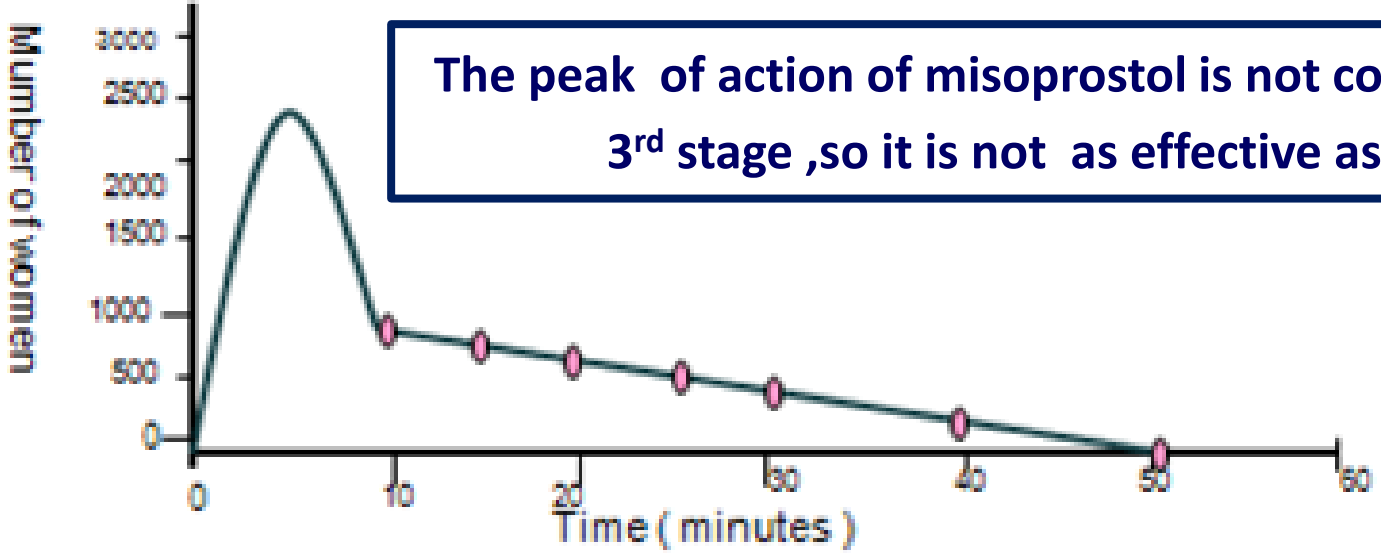
600 µg orally or sublingually.

WHO Clinical Guidelines Bellagio, Italy in Feb 2007
Gómez et al., Int J Gynecol Obstet(2007) 99, (supp 2):S190.

Pharmacodynamics of misoprostol & oxytocin



Length of third stage of labour



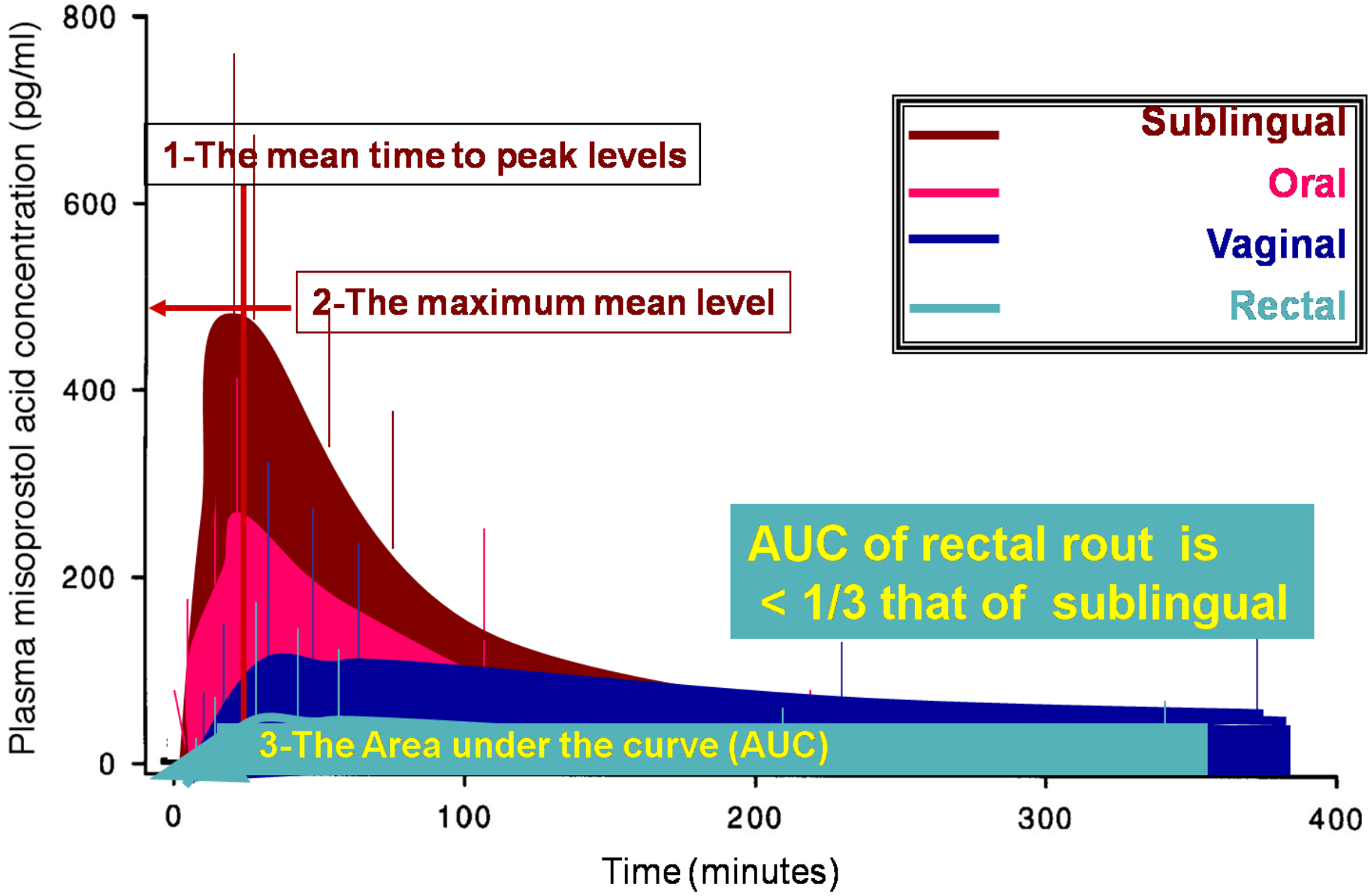
The peak of action of misoprostol is not consistent with the 3rd stage ,so it is not as effective as oxytocin

Why Orally Or Sublingually?

Pharmacokinetic Profiles of Misoprostol

Route	Onset of action	Duration of action
Oral	8 min	~2 h
Sublingual	11 min	~3 h Highest area under the curve
Vaginal	20 min	~4 h
Rectal	20-100 min	~4 h Lowest area under the curve

Tang et al., Int J Gynecol Obstet (2007) 99, S160–S167



Mean plasma concentrations of misoprostol acid over time..

Tang et al :Human Reproduction, Vol. 17, No. 2, 332-336, February 2002

1- What Is The Best Line For Managing her 3rd Stage ?

a- IM 10 u oxytocin

b- IV 5 U oxytocin

c- IM 10u Oxytocine + Methergin

d- Carbetocin (oxytocin analogue) 100 µg IM

e- Misoprostol 1000 µg rectally

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a- IM 10 u oxytocin

b- IV 5 U oxytocin

c- IM 10u Oxytocine + Methergin

d- Carbetocin (oxytocin analogue) 100 µg IM

e- Misoprostol 1000 µg rectally

She had received

Oxytocin 5 iu IV over 5min.+

500 ml saline+10 u oxytocin+ +

Methergin 0.2 mg IM

- After delivery of the placenta she had lost about 500ml of blood within one hour .
- The uterus is intermittently atonic Bp 110/80 mmHg,pulse 94/min. and the patient is anxious

What do you consider this blood lose?

A- The maximum normal average

B - PPH3

Primary PPH: Definition?

1-Quantification of blood loss

Any blood loss from the genital T. during delivery above 500 ml.

Traditionally &WHO 1990

A blood loss of ≥500 ml for vaginal delivery and ≥ 750 ml with CS delivery.

Australian Coding Standards2002

Either a 10% change in hematocrit, or a need for erythrocyte transfusion

ACOG 1989

Primary PPH: Definition?

1-Quantification of blood loss

But

Visual inspection: is inaccurate. It is about 50% of the true loss.

Hematocrit: It needs:

- **4 h for significant changes**
- **2-3 days for peak drop**

Kodkany &Derman, B-Lynch et al. Postpartum Hemorrhage 2006

Primary PPH: Definition?

2- Clinical Parameter

Excessive bleeding that has the potential to produce hemodynamic instability.

SOGC Guidelines No.88 2000& No.235 2009

Primary PPH: Definition?

2- Clinical Parameter

For blood loss estimation, clinicians should use clinical markers (signs and symptoms) rather than a visual estimation.

Grade B

SOGC Guidelines No.88 2000& No.235 2009

Primary PPH: Definition?

2- Clinical Parameter

What Are the degrees?

- Compensated Hemorrhagic Shock
- Mild Hemorrhagic Shock
- Moderate Hemorrhagic Shock
- Severe Hemorrhagic Shock

SOGC Guidelines No.88 2000& No.235 2009

Compensated Hemorrhagic Shock

Loss of ≤ 15% of blood volume may not be associated with any change in blood BP, pulse, or capillary refill.

As symptoms usually precedes the sign, these symptoms may be presented :

- **Anxiety**
- **Restlessness**
- **Feeling of breathlessness .**

Urinary output > 30 mL/h

SOGC Guidelines No.88 2000& No.235 2009

Signs And Symptoms Of Shock

Degree of shock	Blood loss	Signs & symptoms
Mild	<20%	Anxiety , Sweating & Palpitation Increased capillary refilling Cool extremities
Moderate	20% to 40%	+ Tachycardia& Tachypnea Postural hypotension Oliguria (< 20 mL/h)
Severe	>40%	+ Hypotension Agitation/confusion Collapse& Anuria

NB. Blood volume at term: ± 100 ml/kg

SOGC Guideline: No.115 & No.235 October 2009

Primary PPH: Definition

Should Blood Loss Be Routinely Quantified For The Purpose Of Diagnosing PPH?

After childbirth, blood loss and other clinical parameters should be closely monitored.

At present, there is insufficient evidence to recommend quantification of blood loss over clinical estimation.

WHO Guidelines 2009

Primary PPH: Definition

Minor PPH

I -Estimated blood loss 500- 1000 ml &
No clinical signs of shock

Measures to facilitate resuscitation should it become necessary.

- Close monitoring
- IV access
- CBC ,Blood group and screen
-

Management dependent definition

RCOG Guideline PPH No.52 May 2009 (Grade C)

Primary PPH: Definition

Major PPH

II-Estimated blood loss >1000 ml or clinical signs of shock

Protocol of measures to achieve resuscitation and haemostasis.

Management dependent definition

RCOG Guideline PPH No.52 May 2009 (Grade C)

- **After delivery of the placenta she has lost about 500ml of blood within one hour .**
- **The uterus is intermittently atonic Bp 110/80 ,pulse 94/m and the patient is anxious**

What do you consider this blood lose?

A-The maximum normal average

B –PPH

- After delivery of the placenta she has lost about 500ml of blood within one hour .
- The uterus is intermittently atonic Bp 110/80 ,pulse 94/m and the patient is anxious

What do you consider this blood lose?

A-The maximum normal average

B –PPH

What Is The Next Step?

Management Of

Established PPH

Management Of Established PPH

4 components, Undertaken Simultaneously:

1. Communication
2. Resuscitation
3. Monitoring and investigation
4. Arresting the bleeding

RCOG Guideline PPH No.52 May 2009 (Grade C)

Management Of Established PPH Depends On Degree of Blood Loss

1-Minor PPH

Estimated blood loss 500- 1000 ml & No clinical signs of shock (Compensated Shock)

2-Major PPH

II-Estimated blood loss >1000 ml or clinical signs of shock

RCOG Guideline PPH No.52 May 2009 (Grade C)

2-Resusetation

Minor PPH <1000 ml &Compensated	Major PPH >1000 ml or Shock
Intravenous access one 14-gauge cannula Crystalloid infusion. She had received one L lactated Ringer solution	AB,C : Assess: Airway, Breathing& Circulation O_2 by mask at 10–15 L/M 14-gauge cannula x2 orange Transfuse blood rapidly Until blood is available, IV up to 3.5 L crystalloid lactated Ringer (± one L of it is colloid) Keep patient& infusions warm

RCOG Guideline PPH No.52 May 2009 (Grade C)

3-Monitoring and Investigation

Minor PPH <1000 ml &Compensated)	Major PPH >1000 ml or Shock
Venepuncture (20 ml) for: ➢ Group ➢ CBC ➢ Coagulation screen Pulse and BP/15m	Venepuncture (20 ml) for: ➢ Crossmatch (≥4 units) ➢ CBC & Coagulation screen ➢ Basal renal and liver F Ts. Continuous:P ,BP,RR Temperature /15 m Foley C. : urine output 2 cannulae, 14- or 16-gauge All recorded on a flow chart

RCOG Guideline PPH No.52 May 2009 (Grade C)

Management Of Established PPH

4 components: undertaken simultaneously:

1. Communication
2. Resuscitation
3. Monitoring and investigation
4. Arresting the bleeding

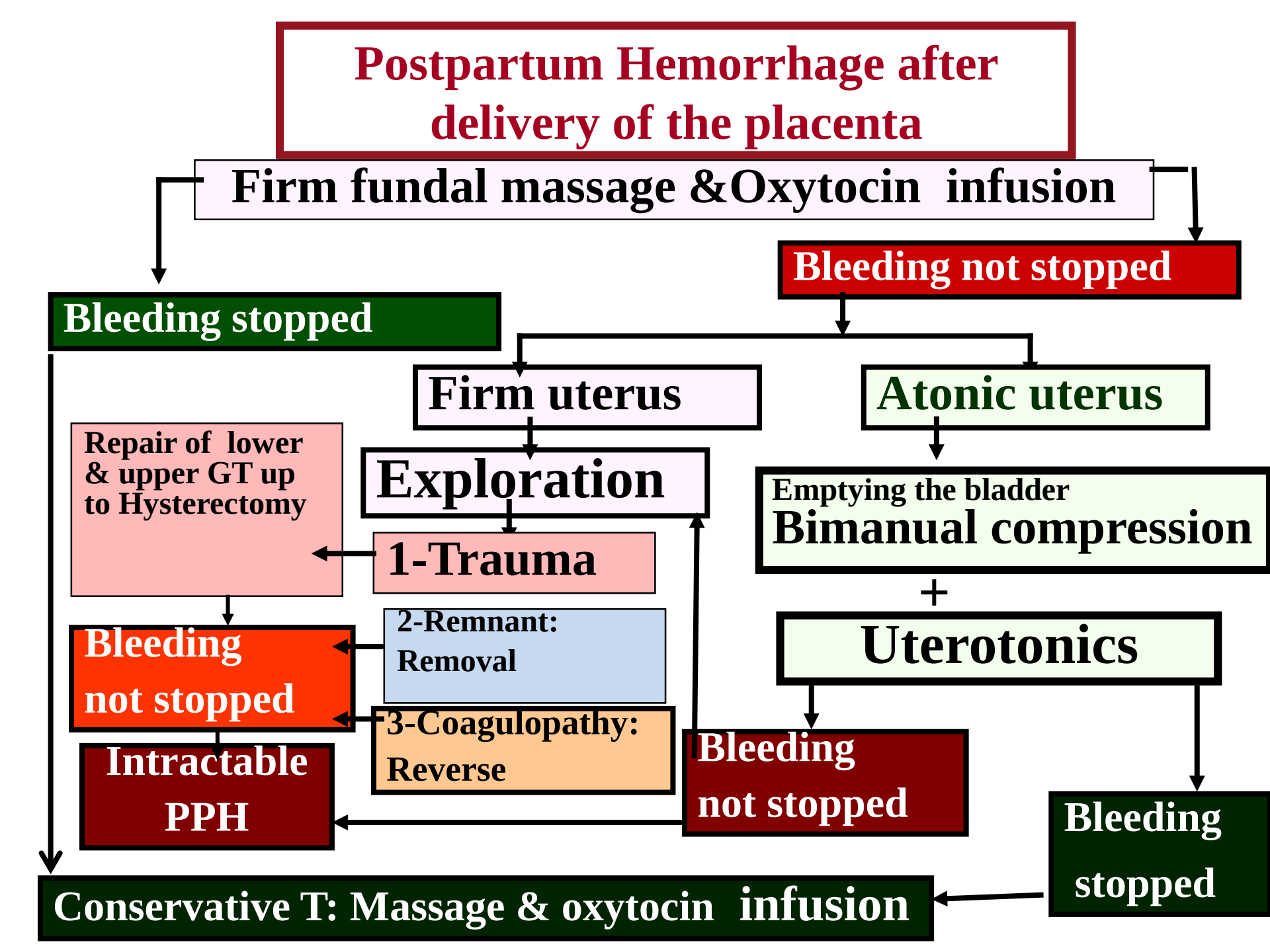
- Treatment of the underlying disorder (4Ts)
- Management of Intractable PPH

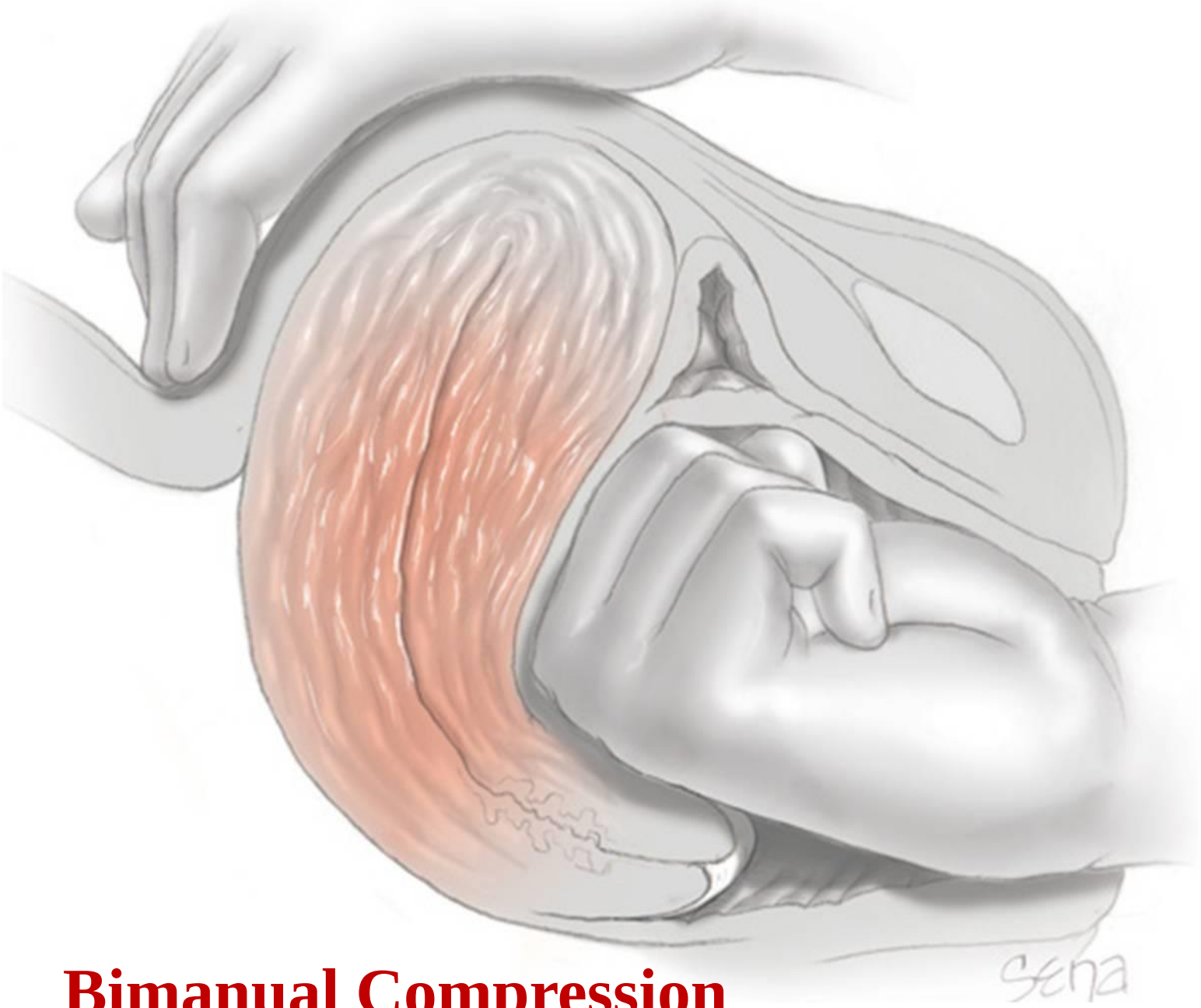
RCOG Guideline PPH No.52 May 2009 (Grade C)

Arresting The Bleeding

Causes for PPH may be considered to relate to one or more of 'the four Ts':

- **Tone (abnormalities of uterine contraction)**
- **Tissue (retained products of conception)**
- **Trauma (of the genital tract)**
- **Thrombin (abnormalities of coagulation).**


Postpartum Hemorrhage after delivery of the placenta
Firm fundal massage &Oxytocin infusion
Bleeding not stopped
Bleeding stopped
Firm uterus
Atonic uterus
Repair of lower & upper GT up to Hysterectomy
Exploration
Emptying the bladder
Bimanual compression
1-Trauma
+
Uterotonics
2-Remnant: Removal
Bleeding not stopped
3-Coagulopathy: Reverse
Intractable PPH
Bleeding not stopped
Bleeding stopped
Conservative T: Massage & oxytocin infusion



Bimanual Compression

Uterotonics

(3 lines)

First Line Uterotonics

For management of PPH, oxytocin should be preferred over :

- Ergometrine alone
- Fixed-dose combination of ergometrine and oxytocin,
- Carbetocin
- Prostaglandins.

WHO Guidelines PPH 2009

RCOG Guideline PPH No.52 May 2009 (Grade C)

First Line Uterotonics

- Oxyocin (Syntocinon®) 5 units IV over 5 m (± repeated) Or
- Infusion (40 u in 500 ml L Ringer at 125 ml/hour).
- Not more than 3 L of IV fluids containing oxytocin.

WHO Guidelines PPH 2009

RCOG Guideline PPH No.52 May 2009 (Grade C)

First Line Uterotonics

Carbetocin (Pabal®) , 100µg given as an IV bolus over 1 minute (Can be repeated)is an alternative

SOGC Guideline No. 235 PPH 2009

Second Line Uterotonics

If the bleeding does not respond to the 1st-line, Ergometrine will be the second line:

- **Ergometrine (Methergin®) IM / IV (slowly): 0.2 mg**
- **Repeat 0.2 mg IM after 15 minutes**
- **If required, give 0.2 mg IM or IV slowly / 4 H**

Maximum dose :5 doses (Total 1.0 mg)

Contraindications :Pre-eclampsia, hypertension, heart disease

WHO Guidelines PPH 2009

RCOG Guideline PPH No.52 May 2009 (Grade C)

Third Line Uterotonics

If the bleeding does not respond to the 2nd-line treatment: Prostaglandin / Misoprostol should be offered.

WHO Guidelines PPH 2009

RCOG Guideline PPH No.52 May 2009 (Grade C)

Misoprostol

Cytotic®,Mesotac® ,Mesoprost®

The recommended dose:

- **600 µg oral or sublingual**
- **1000 µg rectal my be used if these routes are not suitable (efficacy < 50%)**

WHO Guidelines PPH 2009

RCOG Guideline PPH No.52 May 2009 (Grade C)

Misoprostol Versus IV Oxytocin

Sublingual misoprostol (800 µg) is clinically equivalent to IV oxytocin (40iu) when used to stop atonic PPH in women who have received oxytocin during the 3rd stage of labour.

Blum et al Lancet. 2010 Jan 16;375(9710):217-23 D.B.v RCT Multicenter Burkina Faso, Egypt (El-galaa H), Turkey& Vietnam

Misoprostol Versus IV Oxytocin

In settings in which use of oxytocin is not feasible, misoprostol might be a suitable first-line treatment alternative for post-partum haemorrhage.

Winikioff et al Lancet. 2010 Jan 2010 Jan 16;375(9710):210-6 D.B.RCT Multicenter Ecuador, Egypt ,

Misoprostol

- A repeated dose should not be given unless at ≥ 2 h since the first dose.
- If the initial dose was associated with pyrexia or marked shivering, then at least 6 hours should lapse before the second dose is given.

rFVIIa

Recombinant human coagulation Factor VIIa (rFVIIa): NovoSeven®

90 µg/kg given/2 hours bolus infusion

Unproven Effect

Tranexamic Acid For The Treatment Of Postpartum Haemorrhage

- Tranexamic acid decreases postpartum blood loss after vaginal birth and after CS based on two RCTs of unclear quality which reported only few outcomes.
- Further investigations are needed on efficacy and safety of this regimen for preventing PPH.

Novikova and Hofmey , Cochrane Systematic Reviews 2010, Issue 7 .

Tranexamic Acid For The Treatment Of Postpartum Haemorrhage

"The WOMAN Trial" : Waiting the result

An international randomised, double blind placebo controlled trial.

The trial will be a large, pragmatic, randomised, double blind, placebo controlled trial among 15,000 women with a clinical diagnosis of PPH

Shakur et al Trials. 2010 Apr 16;11:40 UK

Return to The case Scenario

The patient received :

1-Syntocinon 5 units IV over -5iu & (40 u in 500 ml L Ringer at 125 ml/hour).

2-Methergin 0.2 mg/slow IV and other 0.2 mg IM and repeated after 15 minutes

3-600µg misoprostol sublingually

The bleeding subsided for 30 minutes Then the uterus was not responding to treatment or massage and other ± 500 ml of blood were lost.

The case is now categorized as "Major PPH"

What is the best line of management?

Management Of Established PPH Depends On Degree of Blood Loss

1-Minor PPH

Estimated blood loss 500- 1000 ml & No clinical signs of shock (Compensated Shock)

2-Major PPH

II-Estimated blood loss >1000 ml or clinical signs of shock

RCOG Guideline PPH No.52 May 2009 (Grade C)

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RCOG Guideline PPH No.52 May 2009 (Grade C)

Management Of Established PPH

4 components: undertaken simultaneously:

1. Communication
2. Resuscitation
3. Monitoring and investigation
4. Arresting the bleeding

- Treatment of the underlying disorder (4Ts)
- Management of Intractable PPH

RCOG Guideline PPH No.52 May 2009 (Grade C)

1-Communication

Minor PPH <1000 ml &Compensated	Major PPH >1000 ml or Shock
Alert first-line obstetric and anaesthetic staff trained in the management of PPH.	ØCall obstetric middle grade & alert consultant ØCall anaesthetic middle grade & alert consultant. ØAlert consultant clinical haematology ØAlert blood transfusion laboratory.

RCOG Guideline PPH No.52 May 2009 (Grade C)

2-Resusetation

Minor PPH <1000 ml &Compensated	Major PPH >1000 ml or Shock
ØIntravenous access one 14-gauge cannula ØCrystalloid infusion.	ØAB,C : Assess: Airway, Breathing& Circulation ØO_2 by mask at 10–15 L/M Ø14-gauge cannula x2 ØTransfuse blood rapidly ØUntil blood is available, IV up to 3.5 L crystalloid lactated Ringer (± one L of it is colloid) ØKeep patient& infusions warm

RCOG Guideline PPH No.52 May 2009 (Grade C)

2-Resusetation

- Volume replacement must be undertaken on the basis that blood loss is often grossly underestimated.
- Compatible blood (supplied in the form of packed RBCs) is the best fluid as soon as available,
- If necessary Rh negative O blood.

RCOG Guideline PPH No.52 May 2009 (Grade C)

Massive Blood Loss : What Are The Main Goals Of Management ?

The Main Goals is to maintain:

- Haemoglobin > 8g/dl
- Platelet count > 75 x 10^9/l
- Prothrombin T < 1.5 x mean control
- Activated prothrombin times (APT) < 1.5 x mean control
- Fibrinogen > 100mg/dl

British Committee for Standards in Haematology
Management of Massive Blood Loss 2006

Indications For Blood Component Therapy

Component	Usual Indication	starting dose
Packed RBC	Replacement of oxygen-carrying capacity	2– 4 Units IV
Fresh frozen plasma	Documented coagulopathy	2–6 Units IV
Cryoprecipitate	Coagulopathy with low fibrinogen	10–20 Units IV
Platelets	Thrombocytopenia / thrombasthenia with bleeding	6–10 Units IV

SOGC Hemorrhagic Shock Guideline No 115 2002

2-Resusetation

Colloids versus crystalloids ?

Intravenous fluid replacement with isotonic crystalloids should be used in preference to colloids for resuscitation of women with PPH.

High doses of colloids :

- **More expensive**
- **May cause adverse effects**

WHO Guidelines PPH 2009

Coagulopathy

Fresh frozen plasma 4 units for:

- Every 6 units of red cells or
- Prothrombin time > 1.5 x normal
- Activated partial thromboplastin time > 1.5 x normal

  (12–15 ml/kg or total 1 litres)

Platelets : if PLT count < 50 x 10^9 /L

RCOG Guideline PPH No.52 May 2009 (Grade C)

Hypovolumeic Shock

- During the wait lactated Ringer :3ml for every one ml of blood lost (*)
- Ringer's lactate is preferred over normal saline to avoid hyperchloremic acidosis(**)
- There is no place for hypotonic dextrose solutions (**)

Smith : in Te Linde's operative gynecology.; 1997,245-6 *

(SOGC) Clinical Practice Guidelines 2002 (Grade I a) **

Whole Blood Vs Component therapy

Component therapy provides better treatment because only the specific component needed is given.

National Institutes of Health (1993)

Whole blood is needed when acute hemorrhage is catastrophic.

(Klein, 1994, Schwartz, 1994).RCOG 2009

Blood Component : Recipient & Donor

Donor	Compatible plasma	Compatible red cells	Compatible platelets	Compatible platelets
Recipient ABO group			1st choice	2nd choice
A	A,AB	A,O	A,AB	B,O
B	B,AB	B,O	B,AB	A,O
O	O,A,B, AB	O	O	A,B,AB
AB	AB	AB,A,B, O	AB	A,B,O

3-Monitoring and Investigation

Minor PPH <1000 ml &Compensated	Major PPH >1000 ml or Shock
Venepuncture (20 ml) for: ➢ Grouping ➢ CBC ➢ Coagulation screen Pulse and BP/15m	Venepuncture (20 ml) for: ➢ Crossmatch (≥4 units) ➢ CBC & Coagulation screen ➢ Basal renal and liver functions Continuous: Pulse , BP & RR Temperature /15 m Foley catheter: urine output 2 cannulae: 14 or 16 gauge All recorded on a flow chart

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Poor Man's" Fibrinogen Assay

- If a clot does not form within 6 m or
- Clot forms and lyses within 30 m.

A coagulation defect is probably present and the fibrinogen level is < 150 mg/dl

(SOGC) Clinical Practice Guidelines 2002

Management Of Established PPH

4 components: undertaken simultaneously:

1. Communication
2. Resuscitation
3. Monitoring and investigation
4. Arresting the bleeding

- Treatment of the underlying disorder (4Ts)
- Management of Intractable PPH

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Intractable PPH

About 10 % of women will not respond to the initial management steps and are considered as intractable PPH.

They are caused mainly by

- **Uterine atony**
- **Placenta accreta at CS scar**
- **Difficult trauma repair**
- **Coagulopathy**

Management of Intractable PPH

Please see Part II

Thank You

Egypt