Foreword

The 3rd Biennial Meeting of Pendidikan Intensif Fertilitas dan Embriologi (PIFE) from the Ikatan Alumni Andrologi Fakultas Kedokteran Universitas Airlangga (IAA FKUA) was held on Aula Fakultas Kedokteran Universitas Airlangga in Surabaya, November 22-24th 2019. This conference had the vision to upgrade knowledge in how to manage a good Artificial Reproductive Technology (ART) lab, provide excellent services, improve skills, understand the regulations and standardize. Besides that discussion in supporting matters such as ethics, law, technology, and finance.

PIFE started since 2018 is expected to be IAA FKUA's routine activity to be able to bring together health professionals, academics, and industry. IAA FKUA cooperates with various other medical associations such as PERSANDI, POGI, PERFTRI, HIFERI, and ISHE. PIFE also cooperates with multiple universities and health institutions in Indonesia and abroad. This partnership is to improve cooperation and better services especially for Indonesian people in need.

The conference includes opening keynote speakers from Kementerian Kesehatan of Republik Indonesia, invited speaker, symposium, workshop, oral and free papers as well as discussions on many related topics in the meet of the expert. In the end, hopefully, all the participants can enjoy the PIFE 2019 and also the city of Surabaya.

dr. Suwasiedo Henry Wibowo, MARS., Sp.And(K)
Head of PIFE and IAA FK UA
ABSTRACT

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Bali Medical Journal

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Sanglah General Hospital
Bali - Indonesia

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Bali - Indonesia

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suwiyoga@unud.ac.id
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ABSTRACT

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Bali - Indonesia

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AmerthaManuaba@gmail.com / Amertha_Manuaba@unud.ac.id
Biomedicine Magister Program, Udayana University, Indonesia

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(Scopus ID), (Google Scholar), (Orcid ID), (Researcher ID), (Researchgate)
Lecturer of Clinical Pathology Department, Faculty of Medicine Udayana University, Indonesia.

**dr. Agha Bhargah, SKed.**
(Scopus ID), (Google Scholar), (Orcid ID), (Researchgate), (Researcher)
Faculty of Medicine Udayana University, Indonesia.

**Editorial inquiries to be addressed to:** editor@balimedicaljournal.org
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Updates on sperm cryopreservation

Aucky Hinting, Agustinus
1Andrology Specialist Medical Education Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
2Ferina - Center for Reproductive Medicine, Surabaya, Indonesia

Abstract
The decline in male fertility is alarming today. Sperm cryopreservation allows us to preserve male fertility before their fertility decline. This method may be also helpful for ensuring sperm availability at the time of assisted reproductive technology procedure. Slow freezing is one of the most commonly used protocols for human sperm cryopreservation. Programmable freezing provides more strict control of freezing rates through the use of automated programmable freezers. The rapid freezing and vitrification technique gives us a more simple protocol.

Several studies agree to the idea of freezing prepared sperm samples, so sperm selection techniques are performed prior to cryopreservation to improve survival after thawing. However, several studies propose performing sperm preparation after thawing as a protocol that leads to an increase in the total amount of spermatozoa with good motility.

Intracytoplasmic sperm injection has allowed spermatozoa obtained during surgical sperm retrieval could be preserved. Testicular spermatozoa are preferably frozen in suspension which received after mechanical or enzymatic treatment procedures.

During the past decade, many researchers attempted to invent new technologies in particular for freezing of individual or limited numbers of human spermatozoa in men with severe male factor infertility. They applied several biological and non-biological carriers including human, mouse and hamster zona pellucida, agarose and alginate microspheres, ICSI pipettes, cryoloops, mini-straws, microdroplets, and many other carriers for cryopreservation of several small aliquots or even small numbers of sperm.

Keywords: Sperm, Cryopreservation, Methods, Carriers

Dyspareunia and vaginismus as hidden causes of infertility

Wimpie Pangkahila
1Department of Andrology and Sexology Center for Study of Anti-Aging Medicine Medical Faculty, Universitas Udayana, Bali, Indonesia

Abstract
One of the causes of infertility is sexual dysfunction, either in male or female. Female Sexual Dysfunctions (FSD) that related to infertility are dyspareunia and vaginismus. These sexual dysfunctions result in inhibition of sexual intercourse. Finally, pregnancy is inhibited. Therefore these are called hidden causes of infertility.

Dyspareunia means recurrent or persistent genital pain associated with sexual intercourse include pain only at sexual entry (penetration), pain with every penetration, including putting in a tampon, deep pain during thrusting, burning pain or aching pain, and throbbing pain, lasting hours after intercourse. One of the frequent causes of dyspareunia is vaginismus. Vaginismus is a recurrent or persistent involuntary spasm of the muscularure of the outer third of the vagina that interferes with vaginal penetration, which causes personal distress. In vaginismus, any forms of penetration into the vagina are impossible, for example, finger, tampon, and sexual intercourse.

The worldwide incidence of vaginismus is about 1–7%, with considering that disorder is cross-cultural. In clinical settings, the incidence may be as high as 5–17%. Treatments of vaginismus include sex counselling, the use of dilators, recently use of Botox (clinical trial). In case there are diseases or pathologic conditions in the genital area, these must be treated first.

Keywords: Dyspareunia, Vaginismus, Infertility

Sexual dysfunction and its relevancy to infertility

Hudi Winarso
1School of Medicine, Universitas Ciputra, Surabaya, Indonesia

Abstract
Globally, 8–12% of couples experience difficulty conceiving a child. Although assisted reproduction technology (ART) provides the possibility of achieving pregnancy, almost 40% of people undergoing ART still cannot conceive. Infertility has been described as a stressor and a life crisis for individuals or couples, which results in a lower quality of life and marital conflicts.

Healthy sexuality is central to psychological well-being and quality of life. Sexuality is not just the state of being physically able to perform a sex act or to conceive a child, but as an integral component of human life with multidimensional content. The relationship between infertility and sexuality were discussed using the following themes. (1) How is sexual self-concept in infertile individual and their partners? (2) Does infertility harm the sexual relationship of infertile couples? (3) Is sexual function affected by infertility?

All dimensions of sexual function (desire, arousal, lubrication, orgasm, satisfaction) were lower in infertile women as compared to fertile women. Sexuality can be significantly affected by infertility and its treatment. The reciprocal relations between sexual self-concept, sexual relationship and sexual function in the context of infertility, necessary for further research examine. Moreover, the sexuality of infertile subjects might be influenced by their partner’s reaction.

Keywords: Infertility, Sexual dysfunction, Sexual relationship

ABSTRACT

ABSTRACT

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Splash pregnancy: is it effective for managing infertility in vaginismus?

Johannes Soedjono¹
¹School of Medicine, Universitas Hang Tuah, Surabaya, Indonesia

Abstract
There is a complex association between sexual behaviour and infertility. Problems in sexual intercourse have an important cause and effect relationship with infertility in a large proportion of infertile couples. Therefore, infertility examination should include an evaluation of the couple’s sexual behaviour. The highest chance of conception is achieved through sexual intercourse on multiple occasions during the fertile period. Vaginismus is a sexual disorder of the female partner that precludes the intravaginal deposition of sperm. Therefore, it can be the result of not conceiving. The data shows that the incidence of vaginismus varies from 2% in the general population to 47% in sex therapy clinics.

The critical point is that often the couple’s first complaint to the practitioner is an inability to conceive, not the vaginismus itself. Consequently, commencement is neither the only treatment goal nor sex therapy the only method. There are couples, however, with vaginismus, who may use the expensive assisted reproductive technologies to bypass regular intercourse and conceive without ever consummating the sexual relationship. In some instances, however, self-insemination or ejaculating the semen as close as possible to the vaginal opening without any actual penetration, which is known as splash pregnancy, like a bedroom procedure, is a treatment option to enable the couple to reach their fertility goal.

There is no study about the success rate of splash pregnancy unless some case reports. It is important to underline that splash pregnancy or ART is not the treatment for vaginismus itself.

Keywords: Splash Pregnancy, Sexual Intercourse, Infertility

Evidence-based medicine of Intracytoplasmic Morphologically Selected Sperm Injection (IMSI)

Tri Bowo Hasmoro¹
¹Mitra Keluarga Bekasi Barat Hospital, West Java, Indonesia

Abstract
The presence of large vacuoles in the sperm head has been associated with acrosome status, chromatin condensation, DNA fragmentation and sperm aneuploidy, but these reports remain contradictory. The nature and the impact of small vacuoles are less understood. The large vacuoles are detected and deselected in conventional intracytoplasmic sperm injection (ICSI) as well. However, the detection of subtle small vacuoles depends on the resolving power of the optical system and may impact oocyte fertilization, embryo development and implantation.

Clinical Expertise in Intracytoplasmic morphologically selected sperm injection (IMSI) depends on morphologically selected sperm criteria advanced equipment, technical experience and skill. IMSI is selected at higher magnification, whereas the sperm can be evaluated for fine integrity of its nucleus and the injection of a normal spermatozoon with a vacuole-free head can be assured. Several comparative studies have indicated that the use of high-magnification sperm selection was associated with both higher pregnancy and delivery rates, whereas also lower miscarriage rates were observed. However, still to date randomized, well-powered studies to confirm these findings are scarce and show conflicting results. IMSI seems to be a time-consuming procedure, depending on the degree of sperm morphology impairment and the number of oocytes to be injected. The cut-off for the fine morphology of the individual spermatozoon to be selected or deselected by the procedure remains unclear. The lack of proof and understanding of its benefit does not justify its routine clinical application at present. Hence, the most relevant indications for IMSI remain to be determined.

In several studies, IMSI procedure: significantly improves embryo morphology, increase day 3 embryo quality, provides more viable blastocysts without chromosomal abnormalities, higher blastocyst development rate, increase the chances of having genetically normal blastocysts. But, increase implantation and pregnancy rates, tendency to reduce miscarriage rates, and maintain an equal aneuploidy rate as compared with ICSI is still unclear and debatable.

Keywords: IMSI, ICSI, Sperm Selection

The efficiency of hyaluronan based for sperm selection

Agustinus¹,²
¹Andrology Specialist Medical Education Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
²Ferina - Center for Reproductive Medicine, Surabaya, Indonesia

Abstract
The selection of sperm with good genomic integrity is an important consideration for improving intracytoplasmic sperm injection (ICSI) outcomes. Sperm are commonly selected by their motility and morphology. Hyaluronic Acid (HA) has a role as “physiologic selector” for spermatozoa.

Developmentally mature sperm were found to bind to HA gels similarly to the binding between sperm and zona pellucida. There are two ready-to-use systems for hyaluronic acid-ICSI (HA-ICSI), HA culture dish (PICSI) and viscous medium containing HA (Sperm Slow). Several shreds of evidence suggest selection based on hyaluronic acid-binding may be beneficial. Injection of HA-bound spermatozoa significantly improves embryo quality and implantation. Preliminary data also reported a higher live birth rate in PICSI group in comparison with the control. However, some studies revealed that HA–ICSI does not significantly improve live birth rates.

Some studies suggest that HA–ICSI may have little or no effect on live birth or clinical pregnancy, but may reduce miscarriage. More studies are needed to determine the benefit of HA–ICSI. The broader use of HA–ICSI, therefore, is not recommended at present.

Keywords: Sperm selection, Hyaluronic acid–ICSI, outcomes
Psychological loads in the infertile couple

Dina Elizabeth Sinaga¹
¹Psychiatrist, Kalawa Atei Mental Hospital, Central Kalimantan Province, Indonesia

Abstract

The condition of infertility is a biopsychosocial phenomenon, which means it covers biological, psychological, environmental problems, including personal relations, so that infertility is not just a matter of organ dysfunction, but a complex condition, and can pose a threat to psychological states and emotional distress.

In the United States, infertile couples become one of the most neglected and silent minority groups. It is important to understand what psychological burden is experienced by infertile couples because this can affect how the couple faces and finds solutions to overcome the condition of infertility. Psychological conditions that are not handled properly from the beginning can affect the success of infertility therapy that will be done. So, the primary purpose is to understand the psychological burden felt by infertile couples.

The conclusion is the psychological burden felt by infertile men is different from the burden felt by infertile women, Cultural factors and parenting can influence the psychological burden on infertile couple, and Understanding the psychological burden felt by infertile couples can help the therapist in dealing with partner infertility conditions.

Keywords: Infertile, Psychological Burden

The best way to tell the bad news in infertility case

Agustina Konginan¹
¹Psychiatric Department, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya, Indonesia

Abstract

One of the difficult tasks of doctors is when they have to deliver bad news relating to the patient’s condition, especially regarding the diagnosis and prognosis of the patient. Even more related to infertility cases.

We must be aware of the fact that delivering bad news to infertile couples means that we will interfere in an already vulnerable process. The infertility crisis is very complex and challenging to resolve, repeatedly receiving bad news during infertility investigations and treatments, even long before seeking medical help, the couple has received monthly bad news in the form of unwanted menstruation. How patients respond to the news as bad news may be coincidental sexual disorder in the infertile couple. The incidence of sexual disorders in infertility depends on many factors, including the attitude of the clinician to sexuality, the degree of reluctance by the patient or clinician to discuss the problem and a detailed sexual history. However, the data show that sexual problems are an important factor in the management of infertility. Studies analyzing the association between infertility and psychological functions have used one of the following models. One of them is psychological infertility model, which asserts the role of an existing psychopathology on the etiology of infertility and the other model claims that psychological problems arise as a result of infertility. Recently direct correlation of mental stress with infertility problems and its impact on the outcomes of infertility treatment has been demonstrated.

Non-organic sexual disorder treatment is holistic, involves patient centered approach and clinicians are expected to consciously adopt the patient's perspective and respect the ideas, feelings, expectations and values of their patients.

Keywords: Infertility, Non-Organic Sexual Disorders, Treatment

How to treat non-organic sexual disorders related to infertility

Soetjipto¹
¹Psychiatric Department, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya, Indonesia

Abstract

According to criteria of World Health Organization (WHO), infertility is defined as inability of a sexually active, non-contraception couple to achieve conception after 12 months of regular sexual intercourse. The culprit factor cannot be identified in nearly 10-20% of infertile couples. Failure to become pregnant after 12 months despite regular unprotected sexual intercourse is called primary infertility.

The relationship between sexuality and infertility is complex. Infertility may cause sexual disorders, sexual disorder may masquerade as infertility or there may be coincidental sexual disorder in the infertile couple. The incidence of sexual disorders in infertility depends on many factors, including the attitude of the clinician to sexuality, the degree of reluctance by the patient or clinician to discuss the problem and a detailed sexual history. However, the data show that sexual problems are an important factor in the management of infertility. Studies analyzing the association between infertility and psychological functions have used one of the following models. One of them is psychological infertility model, which asserts the role of an existing psychopathology on the etiology of infertility and the other model claims that psychological problems arise as a result of infertility. Recently direct correlation of mental stress with infertility problems and its impact on the outcomes of infertility treatment has been demonstrated.

Non-organic sexual disorder treatment is holistic, involves patient centered approach and clinicians are expected to consciously adopt the patient's perspective and respect the ideas, feelings, expectations and values of their patients.

Keywords: Infertility, Non-Organic Sexual Disorders, Treatment

Development of assisted reproduction technology in Indonesia

Dicky Moch Rizal¹
¹Department of Physiology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Association of Andrologist (PERSANDI), Yogyakarta, Indonesia

Abstract

Indonesia is one of the countries in the world that has practiced Assisted Reproductive Technology or better known as IVF technology in handling the problem of wanting children. History of the first IVF through the birth of Lois Brown through the IVF program with Dr. Patrick Steptoe became a milestone in world history. Next Indonesia followed through the birth of Nugraha Karyadi as a baby born through the first IVF program in Indonesia.

The Perfitri organization that houses the paradigm that operates in the field of TRB was born in 2009 in association with POGI for obgyn doctors engaged in the field of TRB and PERSANDI for andrology doctors. Furthermore, ISHE was born which overshadowed the embryological staff from both doctors and non-doctors in 2016/2017. The seriousness of the government in overseeing the TRB
program in Indonesia is very evident in the issuance of the PERMENKES no.39 in 2010 was then updated with PERMENKES no. 43 in 2015. However, various problems that arise along with the development of TRB in Indonesia still exist including the uneven distribution of TRB services in Indonesia, concentrated in Java, the problem of labor or human resources that is still small and requires high costs to produce reliable human resources, facilities in the form of tools and building facilities that are classified as expensive and thus require high investment, expensive medicines which all cause the community to assume that IVF services are only for the rich without access for people with a weak economy to enjoy this program.

Finally, the availability of competent medical and laboratory personnel continues to be developed through various training, among others organized by PIFE (Fertility and Endocrinology Intensive Education) as well as from ISHE. Keywords: Assisted Reproductive Technology, Indonesia, Development

**Treatment of gonadotrophic hormone in male infertility at the recent**

Dicky Moch Rizal

1Department of Physiology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Association of Andrologist (PERSANDI), Yogyakarta, Indonesia

**Abstract**

Male infertility is the problem of sperm production and quality related with the couple attempt to have a child. As a causal factor, male infertility contributes about 30-50% in infertility problem. Many factors cause the decreasing sperm production and quality, such as hormonal disturbance, inflammation of reproductive organ, trauma, genetics and immunology. Hormonal disturbance may be caused by low level of gonadotrophic hormone production (FSH and LH), hypogonadism, hyperprolactinemia, hyper estradiol, thyroid hormone imbalance or hypercortisolemia.

The role of gonadotrophic hormone is very important for spermatogenesis and also has contribution to make of decreasing of sperm quality and embryo quality. Many kinds of research treatment model using gonadotrophic. Injection of LH only, FSH only and combination of LH-FSH is used with the certain purpose especially to increase of sperm count or motility. Menotrophin as a combination of FSH and LH in small dose show the benefit effect of therapy. Also using of LH recombinant and FSH recombinant compare with urine LH or FSH. The duration of the treatment was vary in the research.

The common indication of gonadotrophic treatment usually is sperm abnormality with low of FSH and LH but know it also was used for idioopathic factor, sperm abnormal with normal of gonadotrophic level. The research show that clinical use of FSH for normogonadotrophic have beneficial effect to improve sperm abnormality.

**Keywords:** Male Infertility, Sperm Abnormality, Gonadotrophic Hormone

**Gene cause of male infertility**

Achmad Zulfa Juniarto

1Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia

**Abstract**

As one of the most important physiological processes, reproduction leads to the production of new organisms and the perpetuation of the species. Effective reproduction requires a normal development of the sex organs which is strongly influenced by genetic composition and gonadal development.

Genetic sex, indicated by karyotype, is the chromosomal basis of sex determination and defines the sex-determination system. In man, the normal number of chromosomes is 46, 44 of which are autosomes while 2 distinct chromosomes are acknowledged as the sex chromosomes which define the sex of an organism and various sex-related characteristics. An individual normally has a single pair of sex chromosomes in each cell where males have one Y chromosome and one X chromosome while females have two X chromosomes, making females the homogametic sex. However, other karyotypes do exist. Nowadays, it is generally accepted that the X and Y chromosomes have evolved from and ancestral pair of homologous autosomes. The Y chromosome is considered to have evolved sometime between 170 and 310 million years ago when a sex-determining locus arose on one of the proto-sex chromosomes which led to the accumulation of other sex-specific alleles nearby. This resulted in deletion of large parts of the Y chromosome, with the shrinking of this chromosome.

The process of an undifferentiated gonad passing through a complicated series of steps to develop into a testis or an ovary is called the differentiation of the gonad and depends on the sex-determining pathway succeeding in determining the sex. Numerous investigators have tried to discover genes that are vital in sex determination and differentiation.

**Keywords:** Male Infertility, Genetic

**PLC-zeta: the role, impact and treatment**

Widjiati

1Veterinary Medicine, Campus C, Universitas Airlangga, Surabaya, Indonesia

**Abstract**

PLC-zeta (PLCC) is a protein in spermatozoa that has an important role to increase the concentration of intracellular Calcium (Ca 2+) in cytoplasm in order to stimulate ovum activation and to initiate early embryonic growth. Early release and increase of Ca 2+ oscillation started soon after spermatozoa-ovum fusion, so that series of bio-chemical and morphological processes took place by preparing ovum for early embryo cleavage.

PLCCatalyzed hydrolysis of phosphatidylinositol 4,5-biphosphate that triggered cytochrome Ca 2+ oscillation solc by signaling pathway of inositol 1,4,5-trisphosphate.PLCC, made interaction with phospholipid membrane, phosphatidyserine (PS) to form C2-Ca 2+-phosphatidyserine complex by binding this affinity domain to phospholipidmembrane; phosphatidylinositol 3-phosphate (P13P) and phosphatidylinositol 5-phosphate (P15P), which increased enzymatic activities. Interaction of PLCC–P13P and–P15P enabled to regulate function of PLCCin ovum regarding molecular mechanism in process of ovum activation. Ca 2+ signals during fertilization involved ligand of spermatozoa surface which made interaction with receptor of plasma membrane in ovum.
Receptor membrane paired with ligand which was bound to ovum PLC which stimulated IP3 produced and released Ca^{2+}. Several researches stated that ovum that was injected with PLC-zeta coped with failure that induced Ca^{2+} release. Myc-PLCζ-nanoinjection at different concentration was more effective to produce Ca^{2+} oscillation, increase IVF success and embryo growth at two-cell stage or morula and blastocyst. Keywords: PLCζ, Ovum Activation, Ca^{2+}, Ovum Spermatoza Fusion, Fertilization

How to choose the best culture media and prevent from the contaminant?

Zakiyatul Faizah1
1Department of Biomedical Science, School of Medicine, Universitas Airlangga, Surabaya, Indonesia

Abstract
Culture media is an important thing in the culture system of in vitro fertilization. Development IVF media culture from the past to the future have been rapid and impressive. In the past IVF media culture made in house, nowadays numerous commercial media available around the world.

IVF culture medium component develops from simple salt to complex component including pyruvate, amino acid, vitamins, nutrients, and growth factors. IVF media culture bioassay need to ensure quality and safety. Mouse Embryo Assay (MEA) and Human Sperm Survival Assay (HSSA) were typical assays for quality control. Culture condition plays an important role to optimize culture media such as temperature, PH, air quality including VOC and the way to handling the culture media. The culture media must be stored well, aliquot and prepare under laminar airflow to prevent contaminant — oocyte experience outside the body since opu procedure. Temperature, PH, air quality, time to handling, incubator, VOC, culture media, ICSI procedure, culture time were things caused embryo stress.

Manage that factors can reduce embryo stress, optimize culture systems and result in best embryo development. Keywords: Culture Media, IVF, Contaminant

Which to choose: time lapse or mini incubators?

Ita Fauzia Hanoum1
1Permata Hati Infertility Clinic, Dr. Sardjito General Hospital, Yogyakarta, Indonesia

Abstract
Incubators, in an IVF laboratory play crucial role to maintain stable and appropriate environment in order accommodate optimal embryogenesis. Incubators exist in many types with varying capabilities and different methods in regulating their internal environment. Important variables should be taken into consideration when selecting incubators; recovery/stabilization of temperature, gas atmosphere and humidity, as well as understanding various approaches utilized by each incubator type to regulate the variables.

While patient’s volume and workflow are important factors in optimizing incubator function, other important consideration in selecting incubators, are cleaning and sterilization to reduce chance of contamination. Quality control (QC) maybe another important variable to be considered. Several options features of QC provided in incubator’s system to assist routine monitoring. Existing reports indicate smaller incubator/bench top incubators provide faster recovery for environmental variables. Currently time lapse imaging system has been rapidly take attention in the IVF laboratory culture system, while yet such technology in the routine clinical IVF should be reviewed further. Time lapse imaging as close incubation system, offer consistent observation without opening incubator’s door which is detrimental to embryogenesis.

The following presentation will discuss factors to be considered in selecting incubators of IVF laboratory. Management of utilization is paramount in appropriate functioning and optimizing incubators performance. Keywords: Time-Lapse, Mini Incubator, IVF

Antisperm antibody examination: is it needed in the management of infertility?

Indra Gusti Mansur1
1Biomedicine Program, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Abstract
Pregnancy is a complex process that required female’s immune tolerance toward sperms, embryo, and fetus. Therefore, infertility, recurrent abortions and fetal growth problems might be caused by a failure of the female’s immune system to build up an immunotolerance during the reproductive phase. Before conception, the female is expected to develop a proper immunotolerance toward her husband’s sperms. One of the parameters that can be used to identify it is through a Anti-sperm Antibody (ASA) test of the female’s serum tested in infertile couple.

In normal condition, the ASA titer is 1:64 or 1:128 using HAS-aT method test (Husband’s Sperm Auto Agglutination Test). Based on research worldwide, 12-15% of couples are infertile. Among them, 25% are considered ‘unexplained infertility’. A previous study in 2010 concluded that 60% of infertile couple have an ASA titer of 1:16384 or more. From their next research, it has been proved meaningfully that pregnancy can happens with an ASA titer of 1:1024 and below, in ‘unexplained infertility couple’ group.

As a conclusion, ASA test is needed in infertile couples when through standard test for male and female trying to conceive fail to show an abnormality but never been pregnant or fail to conceive or when through recurrent spontaneous abortions during the first trimester and also for ‘unexplained infertility’ group. Keywords: Antisperm Antibody, Infertile Couples
ABSTRACT

Sperm DNA fragmentation: should it to be routinely?

Yukhi Kurniawan1,2
1Department of Andrology & Sexology, Faculty of Medicine, Universitas Udayana, Bali, Indonesia
2WIN Centre for Reproductive Medicine Puri Hospital, Bali, Indonesia

Abstract
Male factor contributed approximately 20% of infertile couples, with an additional 30% to 40% secondary to both male and female factors. Thus, male factor infertility is present in approximately 50% of all infertile couples.

Conventional semen analysis describes some features of sperm function, but does not fully address functional sperm competence. Evaluation of male factor infertility remains routine semen analysis including seminal volume, pH, sperm concentration, motility, and morphology. However, approximately 15% of patients with male factor infertility have a normal semen analysis and a definitive diagnosis of male infertility often cannot be made as a result of routine semen analysis. Over the past decades, an increasing number of infertile couples seek medical assistance by assisted reproductive technology (ART).

DFI, known as sperm DNA fragmentation index, was established to evaluate sperm chromatin integrity, and has gained increasing application for its diagnostic capabilities of male fertility potential and pregnancy outcome.

Keywords: Sperm DNA Fragmentation, Male Infertility, ART

Total antioxidant capacity: is it applicable in Indonesia?

Taufiqurrachman N1
1Faculty of Medicine, Universitas Sultan Agung Islamic, Semarang, Indonesia

Abstract
Physiologically reactive oxygen species (ROS) is needed to induce capacitation, acrosome reaction, hyperactivity, and sperm-oocyte fusion. However, the increment of ROS level outweigh oxidant capacity in seminal plasma induces oxidative stress (OS), infertility, and sperm damage characterized by DNA fragmentation, reduced sperm motility, decrease in sperm fertilizing ability, and defective sperm membrane integrity. There are growing evidences that OS hitherto constitutes a leading cause of infertility in male. The historical studies showed that increase in ROS has associated with up to 40% of male infertility. Contemporary studies also suggested that the increase in ROS concentration was ensued in 30%-80% of male infertility.

Based on these data, antioxidant treatment to counterbalance OS implication in male fertility has been developed. Nevertheless, the results of antioxidant treatment in infertile male remain inconsistent. It might be due to uncertainty the oxidant and antioxidant status in seminal plasma of infertile male ahead of treatment. In elevated or normal of oxidant-antioxidant status, antioxidant treatment is not suggested, instead cause sperm damage mediated by pathological antioxidant abundant. Otherwise in reduced antioxidant concentration, supplementation is needed to replenish antioxidant level. Therefore, measurement to determine oxidant-antioxidant status before treatment is recommended in order to get appropriate indication.

Measurement of oxidant-antioxidant status can be run by several methods directly or indirectly; however, some of the prevalent ones include chemiluminescence, total antioxidant capacity (TAC), and oxidation reduction potential (ORP) test. In this presentation, will be delivered the assessment of TAC in seminal plasma of infertile male, is it applicable in Indonesia?

Keywords: Oxidative Stress, TAC, Infertility

Total quality and risk management of art clinic

Arief Boediono1,2, Pitra Rahmawati1, Ivan R. Sini1
1Morula IVF, Jakarta, Indonesia
2Faculty of Veterinary Medicine, Institut Pertanian Bogor (IPB), Bogor, Indonesia

Abstract
Quality of care is a multi-dimensional concept, encompassing treatment efficacy and impact on health and welfare of both patients and offspring. In addition, the concept of quality includes the cost in financial and human terms of achieving the desired outcome. To optimize quality using the Total Quality Management approach, it is necessary to map all processes, to thoroughly describe all procedures involved in the processes, and to define performance targets for each procedure.

There should also be an assessment of how the procedures might fail; the impact of the failure and the possible cause(s) of such failure. It is then necessary to ensure that the clinic and its staff have the requisite skills, knowledge and equipment to achieve the performance targets. Finally, the performance must be monitored, both with regard to absolute measures as well as trends. In all instances where performance falls outside the set limits or is trending towards a non-conformance with targets, corrective actions must be taken and documented. As a first step in the corrective action it must be clearly established what has occurred. Then there must be an analysis of possible causes of the failure with a view to identifying deficiencies in the system that allowed the failure to occur. Quality management is a larger concept than quality assurance and quality control, which are subsets of quality management.

There is growing recognition that quality management not only ensures improvement of the clinical aspects of the operations of a clinic, but also leads to improved financial performance and increased staff satisfaction.

Keywords: Quality, Assurance, Control, Risk, Management

Successful way in ovarian stimulation and ovum pick-up

Hendy Hendarto1
1Department of Obstetrics and Gynecology, Medical Faculty of Universitas Airlangga, Dr. Sutomo General Academic Hospital, Surabaya, Indonesia

Abstract
Ovarian stimulation is one step in the procedure of in vitro fertilization (IVF) which is used to stimulate the maturation of oocytes, and is aimed at the collection of obtaining some oocytes with good quality in one IVF cycle. A good understanding of the physiology of ovulation and folliculogenesis cycles is crucial in order to achieve successful ovarian stimulation.

The growth of some ovarian follicles is a key step in achieving IVF success, while avoiding excessive stimulation that can lead to uncontrolled ovarian
response. The main modalities of ovarian stimulation medications are the administration of exogenous gonadotropin (FSH), GnRH agonist or antagonist, and the final oocyte maturation regimen. FSH threshold and window concepts becomes a guide by rational increasing the serum FSH concentration maintained above the threshold. Supraphysiological dose of FSH is indispensable in the ovarian stimulation procedure, but less dosages will result in a slight amount of oocytes when ovum pick-up (OPU). The final oocyte maturation is the re-process of meiosis oocytes which is the transition from metaphase I to phase II metaphase to become fertilizable oocytes. Ovum Pick-Up is usually done under anesthesia and with transvaginal sonography (TVS) guidelines after 36 hours of trigger medication. OPU began by probing aspiration needles into the target ovaries with the “first come-first serve” technique of follicles. The aim of the OPU procedure is to take an adequate amount of egg in order to produce healthy pregnancy rather than accumulate a lot of oocytes for the freezing.

Keywords: Ovarian Stimulation, FSH Threshold, Oocyte, Ovum Pick-Up

Endometrial receptivity assay: clinical and stem cell application

Marinda Suzanta

1 Bocah Indonesia Fertility Clinic, Tangerang, Banten, Indonesia

Abstract

Successful implantation depends on the quality of the blastocyst and the development of the embryo and cannot be separated from receptive endometrium. Communication must exist between the blastocyst and the endometrium which is receptive to be mediated by hormones that work locally and growth factors. The short period of maximum receptivity of the endometrium is called the implantation window, characterized by coordination of biochemical and morphological change events that can be used as markers of endometrial receptivity.

The morphological marker of endometrial receptivity such as: 1. Morphological markers (pinopoda, lumen closure); 2. Biochemical markers (endometrial adhesion molecules; integrins, caderin, selectin, and superfamily immunoglobulin but which are often used and useful as markers are integrins and selectin); 3. Endometrial cytokines (Some of the most important ones are Leukemia inhibitory factor (LIF), interleukin-6, interleukin-11, and coloni-stimulating factor); 4. Growth Factors (Growth Factors; Epidermal Growth Factors; Endometrial Growth Factors: heparin binding-epidermal growth factor (HB-EGF) and Insulin like growth factor binding protein-1 (IGFBP-1); Transforming growth factor-β (TGF -β); TGF β1, TGF β2, and TGF β; 5. Endometrial immune markers; and 6. Transcription factors (Hoxa genes 10, 11, 7 and Kruppel like factors). Integrin is the best marker of endometrial receptivity during the implantation window.

Research shows that stem cells improve endometrial prescriptions by increasing the expression of αvβ3 integrin endometrial tissue in mice of POF (premature ovarian failure) models, stem cells produce growth factors such as VEGF, transforming growth factors-β and placental growth factors. It is suspected that the stems cells expels germ progenitor cells into the circulation then will “homing” to the target organ. Other changes that may occur in the microenvironment in the endometrium.

Keywords: Endometrial Receptivity, Stem Cells

Blastocoele fluid biopsy for Preimplantation Genetic Diagnosis/Screening (PGD-PGS)

Mai tra Djiang Wen

1 Department of Andrology & Embryology, Bocah Indonesia Fertility Clinic, Tangerang, Banten, Indonesia

Abstract

Maternal age has strong correlation with embryo quality, aneuploidy rate and thus reduced fertilization rate. Preimplantation genetic diagnosis/screening (PGD/PGS) as a part of IVF technology has improved as part of the answer to the problem. This technology aims to help to choose best transferrable embryos, decreasing implantation failure, reducing miscarriage during in vitro fertilization (IVF) cycles, and minimize the risks of genetic disease transfer. Recently, several noninvasive methods have been found advanced the conventional invasive biopsy. In this review, we will discuss the new biopsy methods for PGD/PGS and the potential applications in IVF clinics.

Blastocyst stage is preferable, with higher DNA amounts and less mosaicism rate. Blastocoele fluid present in the blastocyst cavity, approximately 120-144 hours post fertilization. Spent culture media collected after embryo in culture till blastocyst stage will contain extruded DNA and proteins from the embryo. Blastocyst fluid collection also can be done to collect samples for PGD/PGS as potential source of biomarkers for embryo viability. Both types of sample taken, if successful, would be less intrusive than conventional embryo biopsy. Success rate of amplification with culture media was 96.4% in one of the study. Although amount of embryonic DNA in the culture medium (CM) is higher than blastocyst fluid (CM), contamination rate with cumulus/granulosa cells, polar body, degenerated cells and possibly sperm is higher.

Fluid biopsy, whether blastocentesis or spent culture media analysis, are new updates in collecting samples for PGD/S use. However, future studies are important to validate the potential use and clinical results of these procedures.

Keywords: Biopsy, Blastocyst, Preimplantation Genetic, Diagnosis, Screening

The growth hormone supplementation in women with poor ovarian response in In Vitro Fertilization (IVF) program

Hartanto B juayuji

1 Division of Reproductive Endocrinology & Infertility, Department of Obstetrics & Gynecology, Faculty of Medicine, Universitas Padjadjaran, Dr. Hasan Sadikin Hospital, Bandung, Indonesia

Abstract

Approximately 9-24% of women undergoing controlled ovarian stimulation in invitro fertilization program will show poor response. This group of patients might need specific treatment to obtain appropriate oocyte yields. Growth hormone (GH) has been proposed to enhance the ovarian response in poor responders’ group.

GH stimulates insulin-like growth factor-I (IGF-I), which plays an important role in ovarian folliculogenesis. Receptors for IGF-I have been found in the oocyte, granulosa and theca cells, suggesting their role in augmenting gonadotrophin actions. Stimulation of IGF-I will lead to the increase in gonadotrophin receptors density, better estrogen secretion and oocyte maturation. From one meta-analysis, GH supplementation in poor responders women correlate with higher
ABSTRACT

The role of luteal phase support in endometriosis

Budi Santoso¹, Muhammad Yohanes Ardianta Widyangrumaha¹
¹Department of Obstetrics & Gynecology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

Abstract
The luteal phase is the period between ovulation and menstruation or the establishment of pregnancy. In IVF, aspirations aimed to gain oocytes and contributes to the removal of a few or more granulose cells in the follicle. It triggers a decrease in the function of the corpus luteum and have a pivotal role in endometriosis.

Endometriosis is a common cause of pelvic pain and is experienced by 10% of women of reproductive age. Some literature states that some women with endometriosis develop resistance to progesterone. The molecular basis may be related to the overall decrease in the number of Progesterone Receptor (PR), and even the absence of Progesterone B (PR-B) Receptors. In addition, the expression of progesterone receptors in endometrial cells is stimulated by an increase in estrogen in the follicular phase through the Estrogen-α (ER-α) receptor, which leads to an increase in progesterone response during the luteal phase. In contrast, ER-α expression in endometrial cells is inhibited by progesterone through progesterone receptors. Progesterone triggers the expression of 17β-hydroxysteroid dehydrogenase-2 (17-HSD-2) and sulfotransferase, which convert estradiol to estrone sulfate. In endometriotic tissue, progesterone does not induce expression (17-HSD-2) in the epithelium due to a defect in the stromal cells. It is caused by the absence of PR-B and low levels of Progesterone A (PR-A) receptors in endometriotic tissue. The final result is a lack of E2 metabolism in endometriosis which causes high local concentrations.

This situation raises the question whether endometriosis will reduce the effectiveness of therapy especially the provision of progesterone as a luteal phase support. The effect of luteal phase support in women with endometriosis and its cellular mechanisms are still in controversy.

Keywords: Luteal Phase, Endometriosis, Progesterone

Aromatase inhibitor for infertile men: experience in Indonesia

Tiara Kirana¹
¹Bocah Indonesia Fertility Clinic, Tangerang, Banten, Indonesia

Abstract
In males, androgens are produced both by the adrenal glands and the testes, whereas estrogen is mostly synthesized locally in peripheral tissues from the local aromatization of circulating androgens.

Estradiol, normally considered a female hormone, appears to play a significant role in men in a variety of physiologic functions, such as bone metabolism, cardiovascular health, and testicular function. As such, estradiol has been targeted by male reproductive and sexual medicine specialists to help treat conditions such as infertility and hypogonadism.

In a certain subset of infertile men, particularly those with hypogonadism, or those who have a low serum testosterone to estradiol ratio, there is some evidence suggesting that SERMs and AIs can reverse the low serum testosterone levels or the testosterone to estradiol imbalance and occasionally improve any associated infertile or sub fertile state.

Keywords: Aromatase Inhibitor, Infertility, Hypogonadism

Selective Estrogen Receptor Modulators (SERMs) for fertility

Maria Paulina Budiyandini Dyah Pramesti¹
¹Andrology Specialist Medical Education Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Abstract
Selective Estrogen Receptor Modulators (SERMs) is group of compounds that modulate testosterone and estradiol levels to treat infertility and hypogonadism due to hormonal imbalance as well.

Clomiphene cytrate (CC) is a preparat of SERMs that works as an estrogen antagonist at the pituitary gland level, which stimulates the realease of LH and FSH and affects steroidogenic and spermatogenic function of the testes. There are two isoforms of CC: zuclomiphen or cisclomiphen and enlomiphen or transclomiphen. Zuclomiphen is a mixture of isomer, have both antagonist and agonist effect, on the other hand enlomiphen is a pure estrogen antagonist, which can improve spermatogenesis better.

Administration of SERMs increases the probability of getting sperm from ejaculate and from testes or epididymis with sperm retrieval technique, wich ultimately changes the status from infertile to subfertile man.

Keywords: SERMs, Infertility, Hypogonadism

‘Nikah siri’: can we treat this infertile couple?

Doddy Moesbadianto Soebadi1
1Department of Urology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya, Indonesia

Abstract
In Islamic religion, if the “nikah siri” is done by the pillars and the conditions under Islamic law are fulfilled, then the marriage is still considered valid. However, in Indonesian law, this marriage is not recorded in the KUA (Office of Religion Affair).

Based on the issue above, it is advisable to marry formally under Indonesian law. It is for legality in the eyes of state law. Here clearly, this marriage is against the Indonesian law, because there is no marriage certificate and official letter relating to the legality of marriage.

For medical practitioners working under medical ethics and under the laws of Indonesia, the treatment of infertility itself is ethically justified, but if for the purpose of obtaining active offspring for the “nikah siri” couple should not be done, because it will bring great moral and legal impacts for both the spouse and the medical practitioner.

Keywords: Nikah Siri, Infertile Couple, Treat

Sex selection: a brief review

Silvia Werdhy Lestari1,2
1Medical Biology Department, Faculty of Medicine, University Indonesia, Jakarta, Indonesia
2Andrology Specialist Program, Medical Faculty of Universitas Airlangga, Dr. Soetomo Hospital, Surabaya, Indonesia

Abstract
Sex selection is defined as the practice of using medical techniques in selecting the sex of offspring. The objective of this work was to systematically review and discuss articles dealing with the subject of selecting sperm or embryo for gender selection.

A search on PubMed database using general term such as gender/sex selection, separating sperm, selecting embryo, unused embryo and prenatal genetic diagnosis (PGD). The practices of “sex selection” could be done pre/post fertilization, such as separating sperm and selecting embryos. Separating sperm was performed by flowcytometry that differentiate between X- and Y-chromosome-bearing sperm, while selecting embryo was performed by blastomere biopsy to determine sex. Even though was done worldwide for some medical and non-medical reasons, sex selection raises ethical, legal and social issues. In selecting embryo, the unused embryo could be discarded or donate for research.

According to Indonesian law, sex selection is allowed for the second child by separating sperm method only, not selecting embryo. So that, sex selection could perform in limited condition, particularly in Indonesia.

Keywords: Gender Selection, Separating Sperm, Selecting Embryo, Unused Embryo, PGD

Preserve embryo in couples with special condition: separated, deceased, surplus, and others

Suwaspodo Henry Wibowo1
1Andrologist, Husada Utama Hospital, Surabaya, Indonesia

Abstract
The increasing number of IVF clinics in the world and in Indonesia, where currently in Indonesia there are already more than 32 units. There is a single embryo transfer trend that makes more and more embryos stored. In certain cases, such as husband died, divorced, what about the embryo? May it be transferred, or how is it stored? In Indonesia, the mention above has been regulated in a Government Regulation.

As we know in the Hippocratic’s oath no. 6 (I will respect every human life since conception), which means we should not treat the embryo carelessly. PP No. 61 of 2014, concerning Reproductive Health, Article 40 states: Reproductive services must be within legal marriage, implanted in the womb of the wife from which the ovum originates, not contrary to religious norms. Article 41 Patients are able/able to give consent for medical action (informed consent) Article 42, in order to obtain reproductive services, must be preceded by counseling and informed consent, including further management of excess embryos, counseling before and after service. Article 43, The excess of the embryo must be stored until the birth of the baby, the storage of the excess of the embryo can be extended, the excess of the embryo is prohibited from being planted in the mother’s womb if the father of the embryo dies or is divorced.

Destruction of excess embryos can be done by means of burial, cremation or other actions according to the wishes of the husband and wife owner of the embryo.

Keywords: Preserve Embryo, Special Condition, Separated, Deceased, Surplus

Cryopreservation in very low number sperm count

Rossy Sintya Marthasari1, Agustinus1, Supardi1,2, Aucky Hinting1,2
1Andrology and Sexology Specialist Programme, Biology Department, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
2Ferina Center for Reproductive Medicine, Surabaya, Indonesia
3Medical Doctor, Soetomo Hospital, Surabaya, Indonesia

Abstract
Background: The aim of this study was to analyze the motility rate and viability in subgroups of cryopreserved spermatozoa from oligozoospermic patient. This study also aimed to analyze the minimum amount spermatozoa to be cryopreserved but still had a good quality to be used.

Methods: This was an experimental pretest posttest group design study and it was a model of a very low sperm obtained from oligozoospermic patients. Thirteen patients were included in this study. All samples were examined for motility, viability and concentration of spermatozoa according to Laboratory Manual for the Examination and Processing of Human Sperm 5th edition. There were 4 groups such as: group of 71-100 sperm, group of 31-70 sperm, group 11-30 sperm and group 1-10 sperm. Moving spermatozoa were aspirated into pippete in certain amount and put into 2 µl microdrops of freezing medium. All
ABSTRACT

Sperm telomere length examination in infertile male: a literature review

I Gusti Ngurah Pramesemara
Department of Andrology and Sexology, Faculty of Medicine, Universitas Udayana, Bali, Indonesia

Abstract
At present, the condition of infertility has become a health problem which is quite unusual in the community. Not only affects physical status alone, but it also affects psychologically. Facts on the ground find an increase in the number of married couples who experience fertility problems. Nearly 15% of couples of childbearing age experience infertility and it is estimated that male factors cause almost half.

The cornerstone to identify the condition of male fertility is through the examination of semen analysis according to WHO guidelines in 2010. However, these standard and routine procedures have not been able to explain the causes of male infertility in full. So, it is necessary to develop additional examination of semen analysis with new markers. One promising new marker is a molecular examination to determine telomere length of sperm. Through searching several literatures, there is a correlation between the length of the sperm telomeres and the abnormalities of the semen parameters. In contrast to somatic cells, sperm telomeres are elongated in older men. However, the reduced length of the sperm telomeres causes fertility disorders in men.

Some studies show that the length of the sperm telomeres is related to the normal development of the embryo and the incidence of fertilization. The length of sperm telomeres by the quantitative PCR method can be a new marker of choice for the examination of spermatogenesis, which is useful for evaluating male reproductive age well.

Keywords: Sperm Telomere Length, Male Infertility

The incidence of irregular hormonal imbalance complications in women hormonal contraception use with limited resources on the JKN era in Woha Health Center of Bima

Priska Yunita Bachtiar
General Practitioner, Woha Health Center of Bima, West Nusa Tenggara, Indonesia

Abstract
Background: Hormonal contraception is commonly used worldwide because of the high effectiveness to prevent pregnancy. There are some complications of hormonal contraception that frequently happen, such as abnormal uterine bleeding, weight gain, sexual disfunction, vomit, nausea, headache and stomach cramp. According to World Health Statistics in 2005-2015, Indonesia has exceeded the average number of contraception used in ASEAN after Vietnam, Kamboja and Thailand. The severe complication of contraception is caused by hormonal contraception used, according to RISKESDAS 2018.

Method: The purpose of this study is to determine the incidence of irregular hormonal imbalance symptoms in women hormonal contraception use with limited resources on JKN era in Woha Health Center of Bima, during January to

Keywords: Sperm Telomere Length, Male Infertility
June 2019. This research used descriptive design data retrieval by observation and recording of medical records. The sample is 120, which took by using purposive sampling technique depend on inclusion criteria.

**Result:** The research showed that 90% of women with hormonal contraception and 10% women with non-hormonal contraception of the sample, have irregular hormonal imbalance complication.

**Conclusion:** The complication in hormonal contraception used are caused by unstable hormone function in the body.

**Keywords:** Hormonal Contraception, Irregular Hormonal Imbalance, Complication.

### Varicocelectomy as the treatment reduces sperm DNA damage: a literature review

**Putu Agoes Adi Ariestyawan**
General Practitioner, Medical Faculty of Universitas Udayana, Bali, Indonesia

**Abstract**

**Background:** A varicocele were identified by the presence of tortuous and dilated veins in the spermatic cord. This condition, as an important cause of male infertility, occurs in nearly 40% of infertile males, can impair sperm quality and fertility via various oxidative stress mechanism. Alterations in nuclear and mitochondrial sperm DNA because of imbalance between excessive reactive oxygen species production and antioxidant protection. High level of DNA damage in sperm cells may represent a cause of male infertility that conventional examinations cannot detect.

**Method:** This is a literature review that took four journals where discuss DNA fragmentation index (DFI) result after varicocelectomy with infertile men with a clinical varicocele.

**Results:** A study prospectively evaluated changes in sperm chromatin structure in infertile patients before and after surgical repair. There were 49 varicocele men with at least a 1-year history of infertility. A palpable varicocele and oligospermia, and the DNA fragmentation index was found decreased significantly after surgery from 35.2% to 30.2% (p = 0.019). From a retrospective study where evaluated 25 who underwent microsurgical varicocelectomy for treatment of clinical varicocele, sperm DNA integrity improved significantly after surgery (percentage DFI decreased from 18±11% before surgery to 10±5%, and 7±3%, at 4 and 6 months after surgery respectively). A prospective cohort study with 120 infertile patients associated with varicocele (grade II in 45 men and grade III in 75 men) show reduced sperm DFI after surgery on patient with varicocele grade II (32.7 ± 1.6% pre-surgery to 28.0 ± 2.3 post-surgery with p < 0.05 ) and on patient with varicocele grade III (35.5 ± 4.7% pre-surgery to 28.5 ± 6.3 post-surgery p < 0.05).

**Conclusion:** A varicocelectomy can improve sperm DNA integrity. Also, all sperm parameters such as mean sperm count, sperm concentration, progressive motility and sperm morphology significantly increased.

**Keywords:** Varicocele, DNA Fragmentation Index, Varicocelectomy

### Successful fertilization and embryo development after round spermatid injection in azoospermic Testicular Sperm Extraction (TESE) patient: a case report

**Ahmad Ricardo**<sup>1,2</sup>, **Ninik Darsini**<sup>3</sup>, **Zakiyatul Faizah**<sup>2</sup>, **M. Aminuddin Azis**<sup>2</sup>, **Hendy Hendarto**<sup>3</sup>

<sup>1</sup>Andrology Study Program, Dr. Soetomo General Hospital, Surabaya, Indonesia
<sup>2</sup>Biology Department of Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
<sup>3</sup>Obstetric dan Gynecology Department, Dr. Soetomo General Hospital, Surabaya, Indonesia

**Abstract**

**Background:** Obstructive azoospermia is a common cause of male infertility and can result from infection, congenital anomalies, or iatrogenic injury. Microsurgical techniques were reported could give an improvement to the patient with obstructive azoospermia. This case report aims to evaluate the effect of round spermatid azoospermic Testicular Sperm Extraction (TESE) patient.

**Case Description:** We report 36 years old patient with obstructive azoospermic who performed TESE without any spermatozoa found. Bilaterally enlarged epididymis found in physical examination. FSH and Testosterone level was normal. His wife was 26 years old without an abnormal finding. Ten oocytes were fertilized with round spermatids. Two embryos cleavage became four cells and two cells, and then both were transferred in day 2. The pregnancy test still negative.

**Conclusion:** Even, the pregnancy rate of Round Spermatid Injection (ROSI) is still very low, this technique can become optional for azoospermic in TESE patient.

**Keywords:** Azoospermia, Round Spermatid, TESE, Male Infertility

### The role of Intracytoplasmic Sperm Injection (ICSI) in infertile man with Hepatitis-B (HBV) infection: a case report

**I Gusti N gyroah Pramesmara**<sup>1,2</sup>, **Zakiyatul Faizah**<sup>3</sup>, **Ninik Darsini**<sup>3</sup>

<sup>1</sup>Andrologi Specialist-1 Program, Medical Faculty of Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya, Indonesia
<sup>2</sup>Medical Biology Department, Medical Faculty of Universitas Airlangga, Surabaya, Indonesia

**Abstract**

**Background:** We have already known that there is a relationship between chronic infection of the Human Hepatitis-B Virus (HBV) and infertility in men. HBV infection causes instability of spermatozoa chromosomes, interferes the parameters of semen analysis, and have risks to infectious fetus or embryo. The Intracytoplasmic Sperm Injection (ICSI) procedure is an attempt to prevent HBV infection. This case report aims to evaluate the role of ICSI procedure to the infertile man with HBV infection.

**Case Description:** We reported the case of a 42-year-old infertile male who had primary infertility for 11 years with positive HBsAg. Patients were given
ABSTRACT

Tribulus terrestris, and a antioxidant also referred to an internist colleague for the definitive treatment of Hepatitis-B. Then the patient and his wife were prepared to undergo an In-Vitro Fertilization (IVF) procedure by washing spermatozoa and ICSI.

Conclusion: Routine evaluation for 15 days post-ICSI for the first time did not show biochemical signs of pregnancy in wives with negative β-hCG. It was concluded that the ICSI procedure could be considered in the action of IVF in infertile man with HBV.

Keywords: ICSI, IVF, Infertile Man, HBV

Frequent ejaculations option in male infertility cases to decrease oxidative stress: a literature review

Cinta Ayu Abutari1,2, I Gusti Ngurah Pramesemara2, Reny I’tishom1,2, Ahmad Ricardo Silalahi1,2, Agustinus3

1Andrology Specialist Program, Medical Faculty of Universitas Airlangga, Surabaya, Indonesia
2Medical Biology Department, Medical Faculty of Universitas Airlangga, Surabaya, Indonesia
3Andrology and Sexology Department, Medical Faculty of Universitas Udayana, Denpasar, Indonesia

Abstract

Special preparations in male infertility cases are needed before semen analysis, one of which is an explanation of sexual abstinence. Sexual abstinence is one of the factors that can affect semen parameters.

WHO guidelines recommend a period of sexual abstinence 2-7 days before semen testing has become an evaluation standard in semen analysis. There is an agreement that semen volume and sperm concentration will increase with prolonged sexual abstinence, but can simultaneously harm motility and viability of sperm. Spermatozoa will be highly exposed to Reactive Oxidative Stress (ROS) during their maturation and storage process in the epididymis. This correlates impact to decrease in sperm motility, lipid peroxidase, DNA fragmentation and disrupt its fertilization rate. The adverse effects of the duration of sperm transit in the epididymis on sperm motility have been widely reported previously.

Based on the previous studies, decreased ROS levels will improve DNA fragmentation and fertilization rates. So that, frequent ejaculations can be an approach to enhance the quality of sperm DNA and is expected to be applied infertility treatment.

Keywords: Frequent Ejaculation, Sexual Abstinence, Male Infertility, Oxidative Stress