Robotic Surgery in Gynaecology
make CIMS your home page at the point of care

get connected
get addicted

cimsasia.com

cimsasia.com
Journal Watch

377 • Long-acting reversible contraception in the US
- Stress incontinence surgery: Prior urodynamic testing unnecessary
- Third stage of labour: Active management with or without controlled cord traction

378 • Birth defects after assisted conception
- Cervical pessary to prevent preterm birth in women with a short cervix
- First-trimester abortion: Cervical preparation with misoprostol
Review Article
Obstetrics

379 Primary Amenorrhoea

Amenorrhoea is the absence or abnormal cessation of menstruation. It is mainly classified as primary amenorrhoea and secondary amenorrhoea. Primary amenorrhoea is defined either as absence of menses by age 14 years with the absence of growth or secondary sexual characteristics or as absence of menses by age 16 years with normal development of secondary sexual characteristics. Secondary amenorrhoea is defined as the cessation of menstruation for at least 6 months or for at least 3 of the previous 3 cycle intervals. Primary amenorrhoea is a common problem during adolescence. In this article authors will discuss about primary amenorrhoea in detail.

Shikha Joshi, C Hariharan, SA Inamdar

Review Article
Gynaecology

384 Dermatological Manifestation during Pregnancy: A Literature Review

Pregnancy is a physiological and transient period where medical intervention is usually not required, or at least is restrained to checking expected events. However, in the finely tuned, harmonious and extraordinarily complex cascade of molecular and cellular phenomenon that gestation brings, many signs and/or symptoms may target the cutaneous layer. Therefore, it seems logical that during pregnancy, hormonal or other less well-explained pathways may influence one of the skin cell types. By contrast, some diseases originating in the skin may affect the course of the gestation.

Prasoon Soni, Monica Soni, Ekta, Priyanka

In Practice

392 Case of the Month: Woman with Cyst formation in Right Breast

Prabhu Prakash, Asha Mathur, Sneha Ambwani, Seema Surana

Review Article
Paediatrics

393 The Preschool Wheezer

This article addresses the different patterns of preschool wheeze and explains how one might differentiate between them, looks at the risk factors and important preventative measures to take; reviews current therapies; and highlights the paucity of evidence supporting common use.

David Cremonesini, Anne Thomson
400 In Practice (Answer)

Case Study

402 Study of Serum Homocysteine and Vitamin B₁₂ Levels in Eclampsia, Pre-eclampsia, and the Effectiveness of Treatment with Inj. Vitamin B₁₂ on the Outcome of these Patients
Radha Yegnararayan, GS Shekhawat, Hemant S Damle

407 Amelia: A Rare Case
Varsha Deshmukh, KA Yelikar, VY Kalyankar, Neha Golechha, PS Deshmukh

Continuing Medical Education

409 Robotic Surgery in Gynaecology
This article reviews the applications of robotics in various gynaecological procedures, including tubal reanastomosis, hysterectomy, myomectomy, sacrocolpopexy and oncological surgery.
Yuen Pong Mo
GYNAECOLOGY

Long-acting reversible contraception in the US

The US has a particularly high rate of unintended pregnancy (about half of all pregnancies), leading to many abortions and adverse consequences for women’s health. About half of the unintended pregnancies are a result of failure of contraception and half a result of failure to use contraception. The annual failure rate for oral contraceptive pills is about 9% overall and higher in teenagers and other high-risk groups. Long-acting reversible contraceptive methods, including intrauterine devices (IUDs) and subdermal implants, have failure rates of < 1%. A low uptake of IUDs may partially explain the high rate of unintended pregnancy in the US. Now, a US prospective cohort study has underlined the effectiveness of long-acting reversible contraception.

In St Louis, Missouri, a total of 9,256 women aged 14–45 at risk of unintended pregnancy were recruited between August 2007 and September 2011. They were provided with a contraceptive method of their choice free of cost with an emphasis on the advantages of long-acting reversible contraception. A total of 7,486 participants were included in the analysis. There were 334 unintended pregnancies. The contraceptive failure rate was 4.55 per 100 person-years with pills, patch, or ring, and 0.25 per 100 person-years with long-acting reversible contraception, a significant 22-fold improvement with long-acting reversible contraception. The risk of unintended pregnancy in participants using pills, patches, or rings was almost twice as high in younger women (< 21 years) as in older women. Among women using long-acting reversible contraception, age did not affect the failure rate.

The use of long-acting reversible contraceptive methods reduces the risk of unintended pregnancy.


OBSTETRICS

Third stage of labour: Active management with or without controlled cord traction

Postpartum haemorrhage (PPH) is an important cause of maternal morbidity and mortality, especially in developing countries. Active management of the third stage of labour reduces the risk of PPH by > 60%. Active management includes administration of oxytocin and controlled cord traction, but the importance of controlled cord traction is unknown. Omitting controlled cord traction might simplify and improve services in resource-poor countries. A randomized trial in eight countries (Argentina, Egypt, India, Kenya, the Philippines, South Africa, Thailand, and Uganda) has suggested that controlled cord traction might be omitted safely.

A total of 24,390 women with singleton pregnancies were randomized to full package (FP) or simplified package (SP) management of third stage. All women were given oxytocin 10 IU immediately after the birth, with cord clamping at 1–3 minutes. The SP consisted of placental delivery with gravity and maternal effort. The FP consisted of controlled cord traction immediately after uterine contraction and cord clamping. Blood loss of 100 mL or more occurred in 239/11,621 (2%) in the SP group and 219/11,621 (2%) in the FP group. The risk ratio of 1.09 (0.91–1.31) had a 95% confidence interval up-to-date

per margin exceeding the pre-stated non-inferiority margin of 1.3. There was one case of uterine inversion in the FP group.

Although the pre-stated non-inferiority limit was exceeded, these researchers conclude that omitting controlled cord traction had very little effect on the risk of severe PPH, and haemorrhage prevention programmes in non-hospital settings could safely focus on the use of oxytocin.


Birth defects after assisted conception

Evidence suggests that assisted reproduction technologies, ie, in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), are associated with increased risk of birth defects. This could be due to factors within the technologies or to factors in the patients who take up the technologies. A study in South Australia has provided more data.

Out of a total of 308,974 births, 6,163 were the result of assisted conception. The rate of any birth defect was 8.3% after assisted conception and 5.8% without assisted conception. Unadjusted data showed a 47% increase in risk after assisted conception, but after adjustment for parental factors the increase fell to 28%. There was no significant increase in adjusted risk after IVF, but after ICSI this risk was increased significantly by 57% after adjustment. The risk was increased for a wide variety of defects including cardiovascular, musculoskeletal, urogenital and gastrointestinal abnormalities and cerebral palsy. Women with a history of infertility had an increase in risk irrespective of whether or not they had had a previous birth after assisted conception.

Factors in the parents may be responsible for much of the increased risk, but ICSI may be independently associated with increased risk.


Cervical pessary to prevent preterm birth in women with a short cervix

Cervical pessaries have been used for 50 years to prevent preterm births associated with short cervix, but there has been no randomized trial. Now, a multicentre trial in Spain has confirmed the effectiveness of this method.

The trial included 385 women with a cervical length of 25 mm or less on routine transvaginal scanning at 18–22 weeks’ gestation. Randomization was to insertion of a cervical pessary at 20–23 weeks or no intervention. Spontaneous delivery before 34 weeks occurred in 6% (pessary) vs 27% (controls), a highly significant difference. There were no serious adverse effects from use of a pessary.

Insertion of a cervical pessary reduces the risk of preterm birth in women with a short cervix.


First-trimester abortion: Cervical preparation with misoprostol

Almost a third of all pregnancies worldwide end in induced abortion, often by vacuum extraction in the first trimester. It is important to prepare the cervix for cervical dilation, and osmetic dilators, mifepris-tone, and prostaglandin analogues are used for this purpose. Misoprostol, a prostaglandin E, analogue, is cheap and widely used orally, sublingually, or vaginally. A multinational study has shown that vaginal misoprostol is effective in reducing the risk of complications after first-trimester vacuum extraction abortion.

A total of 4,972 women were randomized at 14 centres in nine countries to vaginal misoprostol (two 200-µg tablets) or vaginal placebo, 3 hours before first-trimester vacuum aspiration abortion. Follow-up was for 2 weeks, and full data were analysed for 4,858 women. There was a significant 32% reduction in risk of complications in the misoprostol group compared with the placebo group. Incomplete abortion occurred in < 1% (misoprostol) vs 2% (placebo), a significant difference. Uterine re-evacuation was necessary in < 1% vs 2%. Pelvic inflammatory disease occurred in 1% of each group. Three women in the placebo group, but none in the misoprostol group, had cervical tears, and uterine perforation occurred in two (placebo) and three (misoprostol). Abdominal pain occurred in more women in the misoprostol group (55% vs 22%) than did vaginal bleeding (37% vs 7%).

Misoprostol given 3 hours before first-trimester vacuum extraction abortion reduces the risk of complications. A Lancet commentator suggests that it should be used routinely.

Amenorrhoea is the absence or abnormal cessation of menstruation. It is mainly classified as primary amenorrhoea and secondary amenorrhoea.

**Primary Amenorrhoea**
It is defined either as absence of menses by age 14 years with the absence of growth or secondary sexual characteristics or as absence of menses by age 16 years with normal development of secondary sexual characteristics.

**Secondary Amenorrhoea**
It is defined as the cessation of menstruation for at least 6 months or for at least 3 of the previous 3 cycle intervals. Secondary amenorrhoea is more common than primary amenorrhoea.

Primary amenorrhoea is a common problem during adolescence. In this article authors will discuss about primary amenorrhoea in detail.

**Primary Amenorrhoea–Causes**

**Hypothalamic**
- Weight loss–anorexia nervosa
- Primary hypothyroidism
Craniopharyngioma
Cerebral/midbrain injury
Encephalitis/meningitis

Pituitary Causes
Mixed pituitary tumours
Irradiation
Post-intracranial surgery

Adrenal
Congenital adrenal hyperplasia
Adrenal tumours

Ovarian Causes
Turner syndrome (45,X0)
Turner mosaics (45,X0/46,XX)
Premature ovarian failure
Virilising ovarian tumours

Diseases of the Outflow Tract
Non-functional uterus with uterovaginal agenesis Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome
Uterine adhesions–TB endometritis
Functional uterus with obstruction to the outflow tract, septate vagina, imperforate hymen

Depending on Serum FSH Levels
Hypergonadotropic primary amenorrhoea
Eugonadotropic primary amenorrhoea
Hyponadotropic primary amenorrhoea

EVALUATION AND DIAGNOSIS
Diagnostic approach for primary amenorrhoea is described in figure 1.
History
- Age at menarche of other siblings
- History of excessive weight loss of 10–15% loss of body weight—Anorexia nervosa
- Cyclical lower abdominal pain—Cryptomenorrhoea
- Anosmia (Kallmann’s syndrome)
- Headaches, visual disturbances—Intracranial tumours
- Meningitis, tuberculosis (hypothalamic)
- Virilisation, hirsuitism, change in voice
- Radiotherapy to the pelvis or chemotherapy

MRKH Syndrome
Among congenital abnormalities of the female genital tract, a non-functional Uterus with uterovaginal agenesis (MRKH syndrome) being one of the most frequent causes of primary amenorrhoea. It can sometimes be associated with renal agenesis or other renal abnormalities. It is normal secondary development and external female genitalia; absence of uterus and upper vagina and normal ovaries. Karyotype 46,XX Intravenous pyelography (IVP) in 30% cases suggest urinary tract abnormalities

Management
Investigation with clinical examination, karyotyping, ultrasound examination, IVP for the localisation of kidneys and laparoscopy in that order followed by vaginoplasty (Figure 2).

Congenital Adrenal Hyperplasia
- Congenital adrenal hyperplasia (CAH) refers to any of several autosomal recessive diseases resulting from mutations of genes for enzymes mediating the biochemical steps of production of cortisol from cholesterol by the adrenal glands (steroidogenesis) as showed in figure 3. Most of these conditions involve excessive or deficient production of sex steroids and can alter development of primary or secondary sex characteristics in some affected infants, children or adults. Genetic males with 5-ARD are born with ambiguous genitalia (i.e., male pseudohermaphroditism). The described clinical abnormalities range from
infertility with normal male genital anatomy to underdeveloped male with hypospadias to predominantly female external genitalia, most often with mild clitoromegaly. A clitoral index greater than 35 mm² is evidence of increased androgen effect. A clitoral index greater than 100 mm² is evidence of virilisation.

- Associated with metabolic abnormalities, hyperkalaemia and hyponatraemia
- Sex chromatin study depicts positive barr bodies
- Karyotype shows generally 46,XX
- 17 hydroxy progesterone > 800ng/ml

Cryptomenorrhoea
Cryptomenorrhoea or cryptomenorrhea, also known as haematocolpos, a condition where menstruation occurs but is not visible. There will be periodic shedding of endometrium, but menstrual blood fails to come out through genital tract due to causes like:
- Imperforate hymen
- Transverse vaginal septum
- Atresia of upper third of vagina and cervix

Patient presents with periodic cyclical pain, retention of urine, haematocolpos, haematometra and haematosalphinx.

**TURNER’S SYNDROME**

Turner’s syndrome (45,XO) occurs in one out of 2500 to 3000 patients. These patients have streak gonads, usually short with associated somatic abnormalities and eye defects like segmental iridogoniodygenesis without glaucoma.

- Turner’s syndrome is caused by either complete absence or a partial abnormality of one of the two X chromosomes. About 50% have mosaic forms such as 45,X/46,XX or 45,X/46,XY
- Features short stature, poor secondary sexual characters though phenotypically female, web neck, lymphoedema, shield chest with widely spaced nipples, scoliosis, wide carrying angle, (Figure 4) coarctation of the aorta, cubitus valgus and streak ovaries

**Androgen Insensitivity Syndrome/ Testicular Feminisation Syndrome**

Phenotypically female normal breast development without areolar pigmentation, scanty pubic and axillary hair, under-developed labial or inguinal gonads.

**On laparoscopy**: Uterus and tubes are absent. Serum testosterone level is equal to normal male.

**Karyotyping**: 46,XY

**Gonadal biopsy**: Testicular structure

Management includes gonadectomy due to increased risk of seminoma or dysgerminoma. Hormone replacement therapy with conjugated
equine oestrogen (premarin 0.625 mg) is adequate to maintain secondary sexual characters.

**TREATMENT–GOALS**

The treatment objective are as follows:
- Correct the underlying cause
- Correct sexual infantilism and initiate full reproductive potential when possible
- Correct short stature
- Correction of sexual infantilism
- Exogenous oestrogen and progesterone
- Correction of short stature human growth hormone exogenous gonadotropins are given to correct short stature

**Correction of Underlying Cause**

Surgical excision of craniopharyngioma and pituitary tumours along with dopamine agonists in prolactinomas:
- XY Karyotype – Gonadectomy
- Imperforate hymen – Cruciate incisions
- Vaginal atresia/septate vagina – Vaginoplasty

**Unresponsive Endometrium**

*Synechiae of tubercular origin*. Antitubercular drugs with adhesiolysis.

**Thyroid and Adrenal Dysfunction**

Adrenogenital syndrome with enlarged clitoris treated by clitoroplasty corticosteroid replacement in 17α hydroxylase deficiency.

**About the Authors**

Dr Shikha Joshi is an Assistant Professor and Dr C Hariharan is the Head of Department and Professor, Department of Obstetrics and Gynaecology, Datta Meghe Institute of Medical Sciences Sawangi, Wardha.

**REFERENCES**

8 *cryptomenorrhea* at Dorland’s Medical Dictionary.
INTRODUCTION

Pregnancy is a physiological and transient period where medical intervention is usually not required, or at least is restrained to checking expected events. However, in the finely tuned, harmonious and extraordinarily complex cascade of molecular and cellular phenomenon’s that gestation brings, many signs and/or symptoms may target the cutaneous layer. Therefore, it seems logical that during pregnancy, hormonal or other less well-explained pathways may influence one of the skin cell types. By contrast, some diseases originating in the skin may affect the course of the gestation. In this review, cutaneous modifications will be classified as physiological changes, specific dermatoses of pregnancy, cutaneous infections that may modify the prognosis of pregnancy and, finally, miscellaneous skin diseases that may be affected by pregnancy.

Physiological Changes in Pregnancy

It is important to recognise and differentiate physiological changes from diseased states in order to explain them to the patient and avoid unnecessary investigations or treatments.

The 3 main precipitating factors that induce the development of these changes are an increase in circulating hormones or other mediators that are secreted by ovaries and/or placenta, including oestrogens, progesterone, human placental lactogen, placental growth factor (PIGF), intravascular volume expansion and a compression from the enlarging uterus. Oestrogens display pleiotropic effects. They stimulate melanogenesis and keratinocyte growth, cause cutaneous vasodilatation, increase capillary...
permeability and probably enhance angiogenesis. Progesterone acts synergistically with oestrogens on melanogenesis, but intervenes solely to reduce collagenolytic activity. In addition, an enlargement of the pituitary gland results in increased levels of gonadotrophins, adrenocorticotropic hormone and melanocytic-stimulating hormone that have a direct effect on the skin.

**Physiologic Changes of the Skin and the Mucosa during Pregnancy**

**Pigmentary Changes**
- **Non-facial hyperpigmentation**
  - Areolae, nipples, periumbilical skin, anogenital region, axillae, thighs
  - Recent scars, nevi, freckle
  - Linea nigra
  - Pigmentary demarcation lines
- **Melasma**
- **Vascular changes**
  - Spider telangiectasias
  - Palmar erythema
- **Venous hypertension signs**
  - Varicose veins and venous telangiectasias of the legs
  - Hemorrhoids
  - Jacquemier's sign
  - Chadwick's sign
  - Non-pitting oedema
  - Purpura
- **Vasomotor instability**
  - Episodic pallor, facial flushing, hot and cold sensations, dermographism, cutis marmorata
- **Vascular proliferation**
  - Hemangiomas, glomus tumours, hemangiendotheliomas
  - Hyperemia and hyperplasia of the gingival mucosa
  - Oral pyogenic granulomas

**Structural Changes**
- Striae gravidarum
- Molluscum fibrosum gravidarum

**Adnexal Changes**
- **Hair**
  - Reversible hirsutism, postpartum telogen effluvium, male pattern alopecia
- **Nails**
  - Distal onycholysis, transverse grooves, longitudinal melanonychia, subungual hyperkeratosis
- **Glands**
  - Eccrine sweat glands: Hyperhidrosis, miliara
  - Apocrine sweat glands: Decreased activity
  - Sebaceous glands: Increased activity, Montgomery’s tubercles

**Non-facial Hyperpigmentation**
Hyperpigmentation is the most frequent skin modification found in pregnancy and is one of its earliest signs. It takes place usually during the first trimester. The exact pathogenesis, although unclear, is considered to rely on increased serum levels of melanocytic-stimulating hormone, oestrogens and possibly progesterone, which stimulates melanocytic activity contributing to pigmentation. Changes are more pronounced in women with a dark complexion. Areas normally displaying pigmentation become darker in pregnancy. However, hyperpigmentation is usually more localised, targeting the areola and/or nipples, which are the most commonly affected sites (40%). Other sites of predilection include the face, the periumbilical skin, the anogenital region, the axillae and the inner thighs. Recent scars, nevi and freckles may also darken during gestation. Linea alba that corresponds to an aponeurosis extending from the symphysis pubis to the xiphisternum often becomes hyperpigmented during pregnancy, most markedly
below the umbilicus. It is referred to as linea nigra and found in 75% of pregnant females. Increase of the pigmentary demarcation lines is frequently observed in black pregnant women, but very rarely in white subjects. After delivery, pigmentation usually resolves spontaneously even though the outcome may differ widely among patients.

Melasma
Melasma, chloasma or mask of pregnancy may affect up to 70% of pregnant women. Facial hyperpigmentation display various symmetrical distributions. The most common is centrofacial melasma developing on the forehead, cheeks, upper lip, and chin. Maxillary and mandibulary patterns are less frequent. Pigmentation consists of grey-brown, poorly demarcated plaques. The diagnosis is very easy. Pigmentation usually regresses in postpartum, but may persist in some cases and/or worsen again after sun exposure. Recurrence in future pregnancies or with oral contraception is common. The genetic background, dark complexion and exposure to UV light are aggravating factors.

Vascular Changes
Various molecules can cause functional modifications in the arteries with a decrease in smooth muscle tension and consequent decrease in vascular resistance. Proliferation of the cutaneous microvasculature also occurs. Alternatively, expanding intravascular volume and compression from the enlarging gravid uterus explains venous congestion, dependent oedema and varicosities. Thus, hyperemia, vasomotor instability, vascular proliferation and venous hypertension can cause skin lesions that usually regress postpartum.

Spider Telangiectasias
Spider telangiectasias, also termed spider angiomas, develop in approximately 60% of white pregnant women, but are found much less frequently in dark-skinned women. They are easily recognised by their punctiform central redness-corresponding to a dilated afferent arteriole with radiating capillaries and surrounding erythema. Typically, spider nevi appears at the end of the first trimester in the area of skin drained by the superior vena cava, namely the face, neck, arms and hands. Their number increases throughout pregnancy. They often disappear within weeks after deliver. It should be mentioned that when abnormally numerous spider telangiectasias manifest in pregnant women, liver status should nevertheless be checked, since in hepatic diseases oestrogen catabolism may decrease.

Acral Erythema
Palmar erythema appears within the first trimester along with spider telangiectasias. It is more frequent and noticeable in white than black women. Two patterns have been described; erythema may either be restricted to the thenar and hypothenar eminences, the metacarpophalangeal joints and the finger pads or, by contrast, it may present as a diffuse mottled redness of the entire palms. Hyperthyroidism, cirrhosis, lupus and salbutamol intake are the main differential diagnosis. Palmar erythema in pregnancy is attributed to venous capillary engorgement and fades within 1 week postpartum.

Venous Hypertension Signs
Secretion of pregnancy-related hormones induces an increased fragility of the elastic fibres in vessel walls. Furthermore, the enlarging uterus compresses the pelvic and abdominal vessels, increasing venous pressure. These, as well as other precipitating factors, including genetic predisposition and prolonged standing, lead to saphenous, vulvar and anal (hemorrhoidal) varicosities.
ing from the second month of pregnancy, varicose veins and venous telangiectasias appear in 40% of women. They are localised on the legs, the pelvis and the perineum. Thrombosis can complicate the situation in less than 10% of cases. Varicosities usually regress postpartum. Uses of elastic stockings are therefore recommended to prevent this phenomenon. Prevention of constipation may help to prevent their exacerbation. In the same way, vascular dilatation of the vestibule and vagina is responsible for varicosities (the Jacquemier’s sign) and a bluish purple tint of the mucosa (the Chadwick’s sign), two early diagnostic features of pregnancy. The increased hydrostatic venous pressure detailed above may also lead to fluid leakage in the extracellular milieu. This results in non-pitting oedema mainly affecting the legs, but possibly affecting the face and the eyelids also. It is more pronounced in the morning and is observed in almost half of all pregnant women during the last few months of pregnancy. However, one has to keep in mind that oedema of the face and hands may be indicative of pre-eclampsia. Purpura is due to the excessive fragility and permeability of capillaries and is common on the legs during the second half of pregnancy; although, it spontaneously regresses postpartum, if persists longer, other causes of purpura should be ruled out.

**Vasomotor Instability**

Vasomotor instability is frequently observed and includes alternating episodes of pallor, facial flushing, hot and cold sensations and dermatoglyphism. Exaggerated response to cold is sometimes associated with a reticulate bluish erythema of the lower legs, referred to as cutis marmorata, which usually resolves after delivery.

**Vascular Proliferation**

Superficial or subcutaneous hemangiomas are reported in 5% of pregnant women. They develop at the beginning of the third month of gestation, particularly affecting the hand and neck. These hemangiomas grow slowly until delivery, which is followed in most cases by spontaneous involution. Hyperaemia and hyperplasia of the gingival mucosa is observed in pregnant women. It may present with various degrees of severity, ranging from mild asymptomatic inflammation to intense pain with bleeding. It develops in the third trimester of pregnancy and progressively resolves postpartum.

Similarly, pyogenic granulomas appear to be relatively frequent during pregnancy. They are also known as pregnancy epulis, epulis gravidarum or granuloma gravidarum and usually develop during the second trimester. Pyogenic granulomas are painless but may bleed. Spontaneous regression is observed in the months after postpartum, but their recurrence is possible in later pregnancies. Surgical excision is allowed if necessary (e.g., considerable bleeding).

**Structural Changes**

**Striae Gravidarum**

Striae distensae (striae gravidarum) is a cause of great concern for pregnant women. They occur in 60–90% of white women, but less commonly in black or Asian women. However, Chang et al., found that dark-skinned women had more striae gravidarum than Caucasian females. The most significant risk factors for striae in primiparous women include young maternal age and elevated maternal BMI, as well as maternal weight gain and high neonatal birth weight. Women with a history of breast or thigh striae, or a family history of striae gravidarum are also at higher risk. The diagnosis is readily performed, but the mechanisms remain poorly known. These seem to be multifactorial and include physical trauma, such as stretching of the
skin, and hormonal mediation through steroids, oestrogens and relaxin, leading to reduction in the elastic fibre network.12

Molluscum Pendulum (Acrochordons)
Molluscum fibrosum gravidarum corresponds to the skin tags or acrochordons that grow during pregnancy. As in non-pregnant females, these appear as multiple small, cutaneous, fibrous, pedunculated, lightly pigmented polyps located on skin folds, such as the neck, the axillary, inframammary and inguinal folds. They begin during the second half of pregnancy and often shrink after delivery. When persisting, these may enlarge in future pregnancies.4 They have no malignant potential.

Adnexal Changes

Hair
During pregnancy, hair cycle changes resulting in fewer anagen hair follicles entering the telogen phase. This leads to thickening and brightening of hairs. In addition to the thickening of scalp hair, body hair follicles increase in size and number, especially on the face, and less often on the arms, legs, and back. This kind of hirsutism is reversible within 6 months postpartum.4

Postpartum, scalp hair enters a prolonged telogen phase causing increased shedding (telogen effluvium), that may begin 2–4 weeks after delivery and last 3–4 months. After this period, hair completely grows again within 6–15 months.7 Evaluation of the possibility of an iron deficiency should usually be performed.

Nails
Nails grow faster during pregnancy and rapidly become brilliant and brittle. Pregnant women may notice distal onycholysis, transverse grooves, longitudinal melanonychia and subungual hyperkeratos- sis. Most of these conditions are uncommon and resolve postpartum.4

Sudoral and Sebaceous Glands
Sebaceous gland activity appears to increase in the third trimester since many pregnant women complain of greasy skin, especially on the face, and in many of these, acne develops for the first time during pregnancy. However, the effect of gestation and hormonal disturbances is unpredictable on pre-existing acne.4 In approximately half of pregnant women, the sebaceous glands on the areola enlarge and appear as multiple elevated brown papules called Montgomery’s glands or tubercles.4 They are visible starting from the 6th week of gestation, representing an early sign of pregnancy.7 Regression is classical after delivery.

Specific Dermatoses of Pregnancy
These conditions are peculiar in the way they represent cutaneous diseases strictly developing during pregnancy or shortly after. They may, or may not recur in later pregnancies. Their mechanisms are, therefore, related to the development of the gestation, although the precise pathways are not yet well understood.

Polymorphic Eruption of Pregnancy (PEP)/Pruritic urticarial papules and plaques of pregnancy (PUPPP)
• Urticarial papules and plaques, usually develops during late term. This disease is characterised by the development of pruritic disseminated cutaneous lesions that usually begin on the lower abdomen, particularly on the striae distensae. Unlike pemphigoid gestationis (PG), the periumbilical area is nearly constantly spared in PEP
• Most frequent in primiparous women
• No maternal or foetal risks
• Resolves spontaneously and rapidly postpartum
• Rarely recurs

Pemphigoid Gestationis
Intensely pruritic vesiculobullous eruption developing during late pregnancy or the immediate postpartum period. The disease usually develops in multiparous women, in contrast to PEP, and mainly during the second or the third trimester. Pruritus classically precedes skin manifestations. Later, urticarial lesions develop initially on the abdomen and the umbilical skin (50–80% of cases). These are erythematous and pruritic papular plaques sometimes displaying an annular pattern. The lesions secondarily extend to the trunk, the limbs, and more rarely the palms and soles. Clear and tense bullae may rise on the edematous plaques. The face and mucous membranes are usually unaffected. Then, more recent series gave much higher figures, raising the incidence up to one in 1600. If PG is not treated, it regresses after delivery, although a flare in postpartum is frequently reported (75–85% of the cases). Persistent PG with a protracted autonomous course may evolve for several years after pregnancy. PG relapses in 50–70% of later pregnancies, appearing earlier in gestation and in a more severe form. Recurrences have been reported in 20–50% of cases with subsequent use of oral contraceptives. The foetal prognosis is good in PG. Neonatal vesicles may appear but the eruption is usually mild, self-limited and linked to the transient passage of maternal antibodies. At least 4 studies found high percentages of preterm labour ranging from 7–43%. Reduced birth weight and low birth weight were associated in one series with early onset of disease and blister formation. Caesarean section incidence was also high, ranging from 3–39%. Of note, the case-control study of Mascaro et al., found a significantly higher incidence of preterm labour and caesarean sections in women with PEP. Recurrences of PG may occur either if an oestroprogestative contraception is given or at later pregnancies, at levels of 20–50% and 50–70%, respectively.

Prurigo of Pregnancy
Prurigo of pregnancy (PP) was formerly known as prurigo gestationis of Besnier or early PP. The incidence of PP varies from one in 300 to one in 450 pregnancies. It presents as excoriated papules and affects the extensor surfaces of the extremities and the abdomen. As previously mentioned, such manifestations are part of other skin diseases related to atopy or various other causes (e.g., scabies).

Pruritic Folliculitis of Pregnancy
Pruritic folliculitis of pregnancy (PFP) is a very rare eruption, with only 24 reported cases, which develops during the third trimester of pregnancy. It is characterised by papules and sterile follicular pustules on the trunk and sometimes the upper limbs. PFP clears spontaneously after delivery. There are no risks for the mother or the baby except a decrease in the foetal birth weight.

Intrahepatic Cholestasis of Pregnancy
Intrahepatic cholestasis of pregnancy (ICP) is not strictly part of the dermatoses of pregnancy since there are no primary skin lesions. The aetiology of ICP is complex and not fully understood, but it is likely to result from the cholestatic effects of reproductive hormones and their metabolites in genetically susceptible women. ICP usually manifests in the third trimester by nocturnal itching. Skin lesions are found in only a third of cases. These are secondary to scratching and correspond to excoriated lesions or prurigo. Symptoms resolve after delivery. Recurrence occurs in 60–70% of subsequent pregnancies. Hepatitis C infection was
over 3 folds more common in patients with ICP than in controls. As for PG, oral contraceptive intake may also cause recurrences, and this raised the hypothesis that oestrogens are mediating the development of this disease. The diagnosis relies on biochemical tests. Alanine aminotransferase level is increased in 95% of cases, and the serum fasting bile salts level is always increased. Bile acid synthesis appears to be reduced in patients with ICP, in whom primary conjugated bile acids are retained in the blood. The major bile acid in the blood and urine of these patients is cholic acid instead of chenodeoxycholic acid present in normal pregnancies. This test is essential for diagnosing cholestasis and quantifying its intensity. It has been demonstrated that for the evaluation of foetal status, increased total bile acid levels in the mother and increased exposure time for the foetus to these increased values of total bile acid within the maternal circulation system help to predict increased risk of asphyxia in newborns to ICP mothers. In contrast with other dermatoses of pregnancy, ICP harbors a risk of intrauterine growth retardation (17–50%), stillbirth (0.75–3.2%), perinatal death (0.75-6.4%) and preterm delivery (12-50%). Indeed, most authors recommend the induction of labour in week 38 of gestation in mild cases and even earlier (in week 36) in severe cases. Meanwhile, cholestyramine, a resin that binds bile salts, may be given, a partial response being observed in 70% of patients. Furthermore, cholestyramine is responsible for a malabsorption of vitamin K, inducing a risk of haemorrhage. Ursodeoxycholic acid seems to work faster than cholestyramine and also controls pruritus and plasma abnormalities. It appears to be safe for mother and foetus and may decrease foetal mortality associated with ICP.

Impetigo Herpetiformis
The onset of impetigo herpetiformis (IH) occurs most commonly in primiparous women during the third trimester of pregnancy. IH presents with symmetric, erythematous patches the borders of which sterile pustules secondarily develop. The lesions start in the folds and extend centrifugally. Hyperthermia, nausea, vomiting and diarrhoea are common. Hypocalcaemia, hypoalbuminemia or low serum levels of vitamin D should be systematically sought. True hypocalcaemia remains rare and is usually the reflection of hypoalbuminemia. Recurrence in successive pregnancies may occur with earlier onset. Oral contraception can be another triggering factor. Replacement treatment is mandatory if low levels of calcium are found.

CONCLUSION
Skin is constantly modified during pregnancy and/or postpartum. These changes are usually only physiological, expressing changes in hormones or other factors secreted through the placenta, ovaries or enlarged pituitary gland. However, various dermatoses may specifically develop during this period and may influence the foetal outcome or, more rarely, the mother’s health. Therefore, being able to diagnose and manage them is of high importance. Of note, to perform skin biopsy with direct immunofluorescence remains requested when facing urticarial or eczematous plaques. In the same way, it is mandatory to evaluate the bile salts levels when facing generalised pruritus.

About the Authors
Dr Prasoon Soni is a Senior Resident, Department Skin and VD, Dr Monica Soni is an Assistant Professor, Dr Priyanka is a Senior Demonstrator and Dr Ekta is a Medical Officer, Department Obstetrics and Gynaecology, SP Medical College and PBM Hospital Bikaner.
REFERENCES

A 32 years female, came to surgical OPD, with a complaint of cyst in right breast since last 6 month, which was gradually increasing in size and was tender. The cyst was fixed to chest wall (not freely movable like lipoma or fibroadenosis). Excision of the cyst was done under local anaesthesia and sent for histopathological examination. As patient was not having any other complaints, she was not hospitalised.

On gross examination, received greyish white cystic soft tissue piece with grey brown area, measuring 2–2.5 cm. HPE was done and it showed encysted larvae of Trichinella spiralis with its characteristic morphological features and scanty muscle tissue was also seen (Figure 1, 2).

(Continued on page 400)
All children cough and around 50% of children will wheeze before reaching school age, but the majority of these children will be normal. Up to 40% of infants experience wheeze in the first year of life. A UK population-based study showed the prevalence of reported wheeze in 1998 was 29%, a significant increase from the same survey in 1990 when it was 16%. The cost of treating preschool wheezing children is a considerable one, estimated to be 0.15% of the UK National Health Service budget. An asthma diagnosis is more common in this age group than in older children. (Figure 1)

There is good evidence-based treatment for asthma in older children, but only a proportion of preschool wheezers fit an asthma diagnosis. Different patterns (or phenotypes) of preschool wheeze have been determined and are described below. These evolve with time and it can be difficult to distinguish one from another at presentation.

PHENOTYPES OF WHEEZING IN YOUNG CHILDREN

A series of studies from Tucson, Arizona, United States, on a cohort of over 1,000 newborn babies followed throughout childhood has clarified the natural history. In the first 6 years of life, 50% of children never wheezed, small numbers (approximately 1%) had atypical wheezing related to other abnormalities or disease states (see Table 1) and the remainder with typical wheeze could be divided into three groups: transient early wheeze, persistent atopic wheeze and late-onset non-atopic wheeze.
Transient Early Wheeze

In the Tucson study, the largest group had transient early wheeze, making up 20% of the cohort. These children generally started wheezing in their first year of life and stopped by 3 years of age. The primary risk factor is reduced pulmonary function in infancy, with lung function tests shortly after birth showing reduced forced expiratory flow indicating small airways. This is not associated with a family history of asthma or atopy, and airway function in this cohort remained low up to the age of 16 years.

Other risk factors for transient early wheezing include prematurity, male gender, exposure to siblings and other children at day-care centres, pre-natal maternal smoking and post-natal exposure to tobacco smoke.

Persistent Atopic Wheeze

Children with persistent ‘atopic’ wheezing made up 14% of the Tucson cohort. More than half started wheezing before the age of 3 years, and asthma persisted through childhood. They had normal lung function in infancy but developed airways obstruction in the first years of life. These children wheezed without viral infections and were more likely to have a family history of asthma, elevated serum IgE and peripheral eosinophilia. Early allergic sensitization plays an important role in persistent wheeze/asthma. A European cohort of 1,300 children studied from birth to 13 years found that sensitization to perennial (eg, house dust mite, cat and dog hair) but not seasonal allergens developing in the first 3 years of life was associated with a loss of lung function at school age. Such exposure to high levels of allergens in early life led to the development of airway hyper-responsiveness with wheeze in sensitized children. Exposure in later years had a much weaker effect. Interestingly, there is evidence that factors which decrease the risk of atopic sensitization include exposure to other children and farm animals.

Late-onset Non-atopic Wheeze

These made up 15% of the Tucson cohort. Their cumulative prevalence increased in the first 6 years but then started to decline. These children had normal lung function early in life before any respiratory insult. Then, as they were exposed to viral respiratory agents, they developed wheeze independently of allergic sensitization. This phenotype appears to be almost as common as atopic wheezing in the pre-school group but is associated with less severe and less persistent wheeze and becomes less common among school-aged children. (Figure 2)

CLINICAL FEATURES

The child is likely to present with a history of noisy breathing but may not be making any noise when seen. It is important to determine what the family means by the word wheeze as parents often use
this word to describe other noises, such as hearing or feeling a loose rattle on the chest or nasal snuffling. Studies using a video questionnaire or objective recording of lung sounds have shown poor parental recognition of wheeze. From the history, it is important to determine the pattern and duration of wheezy episodes and the severity when they occur. Any precipitants of episodes should be identified (eg, viral infections). History and examination should elicit whether the child or family are atopic (eg, evidence of eczema) and whether there is evidence of any other systemic disease (eg, cystic fibrosis, heart disease). At acute presentation, the child will be tachypnoeic and hyperinflated with lower intercostal indrawing and widespread expiratory wheeze. In addition, generalized inspiratory crackles may be heard in children with viral infections. Severe respiratory distress, evidence of hypoxia (SaO2 <92%) or poor response to treatment warrants referral to hospital. Between episodes, the child may be entirely normal. Persistence or recurrence of focal signs, evidence of inspiratory wheeze or stridor, hypoxia between episodes or failure to thrive are all indications for further investigation in secondary care. It may be difficult at presentation to fit the child into the phenotypes described above, but for management purposes, there are two main patterns:

- Acute episodic wheeze and cough with no interval symptoms; main/only trigger viral infections and no evidence of atopy
- Chronic symptoms or frequent episodes with interval symptoms; evidence of atopy and a variety of triggers which may include viral infections

INVESTIGATION

Most preschool children with wheeze do not require any investigation. A chest X-ray should be performed if there are persistent signs. Oximetry is useful during acute episodes. A sweat test should be performed if cystic fibrosis is suspected. Where there is suspicion of structural abnormalities or unusual diagnosis, then special investigations including bronchoscopy and CT scanning are carried out in secondary/tertiary centres. Further tests should be guided by the history and examination if other causes of ‘atypical wheeze’ are suspected. (Table 1)

TREATMENT OPTIONS

The pathophysiology of wheeze in young children may be multifactorial with bronchospasm, mucus oedema, mucus plugging, abnormal airway architecture and mechanics all contributing. These mechanisms may not be receptive to pharmacological manipulation and so the response to conventional asthma treatments may be highly variable.

Preventative Measures

Passive prenatal smoking results in underdevelopment of the fetal bronchial tree leading to diminished lung function from birth. This is the most important...
Although parents rarely admit to smoking in front of their child, urinary cotinine (a metabolite of nicotine) studies consistently reveal that wheezing children of parents who smoke are significantly exposed. Passive post-natal smoking constitutes a significant risk factor for infection, worsening asthma symptoms and decreased lung function in young children. Unfortunately, interventions to decrease parental smoking are often unsuccessful. Breastfeeding is associated with lower asthma rates during childhood. Primary prevention by reducing the allergen burden in the environment has not been very successful. For secondary prevention, it is clear that if the child is sensitized to an aeroallergen (e.g., cat), then it should be removed from their environment. There is evidence that environments rich in microbacteria, such as farms, protect against the development of allergies. Two bacterial species identified in cowsheds possess strong allergy protective properties. Antibiotic use in the first 2 years of life may be implicated in the development of asthma, and careful antibiotic prescribing is warranted.

**Bronchodilator Therapy**

There is good evidence that beta-2 receptors are present in the airway from birth, and there is definite physiological evidence that at least some children respond to inhaled beta agonists. However, a Cochrane review published in 2002 looked at the efficacy of inhaled short-acting beta agonists for ‘recurrent wheeze’ in children under 2 years old and could not find clear evidence of benefit. The data from the right randomized trials were markedly heterogeneous, which severely limited the performance of between-study comparisons. In clinical practice, it is worth undertaking a therapeutic trial of beta-2 agonists to assess benefit. Ipratropium bromide is no more effective than beta-2 agonists in preschool children. The younger the child, the less likely a response to either agent, but in reality, it is difficult to predict who will respond. There is no evidence that drugs given by a nebulizer are any more effective than those given through a spacer and mask.

### Inhaled Corticosteroids and Oral Steroids

There is no doubt that inhaled corticosteroids (ICS) are beneficial for preventing daily symptoms and improving lung function in schoolchildren. Such effectiveness has not been proven in children with viral-induced wheeze. ICS maintenance therapy is not effective in preventing or treating asthma exacerbations secondary to viral infections in older schoolchildren or adults with established, atopic asthma. In young children, the use of high-dose ICS at the onset of viral colds does not reduce the risk of hospital admission and need for oral steroids but does have a modest beneficial effect on severity of symptoms.

In preschool children with persistent wheezing, the efficacy of ICSs is less clear. Some studies show clinical and physiological benefits, particularly if the child is atopic, whereas others show no benefit. The effect of high-dose ICS on growth is well known, but in animal models, recent evidence suggests nebulized steroids can impair alveolar development, implying the need for increased caution in infants. There is recent evidence that long-term use of ICS has no ef-
fect on the natural history of asthma or wheeze in later childhood.\textsuperscript{21} This important conclusion means ICSs should be prescribed only if the current symptoms are severe enough and then are only continued if shown to be beneficial.

The role of systemic corticosteroids is controversial. A recent randomized controlled trial of parent-initiated oral prednisolone at the time of viral infection showed no evidence of benefit.\textsuperscript{22} However, another randomized trial showed that systemic steroids given to children presenting to the emergency department with preschool viral wheeze reduced the need for additional asthma medication in hospital and reduced length of stay from 3 to 2 days.\textsuperscript{23} A trial of systemic steroids is sensible in a severely wheezing young child, especially when there are risk factors for atopic asthma and the child responds to bronchodilators.

**Leukotriene Receptor Antagonists**

The use of leukotriene receptor antagonists seems logical as there is increased production of cysteinyl leukotrienes at the time of viral infection, and viral infections are a major trigger in preschool children. Physiological studies of the oral leukotriene antagonist montelukast have shown bronchoprotection and a reduction in exacerbations in preschool children.\textsuperscript{24} Montelukast has a rapid onset of action, and a recent study of a 7-day course given from the day of onset of viral symptoms reduced symptoms by 14% and days off childcare or school by 37%.\textsuperscript{25} A trial of montelukast is an appropriate first-line preventative strategy for young children with persistent wheeze and can be considered as an intermittent therapy for those with frequent viral exacerbations.

**PROGNOSIS**

The most common parental question is ‘Will he grow out of it, doctor?’ The long-term cohort studies provide some reassurance. Eighty percent of children who wheeze during the first year of life do not wheeze after the age of 3 years. Sixty percent of children who wheeze in the second year of life and 30–40% of those in the third year have stopped wheezing by school age.\textsuperscript{7} Children who are clearly atopic are more likely to continue with symptoms during childhood.

**CONCLUSION**

The pattern of wheeze in preschool children is an indicator of both likely treatment response and prognosis.

- For children with acute episodic wheeze and cough with no interval symptoms, a trial of treatment during the acute episode is appropriate. These children are unlikely to benefit from prophylactic treatment with inhaled steroids, but exacerbations may be ameliorated in some by the intermittent use of leukotriene receptor antagonists (montelukast).
- For children with chronic symptoms, therapy is dependent on severity. Mild symptoms that do not disturb sleep or feeding may not require treatment. For troublesome chronic symptoms and particularly where there is evidence of atopy, it is reasonable to trial step-wise treatment with leukotriene receptor antagonists (montelukast) as first line followed by low-dose inhaled steroids. Therapy that is not
Figure 3. Management of preschool wheeze in a primary care setting

**Presenting features**
- Wheeze
- Cough
- Breathlessness
- Respiratory distress

**Detailed history**
- Risk factors
- Age of onset
- Only with colds
- Other triggers
- Continuous symptoms

**Detailed history**
- Failure to thrive
- Persistent wet cough
- Recurrent bacterial infections
- Abnormal stool pattern
- Severe symptoms requiring hospitalization

**Examination**
- Generalized wheeze
- May have clear chest
- Eczema
- Normal ENT examination
- No significant chest deformity

**Examination**
- Persistent focal chest signs
- Stridor
- Clubbing
- Asymmetric signs
- Fixed monophonic wheeze

**Management**
- Trial of bronchodilator via a spacer
- Consider montelukast at onset of symptoms
- Reassure family
- No chest X-ray

**Management**
- Trial of bronchodilator via a spacer
- Consider allergen avoidance if clear association
- Consider daily montelukast
- Consider chest X-ray

**Symptoms only with viral colds that completely resolve**
Normal examination
Nothing else in history

**Chronic symptoms which are associated with atopy or are significant**
May worsen with viral colds but persist or resolve for only short periods

**Atypical wheeze likely**
- Chest X-ray
- Refer to paediatrician

**Referral to paediatrician**
- Diagnosis in doubt
- Treatment not working
- Parental or doctor anxiety

**Severe symptoms**
- Oral prednisolone at onset
- Consider ICS if frequent and responsive to treatment
- Stop ICS after 3 months and consider restarting if symptoms worsen
- Use lowest possible therapeutic dose of ICS

**Severe symptoms**
- Oral prednisolone at onset
- ICSs and continue only if clear therapeutic response
- Use lowest possible therapeutic dose of ICS

ICS = inhaled corticosteroids
helpful should be stopped. A referral to an expert in pediatric respiratory disease should be made before escalating therapy.

Some children may have a poor response to pharmacological treatment and avoidance of triggers, and supportive treatment for severe exacerbations (with oxygen ± oral steroids) may be a mainstay of treatment. A management plan is outlined in Figure 3. There is room for new evidence-based therapy for preschool wheeze.


About the Authors
Dr Cremonesi is Specialist Registrar and Dr Thomson is Consultant, both in Paediatric Respiratory Medicine, Oxford Children’s Hospital, Oxford, UK. Dr Thomson has research interests in respiratory infection and cystic fibrosis.

Practice Points

- Wheeze is a very common symptom in preschool children.
- Pre- or post-natal smoking is the single most important risk factor for wheeze in this age group.
- Viral infections are the commonest triggers.
- Bronchodilator therapy via a spacer should be the first-line treatment for acute symptoms.
- Leukotriene antagonists can be effective and should be tried if prophylaxis is warranted.
- Inhaled corticosteroids rarely improve symptoms and have no disease-modifying properties in the long run.
- In all cases where inhaled corticosteroids are started, it is important to stop their use after several months to look for evidence of their efficacy.

REFERENCES

INTRODUCTION
India is the seventh-largest country in the world; an unimaginable disparity exists in the geography, ethnicity, religion, food and personal habits, level of education and standards of living within the country. Livestock plays a pivotal role in the socioeconomic life of India. Parasitic Zoonoses affect human and animal health directly, and consequently affect livestock production. Zoonoses of parasitic origin are prevalent throughout India at varying rates. Factors such as poverty, lack of personal hygiene, defecating in open spaces, scarcity of potable water, abundance of stray animals, high population density, and certain culinary habits are responsible for the rising prevalence of Zoonoses in India.

Among protozoa, Cryptosporidium parvum, Toxoplasma gondii, Leishmania spp., Giardia duodenalis, Sarcocystis spp. and Entamoeba histolytica are the major examples and the main helminth zoonoses include echinococcosis, cysticercosis and rarely few case reports of trichinosis (caused by dogs and pigs respectively). Trichinosis generally presents as muscle cyst with or without eosinophilia but presentation as a breast cyst is a rarity.

DISCUSSION
In Western-Rajasthan, trichinosis is rarely reported, even this may be the first case report, though cysticercous, toxoplasmosis and other Zoonotic parasitic diseases are frequently reported; it may be due to misdiagnosis or under-reporting as all muscle cysts are not sent for biopsy, non-availability of serological test and rare case reports of T. spiralis cyst. In India, Trichinella spp. infection has been documented rarely. Few reports showed the presence of encapsulated larvae of Trichinella spp. in domestic cats, in a wild toddy cat (Paradoxurus hemaphroditus), in a wild civet cat (Viverricula indica), and in domestic pigs. The non-encapsulated species, pseudospiralis was detected in an Indian mole rat (Bandicota bengalensis). But, in India, very few outbreaks are reported in swines and very few case reports of human trichinosis is available from Punjab, West Bengal and Maharastra. Case reports of Psoas muscle and other skeletal muscle involvement are reported but presenting as breast cyst is a rarity and very important differential diagnostic clue for surgeons. Internationally, cases of trichinosis are reported, specially in areas where pork or undercooked pork is consumed or policy regarding inspection of slaughter houses and their hygienic conditions are not good (as epidemic of trichinosis is reported in swines).

Trichinosis is acquired through the consumption of raw or insufficiently cooked meat harbouring infectious nurse cell larva complex. The usual incubation period is 5–15 days. The clinical course of trichinosis has 2 phases: An enteral (gastrointestinal) phase and a parenteral (systemic) phase. During the
enteral phase larvae are released by digestive enzymes in the stomach and passed into the small intestine. Following the invasion of the intestinal mucosa, parasite moults become sexually mature. The mature female begins to expel newborn larvae following copulation. This invasion of the small intestine can cause gastrointestinal symptoms which clinically manifest as nausea, upper abdominal pain, vomiting, diarrhoea, etc. The subsequent parenteral phase begins when the larvae enter the blood circulation and migrate to striated muscles where they encyst. This can cause inflammatory reactions and local tissue necrosis. According to the criteria defined by the Centers for Disease Control and Prevention, a confirmed case of trichinosis is defined as illness with at least 3 clinically compatible manifestations of trichinosis (which includes gastrointestinal symptoms, eosinophilia, fever, periorbital oedema, myalgia, subconjunctival haemorrhages, etc.) and a laboratory confirmed trichinella infection. Laboratory confirmation of infection is made either by a positive serological test for trichinella-specific antibody or by the identification of trichinella larvae in tissue obtained by a muscle biopsy. Most cases occur as outbreaks which is suggestive of a common source of infection, with sporadic cases being the exceptions. A single detected case of trichinosis implies that other people may be infected. Anti-Trichinella antibodies confirmed by the presence of larvae of Trichinella in the digested muscle tissue. Usually the encapsulated larvae in the muscle biopsy can easily be seen by histopathological staining methods, but non-encapsulated ones, e.g., T. pseudospiralis, are difficult to detect. In present case as cyst was present in breast, it was involving chest muscle, was tender and gradually increasing in size, biopsy was sent for histopathology and diagnosis was confirmed. There was no other cyst in body. On direct questioning, patient admitted that she is non-vegetarian and used to have pork in the past. Patient was given antihelminthic drug (albendazole), antibiotics and analgesics.

Conclusion
Attention is drawn to the unusual clinical presentation of trichinosis in this patient that presented as breast cyst. All surgeons must be aware of trichinosis and should include it in their differential diagnosis when examining patients with any type of cyst (spatially involving muscle) in body.

References

About the Authors
Dr Prabhu Prakash is an Associate Professor, Department Microbiology, Dr Asha Mathur is a Professor, Department Pathology, Dr Sneha Ambwani is a Professor, Department Pharmacology, Dr Seema Surana is an Assistant Professor, Department Microbiology, SNMC Jodhpur and Dr PC Gupta is a Junior Specialist, General Surgery, District Hospital, Jodhpur.
Study of Serum Homocysteine and Vitamin B₁₂ Levels in Eclampsia, Pre-Eclampsia, and the Effectiveness of Treatment with Inj. Vitamin B₁₂ on the Outcome of these Patients

Radha Yegnanarayan, GS Shekhawat, Hemand S Damle

INTRODUCTION

Pregnancy-induced hypertension may occur in about 3–10% of all pregnancies.¹ It remains a major cause of perinatal and maternal morbidity and mortality worldwide, because of complications such as eclampsia, foetal growth retardation, premature birth or abruption placentae.¹² An increased concentration of total circulating homocysteine in serum is recognised as an independent risk factor for Pre-eclampsia.³⁴ Moreover, determinants of hyperhomocystinaemia, such as low concentrations of folic acid and vitamin B₁₂ involved in homocysteine metabolism are also associated with increased risk of vascular damage and pre-eclampsia.⁵

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Eclampsia group (n=10)</th>
<th>Pre-eclampsia group (n=10)</th>
<th>Past History of PET/eclampsia group (n=10)</th>
<th>Control group without any past history or PET/eclampsia in present pregnancy (n = 10)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>21.6±2.3</td>
<td>22.1±3.1</td>
<td>25.5±3.3</td>
<td>25.1±2.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Gestation age (weeks)</td>
<td>32</td>
<td>36</td>
<td>36</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td>P1=02</td>
<td>P1=06</td>
<td>Eclampsia=02</td>
<td>P1=04</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P2=06</td>
<td>P2=02</td>
<td>Pre eclampsia=06</td>
<td>P2=4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P3=02</td>
<td>P3=02</td>
<td></td>
<td>P3=02</td>
<td></td>
</tr>
<tr>
<td>SBP (mm of Hg)</td>
<td>158.7±7.1</td>
<td>144.3±4.6</td>
<td>118.1±8.2</td>
<td>120.3±6.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DBP (mm of Hg)</td>
<td>108.1±5.2</td>
<td>96.3±3.1</td>
<td>90.6±2.9</td>
<td>84.0±3.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Proteinuria mg/24 hour</td>
<td>Significant</td>
<td>Significant</td>
<td>Not Significant</td>
<td>Absent</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The results were compared between pre-eclampsia/eclampsia groups and control group. The values are presented as mean ± S.D.
It is uncertain whether hyperhomocysteinaemia per se or low concentrations of vitamin B12 and folic acid are atherogenic factors that trigger pre-eclampsia. The present study was undertaken to determine the levels of serum homocysteine, and vitamin B12 and their correlation in patients with pre-eclampsia. We also studied the effectiveness of treatment with Inj. B12 in patients who showed low levels of vitamin B12.

Material and Methods
This study was carried out at the Department of Pharmacology and Department of Obstetrics and Gynaecology, Smt Kashibai Navale Medical College and General Hospital, Pune, after obtaining Institutional Ethics Committee approval. All participants completed a medical history form and provided informed consent. Forty patients in the age group of 18–35 years were studied for estimation of serum total homocysteine, and vitamin B12 over a period of 18 months. Detailed dietary history with reference to vegetarian or non-vegetarian status and consumption of folate rich foods were recorded in all cases. Peripheral blood smears were examined in all 40 cases for the presence of megaloblasts. In all those cases where homocysteine concentrations were high and vitamin B12 levels were low, we administered Inj. B12, 1500 µgm I/M in 3 divided doses.

Inclusion Criteria
This prospective study was conducted among 40 patients, who were divided into 4 groups. Ten patients with eclampsia, 10 patients with pre-eclampsia, 10 patients with past history of pre-eclampsia/eclampsia and another 10 normotensive patients as control without any signs, symptoms, lab test suggestive of pre-eclampsia were included. Besides routine baseline ANC investigations, all patients were subjected to special investigation including renal, liver and coagulation function tests for pre-eclampsia/eclampsia patients.

Exclusion Criteria
Patients having use of medications (therapy involving S-adenosyl-methionine, carbamazepine, phenytoin, 6-azauridine, xanthopterin, antifolic acids, anticonvulsant agents, tamoxifen, and theophylline) for cancer, severe anaemia, systemic illness and those with major illness were excluded from study.

Blood Sample Collection
Venous blood samples were collected in test tube with aseptic precautions.
After 2 hours of collection, sample was centrifuged at 3000 rpm for 5 min. Serum was separated and collected in polythene tube with cork. The sera with no sign of haemolysis was coded and used for the analysis of total circulating homocysteine and vitamin B₁₂. The investigator carrying the estimation was unaware of the clinical history and treatment status of the patients.

Biochemical Analysis

Serum homocysteine concentration was measured by competitive chemiluminescent enzyme immunoassay method. Serum vitamin B₁₂ concentration was evaluated by solid phase, competitive chemiluminescent assay method. We used fully automated enzyme amplified chemiluminescent immuno assay based immulite 1000 analyzer. Hyperhomocystinaemia was defined as a serum homocysteine concentration greater than 15 µmoles/l. Vitamin B₁₂ deficiency was defined as Vitamin B₁₂ level lower than 223 pg/ml.

Statistical Analysis

Numerical variables were reported in terms of mean and standard deviation or standard error of mean. Statistical analysis of results was done by student’s t test with correction and Yates corrected chi square test wherever applicable. In this analysis, variables showing p value less than 0.05 and 0.001 were considered to be statistically significant and highly significant, respectively. Pearson correlation test was used to test correlation.

Results

Demographic data of pre-eclamptic patients such as mean age of patients showed significant fall (p<0.05). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly increased (p<0.05) in pre-eclamptic/eclamptic group as compared with control group (Table 1). Table 2 depicts changes in serum profile when control group was compared with study group of pre-eclampsia. As can be seen, significant increase (p<0.05) were observed in serum homocysteine whereas, vitamin B₁₂ levels showed significant decrease (p<0.05). A negative and significant correlation was observed between serum homocysteine when compared with vitamin B₁₂ (Table 2 and 3). All patients of eclampsia and pre-eclampsia were treated with vitamin B₁₂ whereas only 02 patients with past history of pre-eclampsia needed vitamin B₁₂ treatment as their homocysteine levels were above normal (Table 3).

When pre and post vitamin B₁₂ levels were compared, decrease and normalisation of homocysteine levels and increase and normalisation in vitamin B₁₂ levels were seen after Inj. B₁₂ treatment in both eclampsia and pre-eclampsia patients (Table 4). This improvement was statistically highly significant (p<0.001). A negative and statistically significant correlation (r=-0.335 and p<0.05) was found between serum homocysteine and vitamin B₁₂ in pre-eclampsia (Table 5).

Final outcome of these patients after Inj. Vitamin B₁₂ therapy has improved at par with control group without any neonatal or maternal mortality in all four groups; however, maternal and perinatal morbidity was much higher among pre-eclamptic and eclamptic group because of pre-existing pathology (Table 6).

DISCUSSION

Our findings suggest that levels of serum homocysteine and vitamin B₁₂ are altered in pre-eclampsia and eclampsia patients.
as compared to age-matched normotensive pregnant control subjects. The present study shows that there was significant hyperhomocystinaemia and deficiency of vitamin B12 in patients with pre-eclampsia and eclampsia. Several prospective studies with rather small cohorts of patients with pre-eclampsia have shown an independent association between elevated serum homocysteine level and untoward obstetric outcome.7,8 Several factors may increase homocysteine levels in women with pre-eclampsia.9 Metabolism in the kidney is the major route by which homocysteine is cleared from plasma and this route of elimination may be affected by preeclamptic changes in the kidney.10 Hyperhomocysteinaemia in pre-eclamptic patients found in our study might be due to modulation in homocysteine metabolism, which corroborates with the work of Walker et al., Hogg et al., Vollset et al. Several studies have demonstrated serum concentrations of elevated homocysteine in pre-eclampsia.11 These studies support our results. In our study, the levels of vitamin B12 were also significantly lower in the pre-eclamptic and eclamptic group as compared to control groups, suggesting raised homocysteine was due to vitamin B12 deficiency. Carmel R found differences in folic acid concentrations between pre-eclamptic and normal pregnant women. Similarly, in a systematic review by Mignini et al., folic acid and vitamin B12 concentrations were lower in pre-eclamptic women when compared with those of normotensive women.12 In another study, there was no difference in folic acid and vitamin B12 levels between pooled normal and pre-eclamptic groups, but these levels were significantly lower in patients with the 677 CT mutation of MTHFR.13 The serum homocysteine was found to have negative and insignificant correlation with serum folic acid in pre-eclamptic patients. In our study negative and statistically significant correlation (r = -0.335 and p < 0.05) was found between serum homocysteine and vitamin B12 in pre-eclampsia. There are two pathways by which homocysteine is metabolised: remethylation and trans-sulfuration. Folic acid and vitamin B12 are required for the remethylation of homocysteine to methionine; vitamin B6 is required for the trans-sulfuration of homocysteine to cysteine. A good correlation between serum homocysteine, and vitamin B12 levels observed in our study support this view. It is

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Eclampsia group (n=10)</th>
<th>Pre-eclampsia group (n=10)</th>
<th>Past history of PET/eclampsia group (n=10)</th>
<th>Control group (n=10)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perinatal outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Birth weight</td>
<td>100%</td>
<td>40%</td>
<td>20%</td>
<td>10%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IUGR</td>
<td>60%</td>
<td>30%</td>
<td>20%</td>
<td>10%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IUD</td>
<td>10%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>-</td>
</tr>
<tr>
<td>Abruptio Placentae</td>
<td>10%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>-</td>
</tr>
<tr>
<td>Need for NICU</td>
<td>80%</td>
<td>60%</td>
<td>20%</td>
<td>20%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Need for Resuscitation</td>
<td>60%</td>
<td>40%</td>
<td>10%</td>
<td>10%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 Min APGAR&lt;7</td>
<td>40%</td>
<td>30%</td>
<td>20%</td>
<td>10%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Maternal outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal delivery</td>
<td>40%</td>
<td>60%</td>
<td>70%</td>
<td>80%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td>40%</td>
<td>40%</td>
<td>30%</td>
<td>10%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Instrumental Delivery (Forceps/ Vacuum)</td>
<td>20%</td>
<td>0%</td>
<td>0%</td>
<td>10%</td>
<td>-</td>
</tr>
<tr>
<td>DIC</td>
<td>2%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>
justifiable to administer Inj. vitamin B12, 1500 µgm to all patients developing pre-eclampsia as prophylactic dose to prevent further complications of PIH.

From the above discussion, we can assume that biochemical screening such as homocysteine, vitamin B12 are of paramount importance in pre-eclampsia. The inverse relation between homocysteine, and vitamin B12 indicates that severity associated with metabolic disturbances in pre-eclampsia can contribute to obstetric complications. On the other hand, there is an absolute need for large studies designed to answer the question as to whether hyper homocysteinemia and vitamin B12 deficiency are associated with increased risk for pre-eclampsia and whether therapy of these disorders might influence maternal mortality and morbidity. Further studies should help define the role of genetic polymorphism in enzymes of homocysteine, folic acid, vitamin B12 metabolism and their role in pre-eclampsia.

About the Authors
Dr Radha Yegnanarayan, GS Shekhawat are Professors and Head of Department Pharmacology, and Dr Hemant S Damle is an Associate Professor, Department Obstetrics and Gynaecology, Smt Kashibai Navale Medical College, Pune, Maharashtra.

REFERENCES
INTRODUCTION

Amelia is an extremely rare birth defect marked by absence of one or more limbs.\(^1\) Its incidence is 1.5-11 lakh live birth and 7.9/10000 still birth.\(^2\) Teramelia means absence of all four limbs (Amelia Marranne). We report a very rare case of tetramelia with cleft lip and cleft palate. The aetiological factor for Amelia are thalidomide use, amniotic band syndrome, diabetes, autosomal recessive mutation and consanguineous marriages.\(^3\) Consanguineous marriage is causative agent in our case.

Case

A 25 year old primigravida presented to emergency ward at GMCH, Aurangabad with a USG report showing “foetus with absent limbs,” she was 38 weeks by date. She was in early labour with face presentation. On detail examination, it was found that there is an evidence of consanguineous marriage. She had married with her first cousin. There was no relevant past history, exposure to teratogens or history of fever with rash during pregnancy. She had USG done in a private hospital at 30 weeks of gestation. USG showed single live intrauterine pregnancy of gestation age 30 weeks+1 day ± 3 weeks. Evidence of Amelia (upper and lower limbs not appreciated) with evidence of paramedian cleft lip. Liquor is adequate, placenta situated left laterally, effective foetal weight 2160 gms.

The relatives were counselled about poor prognosis of baby. Patient progressed well and delivered a female baby by face presentation. No evidence of postpartum haemorrhage or any tears. Baby was female 2.2 kg by weight, fresh still birth. Evidence of tetramelia, (Figure 2), cleft lip and cleft palate. Figure 1, spine was normal, external genitalia was normal figure 3, placental weight 500 gms normal in morphology. Umbilical cord had a single umbilical artery.
Autopsy did not reveal any internal organ dysmorphism. A babygram was performed after birth figure 4. Mother’s blood sugar were within normal limits. Parents were counselled about low recurrence rate and advised to have an early anomaly scan in future pregnancy.

Discussion

Amelia is a very rare congenital anomaly. Usually, Amelia is associated with multiple organ systems defects including cardiovascular, gastrointestinal, urogenital, neural tube and respiratory defects like lung hypoplasia, absent kidney. The prognosis is very poor in these babies. Most of them die in first year of their life.

Embyologically, the limb buds appear during 3rd week of gestation, upper limb buds appear few days before lower limb bud. Complete absence of limbs occurs prior to 8th week of gestation. Failure to formation of limb buds during early embryogenesis may be secondary to vascular, mechanical stress or teratogenic exposure. It may also be due to genetic mutation.

In this case, there is history of consanguineous marriage (2nd degree). About 20% of Amelia cases can now be traced with probable genetic causes including recessive or dominant mutation, chromosomal aberrations. Where entire set of chromosomes deleted, duplicated or exchanged. Prenatal diagnosis including detailed anomaly scan and amniocentesis in doubtful cases play a major role in this cases.

CONCLUSION

Amelia is an isolated abnormality, when it is associated with other abnormalities, prognosis is poor. Antenatal anomaly scan and genetic counselling are important to make informed decisions regarding terminations.

About the Authors
Dr Varsha Deshmukh, Dr VY Kalyankar is an Associate Professor, Dr KA Yelikar is a Professor and Head of Department, Dr Neha Golechha and Dr PS Deshmukh is a Resident, Department Obstetrics and Gynaecology, Government Medical College, Aurangabad.

REFERENCES
2. Amelia. Marianee FO connor MT (ASCP),MPH Thompson,Gale.
5. Fetal Amelia. a case report Nihal a’s niyami, Ashfaaq Ahmed Shahilla Tanzeem, mohammedabdul.
INTRODUCTION

Laparoscopy offers advantages of better cosmesis, less blood loss, less post-operative pain, shorter hospitalization time and quicker recovery. Though basic laparoscopic procedures are widely practiced, relatively few gynaecologists possess the skills in performing advanced procedures like hysterectomy and myomectomy, not to mention the more complex procedures such as radical hysterectomy and pelvic reconstructive procedure. This is because laparoscopy is hampered by its two-dimensional visualization, counterintuitive hand movements, limited degrees of instrument motion and inferior ergonomic surgeon position. The steep learning curve and longer operating time are major obstacles to the more widespread applications of this minimally invasive technique. The introduction of robotic technology into surgical practice overcomes the limitations of conventional laparoscopy and facilitates the application of these minimally invasive techniques for more advanced and complex procedures.

A BRIEF HISTORY OF SURGICAL ROBOTICS

The concept of surgical robotics was first developed in the late 1980s at the National Aeronautics and Space Administration (NASA) as a means of performing battlefield surgery, enabling surgeons to remotely carry out surgical procedures over a distance. With the involvement of the Stanford Research Institute (subsequently named SRI International), the robotic telemunipulating system was combined with virtual reality (telepresence) systems to provide a tele-robotic surgical system. Two companies began commercializing the robotic surgical systems in the early 1990s, Computer Motion, Inc., and Intuitive Surgical, Inc.

Computer Motion’s system, ZEUS®, was developed from the very beginning as an integrated robotic surgical system. It used the same type of robotic arm as that which was designed to hold a laparoscopic camera (AESOP) and an integrated operating-room control system (HERMES) to create a suite of systems that provided a complete surgical environment. The system was designed for laparoscopic surgery, and in September 2001, the first transatlantic tele-surgery (laparoscopic cholecystectomy) was successfully performed using the ZEUS® Robotic Surgical System and high-speed fibre optic networking. The system received regulatory clearance from the US Food and Drug Administration (FDA) in October 2001. By February 2003, the world’s first tele-robotic surgical service had been established in Ontario, Canada, between St Joseph’s Healthcare Hamilton, a teaching hospital affiliated with McMaster University, and North Bay General Hospital, a community hospital 400 km away. However, manufacturing of the ZEUS® system was discontinued following the acquisition of Computer Motion by Intuitive Surgical in March 2003.

Intuitive Surgical had developed the da Vinci® Surgical System based upon the original telepresence concept and introduced the product in 1999. FDA approval was received for use in general surgical procedures in July 2000, in urology in June 2001 and in gynaecology in April 2005.

USING THE DA VINCI® SURGICAL SYSTEM

The da Vinci® Surgical System (Figure 1) consists of an ergonomically designed surgeon console, a patient-side cart with four interactive robotic arms, the high-performance InSite® Vision System and the proprietary EndoWrist® instruments.

The mobile surgeon console consists of a stereoscopic viewer, two handles and five foot-pedals. The console is operated by the surgeon in a sitting position and controls the four (or in the previous model, three) mobile arms of the robot for intra-abdominal manipulations, camera movements and electrosurgical coagulation. The surgeon

Figure 1. da Vinci S Surgical System, components

© 2009 Intuitive Surgical, Inc.
operates the master controls naturally under the display with hands and wrists supported by the resting panel (Figure 2), and the movements are seamlessly translated into precise, real-time movements of surgical instruments inside the patient. There is no tactile sensation, so the surgeon has to rely on visual feedback. The console can be positioned anywhere inside or outside the operating theatre. However, the FDA regulations require that except in telesurgery, the console be placed in the same room as the operative table.

The two hand controls operate either the camera or the robotic instruments arms, but not both at the same time. Only two of the three robotic instrument arms can be used at any one time; the third arm is inactive and can only be used for tissue holding and retraction. The four foot-pedals are separated in the middle by an additional long and narrow pedal that adjusts the focus of the camera. The outer left foot pedal uses the clutch mechanism to allow repositioning of the hand controls without moving the robotic arms, similar to raising a computer mouse to reposition the mouse without moving the onscreen pointer. The inner left foot pedal provides a navigation control of the camera movement by moving both hand controls in and out, right and left, up and down. The instrument arms remain still while adjusting the camera position. The two pedals on the right control the monopolar and bipolar diathermy.

The image is provided by the Insite® Vision System (Figure 3) through a 12 mm endoscope (0 or 30 degrees) comprising two laparoscopes fused together. The surgeon operates in a sitting position and looks through a binocular three-dimensional (3D) viewing monitor with optimal hand-eye alignment. The image is displayed above the hands of the surgeon so that it gives the surgeon the illusion that the tips of the instruments are an extension of the control grips, thus giving the impression of being immersed at the surgical site. The high-definition image provides improved clarity and detail of tissue planes.

The patient-side cart provides four robotic arms (three in the previous model)—three instrument arms and one camera arm—that execute the surgeon’s commands. The movements of the surgeon are digitalized, scaled at 1⁄1, 1⁄3 or 1⁄5, and transmitted by computer to the intra-abdominal instruments without noticeable delay. Normal physiological hand tremor is also filtered, making it possible to perform very fine and precise tasks. Attached to the robotic arms are a full range of proprietary EndoWrist® instruments. (Figure 4) The extra-abdominal movements of the instruments controlled by the robotic arms have 4 degrees of freedom. The intra-abdominal articulations of the microinstruments at 2 cm from the tip mimic those of the human hand and wrist. They possess 7 degrees of freedom—and, therefore, function more instinctively—and overcome the fulcrum effects seen with conventional laparoscopy.

The patient-side cart is wheeled in between the patient’s legs, and the robotic arms are attached to the metal robotic trocars so that they are integrated together. The robotic instrument is then put through the trocar and mounted onto the robotic arm so that the multiarticulated instrument tips can be operated by the hand controls. The manipulation of the robotic instruments is like operating with the human hand, together with the capability of grasping, retracting, dissecting, cutting, coagulating and suturing.

The da Vinci® Surgical System is a stand-alone, dexterity-enhancing system with a fully articulated ‘wrist’. The surgeon feels ‘immersed’ in a full 3D experience, operating as if the surgical field is immediately in front of him/her. (Figure 5) The hand motions used for the surgical console exactly replicate the motions of open surgery, even though they are converted into laparoscopic fulcrum-effect motions. There is essentially no learning curve in using the system; the surgeon simply begins using the handles as if performing open surgery.

APPLICATIONS OF ROBOTICS IN GYNAECOLOGY

The world’s first robot-assisted gynaecological surgical procedure reported in a human was a tubal re-anastomosis using the ZEUS® Robotic System in 1999.3 The first gynaecological use of the da Vinci® Surgical System was also for a tubal re-anastomosis in 2000,4 and the first series of robot-assisted laparoscopic hysterectomies were reported in 2002.5 Currently, the da Vinci® system is the only commercially available surgical robotic system. The number of reports on robot-assisted gynaecological procedures has increased dramatically following the FDA clearance in 2005, and the technique has been applied to virtually all abdominal and laparoscopic gynaecological procedures. Besides the common gynaecological procedures, other procedures reported include ovarian transposition,6 abdominal cerclage,7,8...
repair of vesico-vaginal fistula\textsuperscript{8,9} and trachelectomy after subtotal hysterectomy.\textsuperscript{10}

**Tubal Re-anastomosis**

Degueldre \textit{et al} reported the first series of laparoscopic tubal re-anastomoses using the da Vinci\textsuperscript{®} Surgical System in eight patients and achieved a patency rate of 93.8\%, with two pregnancies within 4 months.\textsuperscript{4} The mean operating time was 181.5 min. In a retrospective case-control study, Rodgers \textit{et al}\textsuperscript{12} compared 26 cases of robot-assisted tubal anastomosis with 41 cases by outpatient minilaparotomy. Median surgical time for the robot was significantly longer than by minilaparotomy (229 min vs 181 min). There were no differences in the hospitalization time, pregnancy rate and ectopic pregnancy rate. The time to return to work was significantly shorter in the robotic group by approximately 1 week.

Dharia Patel \textit{et al}\textsuperscript{13} compared 18 patients undergoing robot-assisted tubal re-ansstor, with 10 historical cohorts using open microscopic technique. The mean operating time for robotic anastomoses was significantly longer (201 min vs 155 min), but the hospitalization time was significantly shorter (4 h vs 34.7 h) and the recovery time was quicker (11.1 days vs 28.1 days). There was no difference in the pregnancy rates (62.5\% vs 50\%), but the rate of abnormal pregnancy was higher in the robotic group.

The results of robotic tubal re-anastomosis are similar to the open approach, with a longer operating time but a shorter recovery period.

**Hysterectomy**

Diaz-Arrastia \textit{et al}\textsuperscript{5} were the first to report robot-assisted laparoscopic hysterectomy in 16 patients. The operating time was long, ranging from 270 min to 600 min. Average blood loss was 300 mL, and the average hospital stay was 2 days. Conversion was required in one patient because of bleeding. Beste \textit{et al}\textsuperscript{14} reported 11 robot-assisted total laparoscopic hysterectomies (TLH) with a mean operating time of 192 min and a mean hospital stay of 1 day. There was one conversion because of uncontrolled bleeding and one cystotomy. Similarly, Fiorentino \textit{et al}\textsuperscript{15} reported 20 cases of robot-assisted TLH with a mean operating time of 200 min and a mean hospital stay of 2 days. Conversion was required in two cases because of severe adhesions.

Marchal \textit{et al}\textsuperscript{16} reported 30 cases of robot-assisted laparoscopic hysterectomy; the mean operating time was 186 min, excluding the 30 min of robotic setup time. One patient required conversion because of obesity, and there were five minor post-operative complications. Reynolds and Advincula\textsuperscript{17} compared 26 cases of TLH with four cases of laparoscopic supracervical hysterectomy. The mean operating time (including docking time) was 242 min. There was no conversion and four complications, including one case of bowel and bladder injury.

According to unpublished data from the University of Michigan, robot-assisted laparoscopic hysterectomy took an additional 60 min more than conventional laparoscopic hysterectomy.\textsuperscript{17} Kho \textit{et al}\textsuperscript{18} published the largest series of robotic hysterectomies involving 91 patients. The mean docking time was 2.95 min, and the mean console time (surgeon’s time dedicated exclusively to the performance of the surgery) was 73 min. The total operating time was 122 min—14 min shorter when compared to conventional laparoscopic hysterectomy in their institution. There was one enterotomy and six post-operative complications. Nezhat \textit{et al}\textsuperscript{19} reported 27 hysterectomies out of 87 patients undergoing robot-assisted gynaecological surgery. The removal of ovaries at the time of hysterectomy increased the mean operating time from 192 min to 236 min.

The only comparative study reported was published by Payne \textit{et al}.\textsuperscript{20} They compared 100 patients undergoing total laparoscopic hysterectomy with 100 patients undergoing robotic hysterectomy. Overall, the robotic cohort experienced a longer operating time by an average of 27 min. However, the last 25 robotic cases had a shorter oper-
ating time compared with the laparoscopy cohort (78 min vs 92 min). The mean blood loss was significantly less, and the mean length of hospital stay was significantly shorter in the robotic cohort. The number of exploratory laparotomies (0% vs 11%) and rate of intraoperative conversions (4% vs 9%) were both lower in the robotic cohort.

Early experience suggested that robot-assisted laparoscopic hysterectomy takes longer than conventional laparoscopic hysterectomy, partly because of the extra time required for docking. With experience, both the docking time and console time can be reduced, but it may take up to 75 cases before an operating time similar to conventional laparoscopic hysterectomy can be achieved. Also, the robotic assistance allows more hysterectomy to be performed using the laparoscopic approach.

Myomectomy
Senapati and Advincula\(^21\) recently described their technique in robot-assisted laparoscopic myomectomy as a means to overcome the difficulties encountered with hysterotomy enucleation repair and extraction during conventional laparoscopy. Advincula \textit{et al} reported the first series of robot-assisted laparoscopic myomectomies in 35 patients; there were three conversions and one patient was excluded because of adenomyosis.\(^22\) Of the 31 completed cases, the mean number of myomas removed was 1.6 and the mean diameter was 7.9 cm. The mean estimated blood loss was 169 mL, the mean operating time was 230 min and the median length of hospital stay was 1 day. Two patients developed post-operative complications.

In a recent retrospective case-control study, Advincula \textit{et al}\(^23\) compared 29 cases of robot-assisted laparoscopic myomectomy with 29 cases of abdominal myomectomy. The robotic group had a longer operating time (231 min vs 154 min), less blood loss (195 mL vs 364 mL), a lower transfusion rate (0% vs 6.9%), shorter length of hospital stay (1.5 days vs 3.6 days) and lower complication rate (13.8% vs 41.4%). In another retrospective study, comparing 15 robotic-assisted laparoscopic myomectomy with 35 matched-control laparoscopic myomectomy, Nezhat \textit{et al} also reported a significantly longer operating time with the robotic assistance (234 min vs 203 min).\(^24\) However, there were no differences in blood loss, hospitalization time and post-operative complications.

Published data on robot-assisted myomectomy are limited. Despite the advantage of ease in suturing, robot-assisted myomectomy requires significantly longer operating time compared with both the conventional open and laparoscopic approaches.

Sacrocolpopexy
Robot-assisted laparoscopic sacrocolpopexy was first reported by Di Marco \textit{et al} in 2004.\(^25\) The same authors recently reported the accumulated series of 42 cases with a mean follow-up of 36 months.\(^26\) The mean operating time was 3.1 h. All but one patient were discharged from the hospital after an overnight stay. Two patients were converted to an open procedure secondary to dense adhesions. There were two cases of recurrence and two cases of vaginal extrusion of mesh. Daneshgari \textit{et al}\(^27\) reported 12 successful robot-assisted abdominal sacrocolpopexy or sacrouteropexy in 15 patients with symptomatic stages 3 and 4 pelvic organ prolapse. The mean operating time was 317 min, the mean blood loss was 814 mL, and the mean hospital stay was 2.4 days. At a mean follow-up of 3 months, all patients had their prolapse resolved.

In a retrospective review of open laparoscopic and robot-assisted sacrocolpopexy involving five patients in each group, the robot-assisted group had the shortest operating time (robot, 358 min; open, 418 min; laparoscopy, 510 min) and hospital stay (robot, 2 days; open, 3 days; laparoscopic, 3 days).\(^28\) Geller \textit{et al}\(^29\) retrospectively compared 73 robotic and 105 abdominal sacrocolpopexy. When compared with abdominal sacrocolpopexy, the robotic approach was associated with less blood loss (103 mL vs 255 mL), a longer operating time (328 min vs 225 min), shorter length of stay (1.3 days vs 2.7 days) and higher incidence of post-operative fever (4.1% vs 0%). Short-term vaginal vault support at 6 weeks post-operation was similar between the two groups.
Robot-assisted laparoscopic sacrocolpopexy accomplishes a repair identical to that of the open technique, but with a longer operating time, while preserving the benefits of reduced morbidity and hospital stay of the laparoscopic approach. Clearly, a longer follow-up is needed.

**Gynaecological Oncology Surgery**

Despite the well-accepted benefits of laparoscopic surgery for benign gynaecological pathologies, the use of laparoscopy in gynaecological malignancy is still the exception. However, the application of robotics in gynaecology focuses mostly on oncological procedures, and most of the publications so far are in these areas.

Marchal et al.18 evaluated 12 malignant cases (five endometrial adenocarcinomas and seven cervical carcinomas) undergoing robot-assisted laparoscopic hysterectomy in 2005. Radical hysterectomy was performed in some patients, and bilateral pelvic lymphadenectomy was performed in nine cases. The mean operating time was 181 min, and the mean number of pelvic lymph nodes removed was 11. No port-site metastasis or recurrences were found with a mean follow-up of 10 months. In the same year, Reynolds et al.19 reported 28 patients with carcinomas undergoing robot-assisted laparoscopic hysterectomy. The median operating time was 257 min, mean blood loss was 50 mL and median hospital stay was 2 days. Lambaudie et al.21 reported 28 patients with gynaecological malignancies, 21 for cervical cancer, seven for endometrial cancer, one for ovarian cancer and three for cervical dysplasia. Surgical procedures included total hysterectomy, bilateral oophorectomy, and pelvic and/or lomboaortic lymphadenectomy. The median operating time was 180 min, and the median blood loss was 110 mL. No perioperative complications were observed, and the median hospital stay was 3 days.

Early experience suggests that robotic assistance can be safely applied to gynaecological oncology surgery with encouraging short-term outcomes.

**Endometrial Carcinoma Staging**

Boggess compared 43 patients undergoing endometrial staging robotically with 101 patients staged laparoscopically.33 None of the robotic patients were converted to laparotomy compared to 3% in the laparoscopy group. Significantly more lymph nodes were retrieved (30 vs 23), less blood was lost (63 mL vs 142 mL), a shorter operating time was required (163 min vs 213 min), and a shorter hospitalization period was necessary (1 day vs 1.2 days) with the robotic cohort compared with the laparoscopy cohort. DeNardis et al.22 compared the first 56 robot-assisted laparoscopic hysterectomies with 106 total abdominal hysterectomies with aortic and/or pelvic lymphadenectomy for endometrial carcinoma. Three robotic cases (5.4%) were converted to open procedure secondary to intra-operative factors. Compared with laparotomy, the robotic group had a longer mean operating time (177 min vs 79 min), less blood loss (105 mL vs 241 mL), a lower transfusion rate (0% vs 8.5%) and shorter length of stay (1 days vs 3.2 days). The major perioperative complication rate was also lower in the robotic group (3.6% vs 20.8%). There was no difference in the total lymph node count (19 vs 18). Seamon et al.24 reported the outcomes of their first 105 patients with early-stage endometrial carcinoma who underwent robotic hysterectomy and pelvic-aortic lymphadenectomy for comprehensive staging; 13 (12.4%) were converted. Conversion risk increased with body mass index. The average operating time was 242 min, and the mean blood loss was 99 mL. The median number of lymph nodes recovered was 29 (mean of 21 pelvic nodes and nine aortic nodes). The median length of hospital stay was 1 night.

Boggess et al. compared the outcomes of 322 women undergoing endometrial cancer staging by different surgical techniques: 138 by laparotomy, 81 by laparoscopy and 103 by robotic technique.35 The robotic cohort had the highest lymph node yield, the shortest length of hospital stay and the least blood loss. Operating time was longest for laparoscopy (213 min), followed by robotic technique (191 min) and laparotomy (147 min). Post-operative complication rates were lowest for robotic technique (5.9%), followed by laparoscopy (13.6%) and laparotomy (29.7%). Conversion rates for the robotic and laparoscopic groups were comparable. Similarly, Bell et al.36 compared 110 patients who underwent hysterectomy with bilateral salpingo-oophorectomy pelvic and para-aortic lymphadenectomy via robotic assistance (n=40), laparotomy (n=40) and laparoscopy (n=30) for endometrial cancer staging. All cases were performed by a single surgeon at a single institution. The operating time was longer in the robotic cohort.
than in the laparotomy cohort but similar to the laparoscopic cohort (184 min, 109 min and 171 min, respectively). Estimated blood loss was significantly reduced in the robotic cohort (robotic, 166 mL; laparotomy, 316 mL; laparoscopic, 253 mL). The complication rate was lowest in the robotic cohort (7.5%) relative to the laparotomy (27.5%) and laparoscopic cohorts (20%). Return to normal activity for the robotic patients was significantly shorter (24.1 days) than those undergoing laparotomy (52 days) and laparoscopy (31.6 days). Lymph node retrieval did not differ between the three groups (robotic, 17; laparotomy, 14; laparoscopic, 17).

The quality of lymph node staging using robotic assistance may be significantly more extensive than laparotomy and laparoscopy. Though operating time seems to be longer for robotic assistance than for laparotomy, it is equivalent or shorter than for conventional laparoscopy.

**Radical Hysterectomy**

The first robot-assisted radical hysterectomy (Piver type 3) with bilateral pelvic lymph node dissection was reported by Sert and Abeler in 2006. One year later, the same authors reported the result of seven robot-assisted laparoscopic radical hysterectomies and bilateral pelvic lymph node dissection for early cervical carcinoma compared with seven total laparoscopic radical hysterectomies. No conversions were observed in the robotic group. The median operating time was 241 min (console time) in the robotic group and 300 min in the conventional laparoscopic group. Docking time for the robotic system was 25 min. The number of lymph nodes, the parametrial tissue and vaginal cuff size were similar in both groups. Less bleeding (71 mL vs 160 mL) and a shorter hospital stay (4 days vs 8 days) were observed in the robotic group. Kim et al reported 10 successful robotic radical hysterectomies with pelvic lymphadenectomy for stage 1 cervical carcinoma with no complications. The mean operating time was 207 min, the mean docking time was 26 min, and the mean blood loss was 355 mL. The average number of pelvic lymph nodes removed was 27.6. Fanning et al described 20 consecutive robot-assisted type 3 radical hysterectomies for stage 1B–2A cervical carcinoma with no complications. The mean operating time was 207 min, the mean docking time was 26 min, and the mean blood loss was 355 mL. The average number of pelvic lymph nodes removed was 27.6. Fanning et al described 20 consecutive robot-assisted type 3 radical hysterectomies for stage 1B–2A cervical carcinoma. The median operating time was 6.5 h, and the median blood loss was 300 mL. All patients were discharged on the first post-operative day. At median follow-up of 2 years, 90% of patients are alive and disease free.

Magrina compared a total of 27 patients undergoing robotic radical hysterectomy with 31 patients and 35 patients operated by laparoscopy and laparotomy, respectively. The mean operating time for patients undergoing robotic, laparoscopy and laparotomy radical hysterectomy were 190 min, 220 min and 167 min, respectively; the mean blood loss was 133 mL, 208 mL and 444 mL, respectively; the mean number of removed lymph nodes was 25.9, 25.9 and 27, respectively; and the mean length of hospital stay was 1.7 days, 2.4 days and 3.6 days, respectively. There were no significant differences in intra- or post-operative complications among the three groups, and no conversions were required in the robotic or laparoscopic group. None of the patients had experienced recurrence at a mean follow-up of 31.1 months.

Boggess et al compared the outcome of 51 consecutive robot-assisted type 3 radical hysterectomies with 49 historical abdominal radical hysterectomies for early-stage cervical cancer. All of the robotic procedures were completed successfully without any conversion to laparotomy. There were significantly more lymph nodes recovered robotically than abdominally (33.8 vs 23.3) with a shorter operating time (211 min vs 248 min), less blood loss (97 mL vs 417 mL) and a lower transfusion rate (0% vs 8%). The mean hospital stay was 1 day in the robot-treated patients and 3.2 days for the abdominal group. There were no differences in the incidence of post-operative complications (7.8% vs 13.6%). Ko et al compared the short-term surgical outcome of 16 patients undergoing robotic radical hysterectomy with 20 patients undergoing abdominal radical hysterectomy. The mean operating time was 241 min for the robotic group and 249 min for the abdominal group. Less blood loss was observed in the robotic group (70 mL vs 195 mL). The mean hospital stay was 2.2 days for the robotic group and 3.2 days for the abdominal group. There were no significant differences in the incidence of intra-operative complications (8% vs 0%) or post-operative complications (7.6% vs 15.4%).
Radical Trachelectomy
A total of four cases of robot-assisted total laparoscopic radical trachelectomy for early cervical cancer have been reported so far. Operating time ranged from 172 min to 387 min, with a mean of 315.5 min.

Blood loss was less than 200 mL in all cases. There were no complications reported, and all patients had their period return after the operation. The follow-up period was short, and no pregnancy has yet been reported.

CONCLUSION
Laparoscopic surgery has revolutionized the concept of minimally invasive surgery for the last 3 decades. Robot-assisted surgery is one of the latest innovations in the field of minimally invasive surgery, and studies on different surgical procedures have confirmed its feasibility and potential benefits. The surgical robotic system is an enabling technology that allows surgeons the ability to perform laparoscopic procedures in an open surgery environment. Robotic-assisted surgery establishes a straight foot-hand-eye axis that does not exist in either open or laparoscopic surgeries and restores the 3D view that is lost in laparoscopic surgery. With the da Vinci® system, the surgeon is completely immersed in the operative field without peripheral stimulations. The system seems to be most beneficial for complex and prolonged procedures, especially when intra-abdominal microsurgery or manipulations in a narrow or difficult-to-access space are required.

However, the extremely high cost of the robotic system and its instruments almost prohibit its widespread and routine use. The system is large in size, and the robotic arms are relatively cumbersome, which, in pelvic surgery, limits the surgical assistants’ access to the surgical field. A large operating room, therefore, is required to house both the surgical team and the robot. There is no tactile feedback from the system, and the surgeon has to rely on visual cues to assess the tensile strength of tissue and sutures.

Despite these limitations, robotic surgery has a shorter learning curve than conventional laparoscopy. It is envisaged that surgical robots will make minimally invasive surgery easier and more efficient. Difficult laparoscopic interventions may become easier and safer to perform, with decreased fatigue for the surgeon. As stated by Ahlering et al., the great advantage of robot-assisted laparoscopy is the successful transfer of open surgery to a laparoscopic environment, even for laparoscopically ‘naïve’ surgeons, with a significantly shortened learning curve.

REFERENCES

A complete list of references can be obtained upon request to the editor.

About the Author
Dr Yuen is Director of Minimally Invasive Gynaecology, Hong Kong Sanatorium and Hospital; Honorary Clinical Associate Professor, Department of Obstetrics and Gynecology, The Chinese University of Hong Kong; and Honorary Consultant, Department of Obstetrics and Gynaecology, Kwong Wah Hospital, all in Hong Kong SAR, China.