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The Abstracts for the Poster Presentations of this Conference can be found online at: www.web.squ.edu.om/squmj/index.asp

Male Infertility for a Generalist: *What can you offer?*

Dr. Sandro Esteves
Director, ANDROFERT Referral Center for Male Reproduction in Brazil, Campinas, Brazil. E-mail: s.esteves@androfert.com.br

In the era of assisted reproductive techniques (ART), the current challenge is to accommodate established and new treatment modalities that are both cost-effective and evidence-based. The presentation reviews the evolving concepts in male infertility for gynaecologists involved in the care of men and women experiencing difficulty in conceiving. Novel diagnostic testing allows the identification of a significant proportion of patients previously misdiagnosed as having idiopathic or unexplained male infertility. Sperm deoxyribonucleic acid fragmentation and oxidative stress are two of the tests already available in the modern clinical andrology laboratory; their results aid the clinician to define the best management strategy. When treating the male partner by medical and surgical therapy, our focus is not only to improve the couple's chance of having an unassisted pregnancy but also to ameliorate their chances of success with ART. The use of oral antioxidant supplementation is now commonplace, especially given the evidence that antioxidants improve the outcomes of pregnancy and live birth in subfertile couples undergoing ART. Hormonal therapy, including aromatase inhibitors and recombinant human chorionic gonadotropin, are easy-to-use medications intended to treat hypogonadal infertile males. In the surgical field, we have incorporated microsurgery to treat common male diseases such as varicocele; this not only increases the chances of spontaneous conception, but also increases the likelihood of pregnancy with ART. For azoospermic men with obstructive problems, microsurgery offers the best method to reconstruct the reproductive tract. The method also improves the likelihood of retrieving sperm for use with intracytoplasmic sperm injections for azoospermic men with non-treatable conditions, such as those with non-obstructive azoospermia.

Obesity and Male Infertility: *A problem of pandemic proportions*

Dr. Sandro Esteves
Director, ANDROFERT Referral Center for Male Reproduction in Brazil, Campinas, Brazil. E-mail: s.esteves@androfert.com.br

Obesity has achieved pandemic proportions around the world and is considered a major risk factor for male infertility. This presentation examines the top questions involved in obesity-related male infertility. First, it covers why and how obesity causes male infertility; the effects of elevated aromatase activity and secretion of adipose-derived hormones are also discussed, exploring how hormone imbalance can result in secondary hypogonadism and infertility. Second, the presentation describes how to identify patients who are candidates for medical treatment; for example, the testosterone/estradiol (T/E2) ratio is a practical tool to assess aromatase hyperactivity in men. Finally, modern strategies to treat obese men with difficulties in conceiving are presented, including the use of oral third-generation aromatase inhibitors and assisted-conception modalities.

Tailoring Ovarian Stimulation using Biomarkers

Dr. Sandro Esteves
Director, ANDROFERT Referral Center for Male Reproduction in Brazil, Campinas, Brazil. E-mail: s.esteves@androfert.com.br

Biomarkers are useful tools in the context of controlled ovarian stimulation (COS) not only to predict the ovarian response to stimulation but also to define an individualised treatment strategy. Although several biomarkers are available (hormonal, functional and genetic), two of them, anti-Müllerian hormone (AMH) and antral follicle count (AFC), have dominated the clinical scenario in recent years. AMH and AFC are valid biomarkers because they can identify with similar accuracy (~80%) patients with diminished ovarian reserve (DOR) and those at risk of excessive response. AMH is a dimeric glycoprotein exclusively produced by granulosa cells of preantral (primary and secondary) and small antral follicles. Unlike follicle stimulating hormone (FSH) and inhibin B, AMH correlates to the number of follicles at a gonadotropin independent stage, and therefore reflects the pool of remaining follicles in the ovary. In contrast, AFC assesses the cohort of follicles measuring 2–10 mm in the early follicular phase. These follicles are in an early antral phase and easily detected by transvaginal ultrasound, as they contain a small amount of antral fluid. The number of small follicles at the beginning of the cycle represents the actual functional quantitative ovarian reserve as they can be stimulated by exogenous gonadotropins. A gradual decrease in AMH serum levels and number of sonographically-detectable antral follicles occurs with advancing age. AMH has low intra- and inter-cycle variability, making it possible to assess its levels at any day and in a single measurement. Assays to measure AMH are basically enzyme-linked immunosorbent assays (ELISA); recently there has been an evolution from in-house assays to commercial AMH kits such as DSL and Immunotech. However, because of different monoclonal antibodies and different standards, reported

values can differ substantially. DSL and Immunotech are now one company and produce a single kit to measure AMH, named the Beckman-Couter generation II assay, a hybrid of the previous ones. Yet, in-house assays are still used and an international standard does not exist. Importantly, AMH results can be affected by other factors (improper sample handling, storage and transportation). Before applying the AMH cut-off points, we need to ensure that the assay is the same one used in the reference population and to determine whether the reference population matches our own patient's profile. AFC has moderate to low inter-cycle fluctuation and is associated with high intra- and inter-observer reliability in the hands of experienced observers. Nevertheless, difficulties with interpretation and standardisation have been reported due to the different methods of scanning the ovaries and counting the follicles. We should exercise caution in applying AFC cut-off points because AFC reflects a given potential oocyte yield that can be altered by the stimulation strategy. The main clinical utility of AMH and AFC is to help clinicians correctly identify patients at risk of elevated response and duration of response, and therefore individualise COS accordingly. One example is the use of lower starting doses of recombinant human (rec-h) FSH in association with gonadotropin-releasing hormone (GnRH) antagonists in women at risk of excessive response. This approach is shown to sustain pregnancy rates while minimising the ovarian hyperstimulation syndrome (OHSS) risk. In addition, it allows the use of a GnRH-agonist trigger that can virtually eliminate OHSS. Another example is luteinising hormone (LH) supplementation in women screened as having DOR which can increase pregnancy rates by c. 30% by adding rec-hLH to FSH. An increase in androgen production, for its later aromatisation to estrogens by a dose-dependent LH activity at the follicular level, may improve the follicular *milieu* and oocyte quality, which reflect on embryo quality and implantation. Our strategy has been to individualise COS in accordance with AMH levels. Cut-off points of 2.1 and 0.82 ng/mL have been shown to predict excessive and poor response to COS, respectively. In the former, lower starting doses of rec-h FSH (112.5–150 IU) and GnRH antagonists are used. In the latter, 75–150 IU of rec-h LH is added to the rec-h FSH regimen in both GnRH analogue protocols. Approximately 70% of patients with a predicted high or poor response by AMH then achieve a normal response. Moreover, moderate/severe OHSS has been practically eliminated while cancellation rates have been kept around 10% in patients with DOR. In summary, there is now sound evidence to support the clinical use of AMH and AFC before COS. However, given the limitations of the biomarkers, clinicians should interpret cut-off points cautiously when using AMH and AFC as sole predictors of ovarian response. For pregnancy, none of the biomarkers are accurate predictors. Ovarian response to COS reflects the quantitative ovarian reserve; occurrence of pregnancy after *in vitro* fertilisation is related to several factors including qualitative ovarian reserve, gametes/embryo quality and endometrial receptivity.

Fetal Renal Anomalies

Dr. Greg Ryan
Division of Feto-Maternal Medicine, Mount Sinai Hospital, University of Toronto, Canada. E-mail: Toronto-gryan@mtsinai.on.ca

The ultrasound examination of the normal and abnormal fetal urinary tract are presented. Specific renal abnormalities will be reviewed, including hydronephrosis/pyelectasis, renal agenesis, megacystis and lower urinary tract obstruction (LUTO), megaureter and megalouretha, renal dysplasia, echogenic kidneys, ectopic kidneys and polycystic and multicystic kidney disease. We present the options for evaluation and treatment of LUTO, including the results of the recent Percutaneous shunting in Lower Urinary Tract Obstruction (PLUTO) trial.

Intrauterine Transfusion

Dr. Greg Ryan
Division of Feto-Maternal Medicine, Mount Sinai Hospital, University of Toronto, Canada. E-mail: Toronto-gryan@mtsinai.on.ca

The aetiology, evaluation and treatment of fetal anaemia, including rhesus alloimmunisation, parvovirus infection and transplacental haemorrhage are discussed. We present the role of amniocentesis and discuss both non-invasive and invasive testing. The emerging role of cell-free fetal deoxyribonucleic acid (cFF-DNA) is presented and the optimal timing of delivery and neonatal management reviewed.

Complications of Monochorionic (MC) Twins

Dr. Greg Ryan
Division of Feto-Maternal Medicine, Mount Sinai Hospital, University of Toronto, Canada. E-mail: Toronto-gryan@mtsinai.on.ca

The crucial importance of early correct identification of chorionicity is discussed. National guidelines and standards for monitoring MC twins are reviewed. The aetiology of twin-twin transfusion syndrome (TTTS) are reviewed, and the differentiation between TTTS and selective MC intrauterine growth restriction presented. The therapy for TTTS, including selective laser ablation of placental anastomoses, serial amnioreduction and cord occlusion and the short- and long-term development of fetuses undergoing laser for TTTS are discussed.

Essential Ingredients in Developing a Faculty of Medical Educators

Mr. Hani W. Fawzi
South Tyneside NHS Foundation Trust, UK. E-mail: hani.fawzi@sthct.nhs.uk

This presentation discusses the development of medical education as an emerging interest. It will outline the 12 roles of a medical teacher within a tool that would support development of a faculty of medical educators. It will attempt to define professional development and then highlight how to develop professionally as an individual in the first instance and then how the institute should develop. The conscious competence model and styles of learning, as well as the experiential learning cycle, are discussed in the context of assessing oneself and one's abilities. The presentation will highlight the need for personal development as an individual and have the ripple effect of opportunities to identify gaps in the institute.

Morbid Obesity and Pregnancy

Dr. Lovina Machado
Department of Obstetrics & Gynaecology, Sultan Qaboos University Hospital, Muscat, Oman. E-mail: Lovina1857@gmail.com

The prevalence of obesity has reached pandemic proportions worldwide. In 2005, WHO estimated that worldwide 1.6 billion adults were overweight and 400 million adults obese. Current predictions are that by 2015 a total of 2.3 billion adults will be overweight and 700 million obese. The incidence of obesity among pregnant women is presently estimated at between 18.5% and 38.3%. Adiposity has

a damaging effect on every aspect of female reproductive life. Morbid obesity in pregnancy is linked to a myriad of adverse pregnancy outcomes. During the antepartum period, there is an increased risk of miscarriages, hypertensive disorders, gestational diabetes mellitus, venous thromboembolism, iatrogenic preterm delivery and respiratory complications. Intrapartum risks include an increased incidence of induction of labour, slow progression of labour, higher Caesarean section rates, postpartum haemorrhage and infection. From the fetal perspective, congenital malformations, large-for-gestational-age infants, stillbirths and shoulder dystocia occur with increased frequency. Such newborns are at increased risk of developing metabolic syndrome later in life. Operative delivery in morbidly obese parturients is technically and logistically challenging for the anaesthetist and obstetricians. It is no surprise, then, that maternal and neonatal morbidity and mortality are increasing. The presentation focuses on the adverse impact of morbid obesity on the continuum of pregnancy with special reference to Oman and suggests methods to optimise obstetric outcomes in these women. A concerted effort must be made to promote lifestyle changes and adequate exercise across society, especially among children and young women.

The Role of Laparoscopy in Gynaecological Oncology

Dr. Stephen Dobbs
Belfast City Hospital, UK. E-mail: stephendobbs@yahoo.com

Laparoscopy was developed in the late 1960s. Since then, the applications for laparoscopy have increased dramatically with the development of modern laparoscopic systems. Today in gynaecological oncology, laparoscopic surgery (LS) plays a key role in providing a comprehensive surgical service. LS provides the benefits of shorter inpatient stays, reduced blood loss, reduced postoperative morbidity and equable surgical results compared to open surgery. On the other hand, LS requires a long and steep learning curve for the surgeon and longer operating times compared to open procedures. A recent survey estimated that only 20% of gynaecological oncology operations in the UK were performed laparoscopically. This may in part be due to a lack of mentoring and a deficiency of advanced laparoscopic courses. In gynaecological oncology, LS can be used for diagnostic assessment, the staging of local and advanced disease and assessment for debulking surgery. LS can be utilised in most treatments for endometrial cancer including hysterectomy, pelvic and para-aortic nodal dissection. In cervical cancer, LS is used for radical hysterectomy, radical trachelectomy and para-aortic nodal dissection in locally advanced cancer. There is also a role for LS in the assessment/treatment of isolated recurrent cancers. Recent developments include robotic surgery and 3-D LS. The future of gynaecological oncology will be centred around the provision of LS.

Cervical Screening and the Role of the Human Papilloma Virus (HPV) Vaccine

Dr. Stephen Dobbs
Belfast City Hospital, UK. E-mail: stephendobbs@yahoo.com

Cervical cancer remains the commonest cause of death from gynaecological cancer worldwide. It is accepted that HPV infection is the major risk factor for cervical cancer. There are over 120 different subtypes of HPV and around 20 high-risk types are responsible for over 99% of all cervical cancers. Of the high-risk group, types 16 and 18 are the most prevalent, causing over 70% of cervical cancers. Up to 80% of sexually active women will be infected with HPV at some time during their lives. Exposure is reduced with barrier contraception. Currently, in the UK all 12- to 13-year-old girls are offered HPV vaccinations through a national immunisation programme introduced in 2008. Vaccination offers protection against HPV types 16 and 18. The vaccines are over 98% effective in preventing cervical abnormalities associated with these types. HPV testing is currently utilised in the cervical screening programme in two ways. In women with low grade changes (borderline or mild dyskaryosis) the presence of high-risk HPV indicates a higher risk of occult high-grade cervical intraepithelial neoplasia (CIN) and these patients are referred for colposcopy. Conversely, those patients with mild abnormalities and who are HPV-negative have a negligible risk of cancer and can return to normal screening frequency. The HPV testing is used as a 'test of cure' in women who have undergone treatment for CIN at the six-month post-treatment smear. Those patients who are cytology negative and HPV-negative can return to the normal three-yearly screening, whereas those patients who are HPV-positive are at a higher risk of residual/recurrent CIN and need referral to colposcopy. Despite the advances in HPV immunisation and testing, women still need to attend regular cervical cytology to detect other HPV causes of cervical cancer and pre-cancer. Worldwide, strategies are needed to implement cheap and effective methods of screening for cervical cancer, utilising our knowledge and understanding of the disease process.

Hysterectomy for Enlarged Uteri: *Total laparoscopic or minimally invasive vaginal hysterectomy?*

Dr. Mohamed Mabrouk
Senior Consultant, Gynecologic Oncology & Minimally Invasive Pelvic Surgery Unit, Sacred Heart Hospital, Negrar, Verona, Italy; Lecturer in Obstetrics and Gynecology, Faculty of Medicine, Alexandria University, Egypt. E-mail: mohamed.mabrouk@sacrocuore.it

Hysterectomy remains the second most common gynaecological operation, after Caesarean section. The three main approaches for hysterectomy are the abdominal, vaginal and laparoscopic routes. For the large-sized uterus with benign pathologies, the abdominal approach is the most commonly used, while uterine dimensions are considered a limitation for the laparoscopic and vaginal routes. Laparoscopic hysterectomy (LH) for large uteri has been the subject of controversy. The vaginal approach for hysterectomy (VH) is becoming widely utilised for non-prolapsed uteri with benign uterine diseases. Some studies support the choice of vaginal hysterectomy as a valid alternative to the abdominal hysterectomy for enlarged uteri. Recently, there has been a quest for efficient and fast haemostatic techniques that can safely replace conventional suture ligature in this approach. Bipolar vessel sealing systems (BVSS) are haemostatic control devices that can seal blood vessels up to 7 mm in diameter by denaturing collagen and elastin within the vessel wall and in the surrounding connective tissue. The use of variable BVSS has been evaluated in gynaecological surgery and there is a general consensus about the effectiveness and safety of their use in vaginal hysterectomy, with varying degrees of difficulty.

Endometriosis: *Get to know your enemy better*

Dr. Mohamed Mabrouk
Senior Consultant, Gynecologic Oncology & Minimally Invasive Pelvic Surgery Unit, Sacred Heart Hospital, Negrar, Verona, Italy; Lecturer in Obstetrics and Gynecology, Faculty of Medicine, Alexandria University, Egypt. E-mail: mohamed.mabrouk@sacrocuore.it

Endometriosis prevalence rates in the general population are unknown, because a definitive diagnosis is established only at laparoscopy and diagnostic accuracy depends on the surgeon's skills and experience in the disease. However, based on community prevalence

estimates of symptoms, endometriosis probably affects 10% of all and 30%–50% of symptomatic premenopausal women. This represents 176 million women worldwide. Endometriosis may develop anywhere within the pelvis and on other extra-pelvic sites. Macroscopically, three forms of endometriosis are described: (1) superficial (peritoneal); (2) ovarian endometriosis (endometriotic cyst of the ovary or ovarian endometrioma); (3) and deep infiltrating endometriosis (DIE). In DIE, endometriotic nodules extend >5 mm under the peritoneal surface and may involve the utero-sacral ligaments, vagina, bowel, bladder or ureters. The depth of infiltration is related to the type and severity of symptoms. Where present, endometriotic tissues can be associated with extensive fibrosis and adhesion formation, causing marked distortion of pelvic anatomy. The disease severity can be assessed by simply describing the findings at surgery or quantitatively, using a classification system such as the one developed by the American Society for Reproductive Medicine in 1997. However, there is no correlation between such classification systems and the type or severity of pain symptoms.

Pregnancy-Associated Breast Cancer

Dr. Ikram Burney
Department of Medical Oncology, Sultan Qaboos University Hospital, Muscat, Oman. E-mail: ikramburney@hotmail.com

Pregnancy-associated cancer (PAC) is defined as a cancer diagnosed during pregnancy or within one year post-partum. PAC constitutes 0.07–0.1% of all cancers. Breast cancer is the most common PAC, followed by carcinoma of the cervix, lymphoma, leukaemia, melanoma and ovarian cancer. The incidence of breast cancer during pregnancy is reported to be 1:3,000–1:10,000 pregnancies. Between 0.2–3.8% of all breast cancers occur coincidentally with pregnancy. The prevalence of pregnancy-associated breast cancer (PABC) has been shown to increase with maternal age, especially in the developed countries. The treatment of breast cancer is multi-modal and often involves surgery, sometimes with radiotherapy, systemic chemotherapy and hormone therapy. PABC is unusual; many surgeons, obstetricians and oncologists have only a limited, if any, experience in the management of cancer during pregnancy. The average obstetrician would see 2–3 cases in a 40-year career. For several years, treatment of breast cancer and the continuation of pregnancy were considered mutually exclusive. However, with recent experience in the use of cytotoxic chemotherapy in the second and the third trimester, it is possible to continue the pregnancy and the systemic treatment. However, monoclonal antibodies are contraindicated and exposure to radiation should be minimised and kept to less than 10cGy. Stage for stage, the prognosis of PABC has been shown to be the same as for cancer not associated with pregnancy. The fetal outcome is dependent mainly on the term pregnancy, rather than exposure to surgery and chemotherapy while *in utero*. The risk of recurrence does not increase with subsequent pregnancies. While there is a plethora of data on the incidence, management and outcomes of PABC from the developed world, there are very little data from developing countries, especially in the Middle East, where the demographic features of breast cancer are different. For example, the mean age at the time of diagnosis of breast cancer in Oman is 47 years and almost one-third of patients are in the child-bearing (less than 40 years) age. On the other hand, the fertility rate is high, and the mean number of pregnancies in the country is more than seven. It is plausible to think therefore that PABC may be even more common in developing countries. The incidence, pattern of presentations, the outcomes of breast cancer and of pregnancy of women treated for PABC from Oman are presented.

Use of Ultrasound to Improve Care of Diabetes in Pregnancy

Prof. Badreldeen I. Ahmed
Feto-Maternal Medicine Centre, Doha, Qatar, and Professor of Obstetrics, Weill Cornell Medical College, Doha, Qatar. E-mail: profbadreldeen@hotmail.com

Diabetes mellitus (DM) is one of the most serious non-communicable diseases (NCD). It has been described as a 'slow-motion disaster' and it is associated with morbidity, mortality and long-term disability. Two out of three deaths globally are attributable to NCD. This presentation explores the means by which ultrasound can be helpful to the clinician managing a diabetic pregnancy. The following issues are addressed: (1) Screening for vasculopathy in the first trimester; (2) Deviation in fetal weight; (3) Diagnosis of congenital malformation, and (4) How to monitor diabetic pregnant patients. Regarding fetal weight, the importance and limitations of the transabdominal diameter formula to estimate fetal weight will be discussed. We discuss the role of 3-D technology in improving weight estimation in diabetic pregnancy. Fractional limb volume which is based on 3-D technology and its role in diagnosis of small-for-gestational age infants is also addressed. Congenital anomalies are more common among diabetic pregnant patients. The cardiovascular system is the system most likely to be affected; however, diagnosis of fetal cardiac defect is very challenging. We discuss the role of new techniques of spatial-temporal image correlation (STIC). STIC is an automated device incorporated into the ultrasound probe and has the capacity to perform a slow sweep to acquire a single 3-D volume. This acquired volume is composed of a great number of 2-D frames and can be analysed and reanalysed as required to demonstrate all the required cardiac views. It also provides the examiner with the ability to review all images in a looped cine sequence. It is very critical in this new technology to acquire adequate volume. The monitoring of fetus growth and well-being in a diabetic pregnant patient can be difficult. The standard Doppler test of the umblical and middle cerebral arteries is not very reliable and can give false reassurance. Fetal acidaemia correlates significantly with changes in the *ductus* venous and hepatic artery blood flow. This relationship is explored in this presentation.

Regulating Fertility Treatment

Dr. Maha Al-Khaduri
Senior Consultant, Department of Obstetrics & Gynaecology, Sultan Qaboos University Hospital, Muscat, Oman. E-mail: m.khaduri@gmail.com

Treatment for infertile couples has become widely available in many countries. There are several regulatory bodies around the world for fertility treatments. In the Middle East there are fewer countries with fertility treatment regulations. In the Arabian Gulf, the two countries that have implemented fertility treatment regulations are Saudi Arabia and the United Arab Emirates. As infertility treatment advances in Oman, there is a greater need to have a mechanism to regulate it. The principal tasks of this regulatory body are to license and monitor clinics that carry out *in vitro* fertilisation, insemination, pre-implantation genetic diagnosis, human embryo research and the storage of gametes (eggs and sperm) and embryos, in order to ensure that human embryos are used responsibly and that infertile patients are not exploited at a vulnerable time.

Is there Evidence for Cerclage in Twins and Higher-Order Pregnancies?

Dr. Nihal Al-Riyami
Departments of Obstetrics & Gynaecology and Maternal Fetal Medicine, Sultan Qaboos University Hospital, Muscat, Oman. E-mail: drriyami@hotmail.com

Multiple gestation is increasing due to the expanded use of fertility treatments and older maternal age. It is associated with higher

rates of almost every potential complication of pregnancy, with the exceptions of post-term pregnancy and macrosomia. The most serious risk is spontaneous preterm delivery, which plays a major role in the increased perinatal mortality and short-term and long-term morbidity observed in these infants. Preterm delivery is caused by several risk factors including multiple gestation. In theory, the identification of risk factors for preterm delivery before conception or in early pregnancy provides an opportunity for intervention to prevent this complication. However, many preterm births occur among women with no risk factors and few interventions have been proven to prolong pregnancy in women at risk. These interventions include progesterone treatment modalities and cervical cerclage. The use of cervical cerclage to prevent preterm delivery in multiple gestation is controversial. The presentation includes the evidence of using cerclage in twins and higher-order pregnancies.

Progesterone Therapy for Prevention of Preterm Labour

Dr. Tamima Al-Dughaishi
Department of Obstetrics & Gynaecology, Sultan Qaboos University Hospital, Muscat, Oman. E-mail: aldughaishit@hotmail.com

Preterm birth remains a major clinical problem. The prevalence in the USA increased from 6.3% of live births in 1981–1983 to 6.6% in 1991 and 7.6% in 2000, although a large portion of this increase is related to multiple pregnancies. There are very few interventions that improve the prognosis of preterm labour. The use of antenatal corticosteroids has been consistently shown to have such an effect, but most studies on tocolysis, with the exception of one recent report on nitroglycerin, have very limited clinical applications. Almost 50 years ago, Csapo *et al*. promoted the progesterone see-saw theory, which is that high progesterone levels prevent uterine contractions and low levels facilitate such contractions. This is one reason for the use of progesterone therapy in early pregnancy and the use of RU486, a progesterone antagonist, to induce abortions. It seems that the hormonal control of contractions and labour in humans is more complex than in other animals and that progesterone may have a more limited role than in animal models. Recently several studies on the use of progesterone to prevent preterm labour have been published. The purpose of this presentation is to review these studies and outline the current role for the use of progesterone for this indication.

Breast Cancer Status in Oman

Dr. Adil Alajmi
Consultant Breast Reconstructive Surgeon, Department of Surgery, Sultan Qaboos University Hospital, Muscat, Oman. E-mail: adilalajmi@hotmail.com

Breast cancer is the cancer with the highest incidence among females in Oman. Females with breast cancer in Oman tend to be younger than their Western counterparts. The majority of patients present with advanced stage cancer and the tumours display aggressive features. This presentations describes the clinico-pathological features of the disease in Oman with an analysis of prognostic factors and survival rates. A small propor¬tion of patients have breast conserving surgery; a relatively small number receive preoperative chemotherapy despite the locally advanced nature of disease. The overall survival and disease-free survival rates are favourable compared to other Asian and Arab Countries. The presentation explains in part the inferior survival figures compared to white-American and European females. The following measures are strongly recommended to improve morbidity and mortality: increasing the awareness of breast cancer; the introduction of breast screening programmes; a multi-disciplinary approach to breast cancer management, and research on the molecular biology and genetic aspects of breast cancer to explore further the characteristics of breast cancer in Oman.

Breast Lumps, Bumps and Pain

Dr. Sukhpal Sawhney
Department of Radiology & Molecular Imaging, Sultan Qaboos University Hospital, Muscat, Oman. E-mail: sukh@squ.edu.om

Breast disease in women encompasses a wide variety of benign and malignant disorders. The most common breast problems are lumps, bumps, pain and nipple discharge. The majority of these women have benign breast disease. Irrespective of the type of breast problem, the goal of imaging is to rule out cancer and address the patient's symptoms. During the last decade, there have been tremendous advances in breast imaging. With the introduction of newer technologies, today's breast care specialists are faced with challenges; not only because they have to understand the relative merits and weaknesses of each imaging approach, but also because they have to choose the right imaging modality for each particular patient. Currently, mammography is the gold standard for the detection of breast cancer. Despite recent technical advances and the introduction of digital imaging, mammography may miss as many as 10–25% of cancers, especially in dense breasts. Newer modalities, such as digital tomosynthesis, ultrasound scans and magnetic resonance imaging help to increase cancer detection and to characterise benign and malignant disease, thus decreasing the need to perform invasive procedures and allaying patient anxiety. The presentation will familiarise clinicians with the different aspects of breast disease and their appearances in commonly-used imaging modalities. Further, the Breast Imaging-Reporting and Data System (BIRADS) classification will be introduced to enable a more comprehensive understanding of breast radiology reports. The pitfalls and benefits of advanced imaging modalities will be described.

Thromboprophylaxis in High-Risk Pregnancy as applied to the Middle East

Dr. Salam Alkindi
Department of Haematology, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman. E-mail: sskindi@yahoo.com

Physiologically, pregnancy is a hypercoagulable state. Thromboembolic disease has remained one of the leading major causes of morbidity and mortality in pregnancy and the early post-partum period. Obvious risk factors include a family history of thromboembolic disease, immobilisation, increased maternal age, obesity, sickle cell disease, smoking, assisted-reproduction techniques, twins, intrauterine growth restriction and the presence of a heritable or acquired predisposition to thrombosis. There are different scoring systems adapted to assess the risk of thrombosis, including age, weight, previous thrombosis and the presence of thrombophilia. Thromboembolic prophylaxis is a necessity for at-risk patients; however, the guidelines need to be evidence-based and take into consideration the above mentioned risk factors. Also there needs to be a balance between the risk-benefit evaluation and the resources available to monitor these patients. National as well as regional data are emerging and may help Omani obstetricians to tailor their therapy to the needs of pregnant women in this country.