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Effect of Vaccination on Performance of Dairy Animals with Special Reference to Bulls: A Review

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ABSTRACT

Vaccination stimulates immune system to generate memory cells responsible for immunity against specific antigen. Milk production decreased by vaccination however milk composition not changes significantly. Bull vaccinated against bacterial and viral diseases increases cellular damage and testicular degeneration leading to enhanced sperm abnormalities and decrease sperm motility, concentration and live cells. Exotic and crossbred bulls are more prone to diseases and vaccination. Offshoot of vaccination includes pain, swelling and redness at site of injection together with high temperature, shivering, fatigue and pain in muscles and joints. Marker vaccine help in differentiation or segregation of infected from vaccinated animals. Aversion of pyrexia to maintain normal body temperature can be a preventive measure against the adverse effects of vaccination. Vitamin E supplementation and pre-vaccination levamisole injection was tried to mitigate vaccination stress, though partial positive effect was observed. Therefore temporary suspension of semen freezing is advisable for 2 to 3 months post vaccination to avoid low fertility rate in herd.

Keywords: Antigen, Marker vaccine, Levamisole, Semen profile, Vitamin E.

Vaccination is practice of administration of killed, mild or attenuated microbes in order to stimulate immune system against wild form of infection thereby preventing infection. Vaccination stimulate animals own immune system. Vaccination generates memory cells responsible for immunity against specific antigen on re-exposure (Berek and Ziegner, 1993). Immunization should provide good humeral, cellular and local immune response similar to natural infection and protect against clinical diseases and re-infections with minimal immediate side effect.

Mild local and systemic reactions after vaccination are likely to be natural consequences of spirited stimulation of immune system of body. Moreover, vaccination is one of the major stressors that affect the milk production and semen quality. Vaccination protocols are evolving continuously keeping in view efficacy and safety of vaccine concern. The protocol of vaccination required to be modified as per seriousness of disease, nature of disease and risk exposure to the animals. Risk of vaccination should not exceed the chances of contracting disease. Vaccines are administered to healthy animal as it target protection rather treatment (Chen, 1999). Ultimate goal of vaccination is eradication of disease permanently. Vaccination necessitate limiting of infection only to target animal group with no human or environmental

reservoir and absence of subclinical or carrier state in animals. Immunity achieved by administration of vaccine is called active immunity, produced by own immune system and persist throughout the life; however, passive immunity is transferred from other animals and provide immediate protection which, diminish with time i.e., temporary. Passive immunity may be transferred through placenta and colostrum.

Quality germplasm production requires breeding bulls to be free from diseases. For prevention of diseases, vaccination against communicable diseases is essential component of standard management practices in a bull station expected to reduce the incidence and severity of disease (Smith, 1957). Poor efficacy and adverse reaction locally led to confusion among farmers regarding alternatives of vaccines (Smith and Klose, 1980).

Four important points should be born in mind while looking into health and fertility of bull i.e., nutrition, genetics, disease and stress. If any one of these factors is affected, fertility will be compromised accordingly. Under natural breeding system bull should be vaccinated well ahead of the breeding season. Bull if vaccinated against contagious viral diseases increases cellular damage and testicular degeneration (Rao and Venkataswami, 1974) leading to enhanced sperm abnormalities (Venkataswami and Rao, 1970; Narshimhan *et al.,* 1970). Long lasting significant effect of vaccination with respect to sperm motility, concentration, live cells and abnormalities were also reported (Narasimha Rao, 1974). Local application of heat to the scrotum (Steinberger and Dixon, 1959), retention of heat into scrotum (Gustaffson, 1966) different infections including protozoal (Singleton, 1968), ephemeral fever (Chenoveth and Burgess, 1972) etc. were also reported to affect semen quality.

Vaccination principles

Vaccination protects the animals from communicable disease by introducing agents, which mimic the microbe (highly purified antigen/ mild version of disease) to stimulates memory, plasma, T and B cells providing a level of resistance to disease beyond their inherent immune status. Adjuvant formulation, those specifically focus on augmentation or control of interplay between innate and adaptive immune system along with function of antigen presenting cells (APC) nowadays used with antigens (Zepp, 2016). Vaccination is a form of immune-prophylaxis, which afford protection long time before exposure to wild type infection. Since effectors lymphocyte (T and B) cells are short lived i.e., in days, a prime requisite of vaccine is to generate immunological memory (Ada, 1990).

Memory B cells quickly divide into plasma cells and make more antibody if required. Memory T cells can divide and grow into microbe fighting army during subsequent exposure to the infection.

Types of vaccines

Based on importance of disease, vaccines are divided into three categories (Tizard, 2013)**:**

1. Essential or core vaccine: Vaccines which protect against common, dangerous disease with significant morbidity and mortality.
2. Optional or non-core vaccines: Disease for which risk is low.
3. Special vaccine: Vaccines that may have no application in routine vaccination but may be used under very special cases.

Based on number of antigen

Single Vs. multiple antigen vaccine: Multiple antigen vaccine protects animals against several agents at a time, however, with less satisfactory protection as compared to single antigen vaccine.

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Based on virulence

1. Killed vaccine (KV) or Inactivated or toxoid:	2. Modified live vaccine (MLV)/ Live attenuated vaccine:	3. Chemically altered vaccine:
No risk of spread of organism to other animals. Minimum risk causing abortion to pregnant animals. On farm mixing is not required. **Disadvantages:** Allergic reactions and post-vaccination lump is common. Two initial doses (booster dose) required for proper functioning. Slower onset of immunity. Immunity is not so strong and long lasting as compared to live vaccine. More costly as compared to live vaccine.	One initial dose is sufficient, sometimes booster dose required. Rapid, strong and long lasting immunity is characteristics of this vaccine. Less chances of allergic reactions and lump formation. Vaccines are low cost. **Disadvantages:** There is risk of causing abortion or transient infertility, therefore contraindicated during pregnancy and used 6-8 weeks prior to breeding. Must be mixed on farm and used within an hour accordingly.	Share advantage of live vaccine, safe as killed vaccine minimal risk of causing abortion. **Disadvantages:** Two initial dosages required. Slower onset of immunity as compared to modified live vaccine as well as less durable immunity. More expensive as compared to MLV.

Other types of vaccine

Subunit vaccine: Instead of using whole microbe, subunit vaccines utilizes fraction of antigen (epitopes) which stimulate the immune system best i.e., reduce antigen over load therefore adverse reaction to vaccine is lower.

Conjugated vaccine: Some bacteria possesses polysaccharide coating over actual antigen, therefore conjugate vaccine is desirable for surface polysaccharide. Modern vaccines include DNA vaccine and recombinant vector vaccine. DNA vaccines permit development of protection against disease for which current vaccines are ineffective or not available.

Precautions for improving vaccination efficiency:

Vaccines should be stored correctly at refrigerated temperature before use. Animal should be in good general health before administration of vaccine. Vaccine do not work properly in sick, stressed, thin, heavily parasitized or trace mineral deficient cattle.

Cause of vaccination failure: Low efficacy of vaccine, its improper dosage through improper route along with stress in animals and malnutrition. Vaccination failure is more often due to administration of vaccine to immune-suppressed or immune-deficient individual rather subnormal vaccine efficacy (Day, 2006). Vaccination of calf at too young age may also fail to respond the vaccine.

Vaccination side effect/ adverse effect: Side effect of vaccination includes pain, swelling and redness at site of injection together with high temperature, shivering, fatigue and pain in muscles and joints. Three principle of adverse effect include 1. Effect consistent: clinical response should be similar for different animals, 2. Effect specific: Adverse effect linked specifically to the vaccine and 3. Temporal relationship: Earliest manifestation aggravate with continuing condition.

Side effect discussed in detail by Novak (2007) as follows:

Class	Types of Reaction
I	Not due to vaccine
II	Lump and swelling locally
III	Facial swelling
IV	Systemic sign such as fever vomiting and diarrhea
V	Anaphylactic shock, death.

High temperature after vaccination up to 48 hours is common in cattle and buffaloes after FMD, HS and BQ Vaccination (Pandey *et al.,* 1987; Shah, 1998).

DIVA/ SIVA Test/ Marker vaccine: It helps in differentiation or segregation of infected from

vaccinated animals and therefore referred to as DIVA (SIVA) vaccine (van Oirschot *et al.,* 1986). This is often achieved by excluding an antigen present in pathogen being vaccinated against, thus creating a negative marker of vaccination. Apart from apparent benefit of allowing serological monitoring of vaccinated individuals or population, it also helps in continuous monitoring of efficacy and safety of the vaccine.

Adverse effect of vaccination on production

Adverse effect of vaccination was also common in cow especially during first week post vaccination. Common lesion observed after FMD vaccination was urticaria, necrotic and exudative dermatitis, edema, vesicles formation around teats and loss in milk production up to 21.5% (Yeruham *et al.,* 2001); however, author also reported no effect of blue tongue virus vaccination on milk quality and quantity in dairy cattle (Giovannini *et al.,* 2004). Drop in milk production up to 10 days along with poor conception rate and reproductive efficiency is also reported in crossbred cows and buffaloes due to vaccination (Mavi and Bagha, 2011). In a economic analysis the benefit cost ratio of FMD vaccination in Pakistan with 50 livestock farm was estimated more or less 5.7 (Ferrari *et al.,* 2014).

Vaccination stress in bull with respect to sperm profile

Ambient temperature, humidity, nutrition, managerial practices affect semen quality, besides febrile conditions associated with different diseases such as FMD and Anaplasmosis, Brucellosis (Roberts, 1956), Babesiosis (Singleton, 1968) and traumatic gastritis (Bane, 1954). Subcutaneous injection of pus and absorption of arsenic through skin leads to testicular degeneration whereas, bacterial toxin, vaccination, histamine or foreign protein produces mild fever along with changes in semen quality.

Murugavel (2002) in an experiment with 12 murrah bulls divided in to two group and vaccinated with BQ (formalized and alum ppt.) and FMD (tissue culture) vaccine, reported detrimental effect on post thaw motility of sperm. Singh (2003) in a trial with 4 buffalo bull vaccinated (20 ejaculates pre-vaccination + 72 ejaculates post-vaccination) with tetravalent vaccine@10 ml s/c per animal, reported significant decrease in motility, concentration and HOS positive sperms. Similarly Mathur *et al.* (2003) in an experiment with 10 Frieswal (HF X SW) bulls of more than 24 months of age, observed significant detrimental effect post-vaccination. Significant decrease in the concentration and motility of the spermatozoa and an increase in the proportion of abnormal and dead spermatozoa after the first vaccination in ram; however, after the second vaccination only smaller, non-significant changes were observed (Bread *et al.,* 2007).

In India, as a regular prophylactic measure, breeding bulls are vaccinated against various contagious diseases, but still more emphasis need to be paid on vaccination of exotic and crossbred bulls as they are more prone to FMD, HS, BQ and other diseases (Mathur *et al.*, 2003) and vaccinations. Available reports on the effect of vaccination on semen quality are conflicting. Increased incidence in sperm abnormalities following vaccination were observed by Venkataswami and Rao (1970); Rao and Venkataswami (1974) and Kammar and Gangadhar, (1998). However, Mangurkar *et al.* (2000) observed that vaccination did not affect the ejaculate volume, initial motility, pre freeze and post-thaw motility.

Semen quality is affected by vaccination (Gahlot and Kohli 1981; Venkatareddy *et al.*, 1991 and Murugavel *et al.*, 1997) as it is one of the major stress factors which cause rise in body temperature as well as temperature of the testis increases because of the febrile reaction occurring during post-vaccination period. The causes for febrile reaction after vaccination (Hanly *et al.*, 1997) may be due to adjuvant (contamination,

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quality) and antigen used (not purified bacterial antigen, viral antigen not clarified). When testicular temperature increases, metabolism increases at a greater rate than blood flow and hence the testes become hypoxic. The testes are very susceptible to temperature increases due to endogenous or exogenous factors (e.g. fever, high ambient temperature). As testicular temperature increases, the proportion of defective spermatozoa increases; recovery is dependent upon the nature and duration of the thermal insult. Sperm abnormality especially the acrosomal and pyriform condition due to exposure of rams to heat stress was associated closely with decrease in conception rate, ewes inseminated show high incidence of embryonic mortality (Rathore, 1970). The testis usually operates close to hypoxia. Increased temperature increases metabolism, with a concurrent need for increased oxygen to sustain aerobic metabolism. Blood flow changes little in response to increases in testicular temperature and consequently the testes become hypoxic (Setchell, 1978). Increasing blood oxygen saturation is not practical since the blood is nearly completely saturated under normal conditions. Although increasing blood flow would increase the delivery of oxygen, it would also bring considerable additional heat into the testes. The increased body temperature may affect not only spermatogenesis (Venkatareddy *et al.*, 1991) but also fully formed sperm (Anderson, 2001). Besides this abnormal acrosome development (Bane and Nicander, 1966) occurs temporarily due to induction of testicular degeneration which is particularly common during transformation of spermatids through uncontrolled growth of acrosomal system.

Heating seems to affect Sertoli and Leydig cell function; as germ cells are the most sensitive to heat. All stages of spermatogenesis are susceptible, with the extent of damage related to the exposure of the increased temperature (Waites and Setchell, 1990). Spermatocytes in meiotic prophase are killed by heat, whereas spermatozoa that are mature usually have metabolic and structural abnormalities (Setchell *et al.*, 1971). Heating testis usually decreases the proportion of progressively motile and live spermatozoa, and enhances the occurrence of morphologically irregular spermatozoa with faulty heads (Barth and Oko, 1989). Although there is considerable variation among bulls in the nature and proportion of damaged spermatozoa, the order of appearance of specific defects is relatively consistent (Vogler *et al.*, 1993 and Barth and Bowman, 1994). Unless spermatogonia are affected, the interval from cessation of heating to restoration of normal spermatozoa in the ejaculate corresponds to the interval from the beginning of differentiation to ejaculation (Waites and Setchell, 1990). Abnormality of spermatozoa should not exceed 17-20 percent, which might impairs fertility (Lagerlof, 1934), although Mercier and Salisbury (1946) claimed that the morphology is not the sole factor contributing the fertility. Haq (1949) reported high level (31.4%) of sperm abnormality in unfertile bulls. Semen of vaccinated bulls containing high percentage of abnormality cannot be recommended for use until 45 days of vaccination (Venkataswami and Rao, 1970).

Even though sperm morphology has returned to normal, their utilization may result in decreased fertilization rates and an increased incidence of embryonic death (Burfening and Ulberg, 1968). When scrotal/testicular temperature is increased (regardless of the cause), sperm morphology is generally unaffected initially (for an interval corresponding to epididymal transit time) but declines afterward (Barth and Oko, 1989). In some studies (Wildeus and Entwistle, 1983 and Kastelic *et al.*, 1996), spermatozoa that would have been in the epididymis at the time of scrotal heating were morphologically abnormal when collected soon after heating. In another study (Vogler *et al.*, 1991), changes in these spermatozoa were manifest only after they were frozen, thawed and incubated. Sperm features returns to pre-treatment values within

approximately 6 weeks of the thermal insult. However, a prolonged and (or) severe increase in testicular temperature will increase the interval for recovery. It appears that the decrease in semen quality associated with increased testicular temperature is ultimately related to the severity, the duration of the increased testicular temperature and also individual variation.

This preventive vaccination might be followed by epididymal dysfunction which possibly is the reason for increased number of spermatozoal abnormalities in the initial stage, resulting in reduced motility (Rao and Venkataswami, 1974 and Rao, 1976). This derogatory effect of vaccination resembles those of therapeutic agents on germinal cells resulting in increased number of dead spermatozoa, and leucocytes absorbs through the process of phagocytosis (Mann and Mann, 1981). There is subsequent decline in epididymal sperm reserves (Rao *et al.*, 1980), thus concentration decreases as the resorption of abnormal sperm increase. Very less information is there in concern with the semen quality during post vaccination period. As compared to bacterial vaccine, viral vaccine has more deleterious effects, as both the metabolic activity and 'cold shock' resistance of sperm are reduced to a considerable level (Venkataswami *et al.*, 1972).

Effect of Bacterial vs. Viral vaccination

Type of Vaccine	% Sperm abnormalities			
	Pre-vaccination	Post-vaccinations (Weeks)		
		1	2	3
HS	7.8 (7)	7.1 (10)	9.3 (9)	-
BQ	7.4 (8)	13.5 (12)	20.8 (12)	6.8 (11)
FMD	8.6 (7)	25.6 (10)	20.8 (12)	14.2 (11)

► Value in parenthesis indicates number of sample. (Venkataswami *et al.,* 1972)

Semen quality of exotic (Saxena and Tripathi, 1977; Gahlot and Kohli, 1981 and Gahlot *et al.,* 1990), crossbred bulls (Venkatareddy *et al.* 1991 and Mathur *et al.* 2003) and buffalo bulls (Tripathi and Saxena 1976) is adversely affected by vaccinations against FMD, HS and BQ. Available reports on the effect of vaccination on semen quality are conflicting. Findings of various workers on these aspects have been summarized as follows:

Effect of vaccination on semen quality in different species

Breed	Findings	Authors
Crossbred bull	No significant difference in ejaculate volume after FMD vaccination, but a significant decline sperm number in ejaculate and progressive motility was observed.	Rao (1974)
Crossbred bulls	Decline in motility, concentration and percentage of live spermatozoa during post-vaccination period before returning to normal levels; however, secretory activity of accessory reproductive glands remained unaffected by vaccination. Following Rinderpest vaccination marked decline in *in-vitro* preservability of semen was observed.	Radhakrishnan *et al.* (1975)
Murrah bulls	During 0-45 days post-vaccination of FMD, the abnormalities of sperm increased and semen preservability declined. They also reported impaired maturation of spermatozoa due to vaccination shown by more number of protoplasmic droplets in vaccinated bull sperms.	Tripathi and Saxena (1976)
Jersey bulls	Motility, livability, preservability of sperm declined and abnormalities increased up to 45 days post-vaccination of FMD. High incidence of protoplasmic droplets in sperm and mid piece abnormality was observed.	Saxena and Tripathi (1977)
Jersey bulls	Mild deleterious effects of RP (Rinderpest) vaccination were observed as compared to reports by Radhakrishnan et al. (1975). Pyrexia was not noticed post vaccination.	Gahlot and Kohli (1981), Gahlot *et al.* (1990)
Exotic, Crossbred and Zebu	Clear cut breed variation was observed with adverse effect of vaccination on semen quality. Effect of FMD vaccination in Jersey and Jersey × Ongole was moderate, but in local Ongole bull, it was less severe.	Venkatareddy *et al.* (1991)

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Murrah buffalo bulls	Decrease in sperm concentration, motility and live sperm count was detected. Total spermatozoal abnormalities increased significantly during the period. Adverse effect on sperm profile was noticed up to two months post-vaccination.	Murugavel *et al.* (1997)
Surti buffalo bull	No adverse effect of FMD vaccination on ejaculate volume and sperm concentration during post vaccination period, but there was significant decrease in percentage of progressive motility of sperm.	Kammar and Gnagadhar (1998)
HF, Jersey & their crossbred	During post-vaccination period number of ejaculate volume decreased by 6%; however, other semen characteristics like motility not affected significantly.	Mangurkar *et al.* (2000)
Crossbred	As per the personal observation of author, one bull recovered from FMD, the concentration of spermatozoa was normal, but the motility was poor (20 per cent) and the pH was rather high (6.86); nine weeks later the motility was good (80 per cent) and the pH lower (6.60), since the bull has maintained good sperm production.	Anderson (2001)
Murrah bull	Vaccination stress was prominent i.e., semen was not fit for cryopreservation for five weeks in case of BQ and seven weeks for FMD vaccination.	Murugavel *et al.* (2002)
Frieswal bulls	Semen quality parameters showed a declining trend: mass activity, from 3.1 to 2.5 and mean per cent progressive motility 55.4 to 46.5 at pre FMD and post-HS and BQ vaccination, respectively. On bulls HS and BQ vaccination had more detrimental effects as compared to IBR & FMD.	Mathur *et al.* (2003)
Buffalo bulls	The adverse effects in the spermiogram (concentration, motility, live sperm count, intact acrosome) as exerted by the FMD vaccination was observed up to 1 month after vaccination.	Singh *et al.* (2003)
Sunandini bulls	In Kerala Livestock Development Board also semi-annual vaccination against Foot & mouth disease followed with two weeks sexual rest was done to cope with post vaccination stress.	Krishnan *et al*. (2003)
Karan Fries (KF); Murrah (MU) and Sahiwal (SW) bulls	Application of Raksha Triovac vaccine had adverse effect on sperm motility and mass activity of MU and KF bull semen. Vaccination had no significant (P>0.05) effect on volume and sperm concentration of semen in KF, MU and SW bull semen.	Pankaj *et al.* (2007)
Sahiwal bulls	Significant decrease in mass activity (2.20±0.12 vs. 1.73±0.14) and sperm concentration per ml was observed.	Bhakat *et al.* (2008)
Karan Fries (KF); Murrah (MU) bulls	Significant reduction in seminal attributes including mass motility, initial motility and sperm concentration was noticed. They advocated the suspension of semen preservation till normal fertility of sperm should be restored.	Bhakat *et al.* (2010)
KaranFries (KF); Murrah (MU) bulls	TRIOVAC vaccination reduces the semen quality parameters as a result of increased body temperature.	Bhakat *et al.* (2011)
Holstein Friesean bulls	FMD vaccination using Raksha-Ovac Trivalent showed adverse effect on most of the seminal attributes during initial 10 days, however morphology was unaffected.	Saha *et al.* (2011)
Mithun (Bos frontalis) bulls	FMD vaccination showed adverse effect with respect to sperm functional and biochemical parameters significantly till 10 weeks of vaccination.	Perumal *et al.* (2013)
Murrah buffalo bulls	HS and BQ vaccination affected semen quality parameters like mass activity (1.75±0.12 vs. 1.23±0.14), sperm concentration and individual motility (49.54±0.15 vs. 38.01±0.11) significantly.	Bhakat *et al.* (2015)
KaranFries bulls	FMD vaccination affected semen profile significantly	Rao *et al.* (2017a)

Aversion of pyrexia, so as to maintain normal body temperature can be a preventive measure against the adverse effects of vaccination (Gahlot *et al.*, 1990). The pyretic response to these vaccinations varies from bull to bull, breed to breed and even species to species. To certain extent this adverse effects can also be reduced by immuno-modulators. Therefore, it is advised that vaccination schedule may be followed when the season is unfavorable

as during that time the semen production is usually of poor quality especially for purpose of freezing. Adverse effect of vaccination on semen parameters also reported in mithun (Bos frontalis) which suggest temporary suspension of collection and preservation of semen till 10^{th} week of vaccination to avoid failure in conception rate (Perumal *et al.,* 2013).

Vaccination stress mitigation

Using oral supplementation of antioxidants

Infertility among the animals can be attributed to diminished semen quality and other male factor. The etiology of diminished semen quality is generally poorly understood, although environmental characteristics such as age and diet have been implicated. In particular, dietary intake of antioxidant such as Vitamin E and C has been demonstrated to be critically important for normal semen quality and reproductive functions. Antioxidants protect nutrients (PUFA, Vitamin A) from destructive oxidation which ultimately improve the semen quality. In one small trial of nine infertile men receiving 400mg/day of ά-tocopherol in combination with selenium (Vezina *et al.*, 1996), there were significant increase in sperm motility, live sperm percent and percent of normal sperm where as in other studies, there was no effect of even higher level of vitamin E supplementation (300-1200mg/day), (Moilanen *et al.,*1993; Kessopoulou *et al.*, 1995; Moilanen and Hovatta,1995) or in combination with vitamin C (Rolf *et al.*,1999). Keskes-Ammar *et al.* (2003) reported recommended use of vitamin E and selenium in treatment of male infertility as supplementation of vitamin E and selenium increases the sperm motility. Eskenazi *et al.* (2005) on the basis of Food frequency questionnaire and seminogram of 97 healthy persons reported higher antioxidant intake was associated with higher sperm concentration and motility. Castellini *et al.* (2000) observed that, a combination of increased level of Vitamin E and ascorbic acid in rabbit diet was associated with significant increase in spermatozoal viability, kinetics of spermatozoa movement and fertilizing ability. Velasquez-Pereira *et al.* (1998) observed that, adverse effect of 'Gossypol' feeding can be avoided by vitamin E supplementation to bull. Akmal *et al.* (2006) in a trial with 13 infertile human patient fed vitamin C @ 1000mg twice a day for two month reported significant ($P<0.001$) increase in concentration, motility and normal sperm after supplementation. Biswas *et al.* (2007) in an experiment 180 male Japanese quail chick were randomly divided into three groups (T_1, T2, T3) and fed @15, 150 and 300 IU Vitamin E /kg. Frequency of foam discharge (24 hrs), cloacal gland index and foam weight were significantly ($P<0.05$) higher in T_2 group. Semen characteristics (volume, motility, live sperm, % hatchability and sperm concentration) did not differ ($P<0.05$) significantly. Percentage of abnormal and dead spermatozoa were significantly ($P<0.05$) lower and fertility was higher in T_2 group means moderate supplementation of dietary Vitamin E may be beneficial for foam production, cloacal gland and improve the semen characteristics in male Japanese quail.

Rao *et al.* (2017a) reported positive effect of Vitamin E supplementation to some extent on vaccinated Karan Fries bulls to mitigate stress.

Levamisole treatment

Levamisole is chemically 1-2,3,5,6-tetrahydro-6-phenylimidazo (2,1-b) thiazole. Levamisole is an antibiotics belonging to class of synthetic imidazothiazole derivatives. It has antihelmintic and antinematodal activity. It also modulates the immune system by modifying activity of T-lymphocytes and phagocytes especially in immunologically depressed (aged) animals. Injectable levamisole when used in combination with polyvalent clostridial vaccine heightens antibody response. Bozkurt *et al.* (2004) reported the adverse effect of levamisole. Author reported significant ($p<0.05$) decrease in semen

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volume, sperm motility, concentration and total sperm number at all time. Some reports are that testosterone production by leydig cell was inhibited by levamisole (Schurmeyer and Nieschlag, 1984). Decrease semen volume and motility (Bozkurt *et al.,* 2004). Kavanagh *et al.* (1981) reported that levamisole inhibited sperm motility due to it is a potent inhibitor of seminal diamino oxidase. Acrosomal enzyme play an essential role in fertilization and hyaluronidase being among the acrosomal enzymes is particularly important in dispersing cumulus cells (Tilakaratne and Soory, 2000). Semen hyaluronidase activity could be an index of fertilization ability (Tanyildizi and Bozkurt, 2003). It was also reported that low hyaluronidase activity causes a decrease in fertilizing capability of sperm (Hiryama *et al.,* 1989). Bozkurt *et al.* 2004 reported that levamisole treatment caused significant increase in the semen hyaluronidase activity of rams, means levamisole has significant positive effect on fertilizing capability of sperm. Vaccination to breeding bull deteriorates semen quality pararmeters; however, levamisole treatment in vaccinated bull has positive effect to some extent with respect to semen and blood profile (Rao *et al.,* 2017b).

CONCLUSION

Milk production decreased by vaccination however milk composition not changes significantly. As far as semen production from bull is concerned it is well established that semen quality decreases after vaccination; more over Vitamin E and pre-vaccination levamisole injection was tried to mitigate vaccination stress, though significant effect was not observed. It is therefore recommended that semen should be collected examined and discarded accordingly till the sperm profile is restored after vaccination along with pre-vaccination levamisole treatment and post-vaccination Vitamin E supplementation to achieve the optimum cumulative conception rate in herd.

REFERENCES

Ada, G.L. 1990. The immunological principles of vaccination. *The Lancet,* **335**(8688): 523-526.

Akmal, M., Qadri, J.Q., Al-Walli, N.S., Thangal, S., Haq, A. and Saloom K.Y. 2006. Improvement in human semen quality after oral supplementation of vitamin C. *J Med Food.,* **9**(3): 440-2

Anderson, J. 2001. The semen of animals and its use for artificial insemination. Green world publishers, Lucknow, India, First Ind. Reprint.

Bane, A. 1954. Studies on monozygous cattle twins: sexual functions of bull in relation to heredity, rearing intensity and somatic conditions. *Acta. Agric. Scand.*, **4**(2): 97.

Bane, A. and Nicander, L. 1966. Development of sperm abnormalities. *J. Reprod. Fert.*, **11**: 133.

Barth, A.D. and Bowman, P.A. 1994. The sequential appearance of sperm abnormalities after scrotal insulation or dexamethasone treatment in bulls. *Canadian Vet. J.*, **35**: 93-102.

Barth, A.D. and Oko, R.J. 1989. Abnormal morphology of bovine spermatozoa. Iowa state university press, Ames, pp.17 and 37.

Berek, C. and Zeigner, M. 1993. The maturation of the immune response. *Immunol Today,* **14**(8): 400-4.

Bhakat, M., Mohanty, T.K., Gupta, A.K., Chakarvarty, A.K., Singh, P. and Abdullah, M. 2015. Effect of HS and BQ vaccination on semen quality parameters of Murrah buffalo bulls. *J Infect and Mol Biol.*, **3**(1): 24-27.

Bhakat, M., Mohanty, T.K., Raina, V.S., Gupta, A.K. and Brahma, B. 2010. Effect of FMD vaccination on semen quality parameters in Karan Fries and Murrah buffalo bulls. *Trop Anim Health Prod.,* **42**(7): 1363-1366.

Bhakat, M., Mohanty, T.K., Raina, V.S., Gupta, A.K. and Brahma, B. 2011. Effect of TRIOVAC vaccination on semen quality parameters in Karan Fries and Murrah buffalo bulls. *Indian Vet J.*, **88**(3): 33-34.

Bhakat, M., Mohanty, T.K., Raina, V.S., Gupta, A.K., Mondal, G. and Khan, H.M. 2008. Effect of FMD vaccination on various semen characteristics of sahiwal bulls. *Pak. J. Agr. Sci.*, **45**(2): 327-332.

Biswas, A., Mohan, J., Sastry, K.V.H. and Tyagi, J.S. 2007. Effect of dietary Vitamin-E on the cloacal gland, foam and semen characteristics of male Japanese quail. *Theriogenology.* **67**(2): 259-263.

Bozkurt, T., Tanyildizi, S. and Turk, G. 2004. Effect of levamisole on hyaluronidase activity and sperm characteristics in rams. *Theriogenology,* **62**: 323-329.

Bread, E., Pozzi, N., Sailleau, C., Durand, B., Catinot, V., Sellem, E. Dumont, P., Guerin, B. and Zientara, S. 2007. Transient adverse effect of an attenuated bluetongue virus vaccine on the quality of ram semen. *Vet Rec.*, **160**: 431-435.

Burfening, P.J. and Ulberg, L.C. 1968. Embryonic survival subsequent to culture of rabbit spermatozoa at 38ºC and 40ºC. *J. Reprod. Fertil.*, **15**: 87-92.

Castellini, C., Lattaioli, P., Bernardini, M. and Dal Basco, A. 2000. Effect of dietary alphatocopheryl acetate and ascorbic acid on rabbit semen stored at 5 degree C. *Theriogenology,* **54**(4): 523-533.

Chen, R.T. 1999. Vaccine risks: real, perceived and unknown. *Vaccine,* **17**(3): S41-6.

Chenoveth, P.J. and Burgess, G.W. 1972. Mid-piece abnormalities in bovine semen following ephemeral fever. *Aust. Vet. J.,* **48**: 37.

Chowdhury, A. K. and Steinberger, E. 1964. A quantitative study of the effect of heat on germinal epithelium of rat testes. *Am. J. Anat.,* **115**: 509.

Day, M.J. 2006. Vaccine side effects: facts and fiction. *Vet. Microbiol.,* **117**(1): 51-8.

Eskenazi, B., Kidd, S.A., Marks, A.R., Sloter, E., Block, G. and Wyrobek, A.J. 2005. Antioxidant intake is associated with semen quality in healthy men. *Hum. Reprod.*, **20**(4): 1006-12.

Ferrari, G., Tasciotti, L., Khan, E. and Kiani, A. 2014. Foot and mouth disease and its effect on milk yield: an economic analysis on livestock holders in Pakistan. *Transbound Emerg. Dis.*, **61**(6): e52-9.

Gahlot, P.S., Bishnoi, B.L. and Kohli, T.S. 1990. Semen studies during vaccination stress in jersey bulls. *Indian J. Anim. Reprodn.,* **11**(2): 109-110.

Gahlot, P.S. and Kohli, T.S. 1981. Effect of Rinderpest vaccination (freeze dried) on the semen quality of jersey bulls maintained in the arid zone. *Indian Vet. J.,* **58**: 1001-1002.

Giovannini, A., Conte, A., Panichi, G., Calistri, P., Dessi, M., Foddis, F., Schintu, A. and Caporale, V. 2004. Effect of vaccination against bluetongue on milk production and quality in cattle vaccinated with live-attenuated monovalent type 2 vaccine. *Vet. Ital.,* **40**(4): 648-53.

Gustafsson, B. 1966. M.V.P. *Reference and data Library A.* 7-389.

Hanly, W.C., Bennett, B.T. and Artwohl, J.E. 1997. Overview of adjuvants. *AWIC-Resource-Series*, **3**: 1-8.

Haq, I. 1949. Cause of sterility in bulls in southern England. *Br. Vet. J.,* **105**: 3-6.

Hiryama, T., Hasegawa, T. and Hirror, M. 1989. The measurement of hyaluronidase activity in human spermatozoa by substrate slide assay and its clinical application. *Fertil Steril.,* **51**(2): 330-4

Kammar, N.F. and Gangadhar, K.S. 1998. Effect of foot-and-mouth vaccination on reaction time and some seminal characteristics in Surti bulls. *Indian J. Anim. Reprodn.*, **19**(2): 149-50.

Kastelic, J.P., Cook, R.B., Coulter, G.H. and Saacke, R.G. 1996. Insulating the scrotal neck affects semen quality and scrotal/testicular temperatures in the bull. *Theriogenology*, **45**: 935-942.

Kavanagh, J.P. Brightwell, R., Bardsley, W.G. and Schnieden, H. 1981. Levamisole and other diamine oxidase inhibitors as inhibitors of sperm motility. *Arch. Androl.,* **7**(1): 51-62.

Keskes-Ammar, L., Feki-Chakroun, N., Rebai, T., Sahnoun, Z., Ghozzi, H., Hammami, S., Zghal, K., Fki, H., Damak, J. and Bahloul, A. 2003. Sperm oxidative stress and the effect of an oral vitamin E and selenium supplement on semen quality in infertile men. *Arch. Androl.*, **49**(2): 83-94.

Kessopoulou, E., Powers, H.J., Sharma, K.K., Pearson, M.J., Rusell, J.M., Cooke, I.D. and Barratt, C.L. 1995. A double-blind randomized placebo cross-over controlled trial using the antioxidant vitamin E to treat reactive oxygen species associated male infertility. *Fertil. Steril.*, **64**(4): 825-31.

Krishnan, R., Biju, K., Devanand, C.P. and Xavier, C.J. and Rajesh, V.R. 2003. Effect of Foot and Mouth disease vaccination on semen characteristics of Sunandini bulls. National seminar on Frozen semen technology, Dhoni, Kerala, India, pp. 211-215.

Lagerlöf, N. 1934. Changes in the spermatozoa and in the testes of bulls with impaired or enhanced fertility. *Acta. Path. et. Microbiol. Scand.* Suppl. **19:** 254.

Mann, T. and Mann, C.L. 1981. Male Reproductive Funtion and Semen. Springer- Verlag Berlin. Heidelberg, New York, USA.

Mangurkar, B.R., Phadnis, Y.P. and Bhosrekar, M.R. 2000. Effect of Foot and mouth disease vaccination on semen characteristics of exotic and cross-bred bulls. *Ind. J. Anim. Reprodn.*, **21**(2): 135-137.

Mathur, A.K., Tyagi, S. Mandal, D.K. and Singh, S.P. 2003. Effect of multiple vaccinations on the semen quality of Frieswal bulls. *Indian J. Anim. Sci.* **73**(8): 864-866.

Mavi, P.S. and Bagha, C.S. 2011. Effect of FMD vaccination on milk production and conception rate in dairy cows and buffaloes. *Indian Vet J.*, **88**(9): 152-153.

Mercier, E. and Salisbury, G.W. 1946. The Effects of Season on the Spermatogenic Activity and Fertility of Dairy Bulls. *Cornell. Vet.,* **36:** 301.

Moilanen, J and Hovatta, O. 1995. Excretion of alpha-tocopherol into human seminal plasma after oral administration. *Andrologia*, **27**: 133-136.

Moilanen, J. Hovatta, O. and Lindroth, L. 1993. Vitamin E level in seminal plasma can be elevated by oral administration of vitamin E in infertile men. *Int. J. Androl.,* **16**: 165-166.

Murugavel, K., Rajasekaran, J. and Subramanian, A. 1997. Foot and mouth disease vaccination stress on semen quality in Murrah bulls. *Ind. J. Anim. Reprod.*, **18**: 67-69.

Murugavel, K., Veerapandian, C. and Subramanian, A. 2002. Post thaw motility of buffalo semen following FMD and BQ vaccination. *Indian Vet. Med. J.,* **26**: 241-242.

Narasimha Rao, A.V. 1974. Vaccination stress in crossbred bulls. *Indian Vet. J.,* **51**: 75.

Narshimhan, K.S., Krishan, A.R. and Syed, A.Q. 1970. *Ibid.* **47**: 19.

Novak, W. 2007. Predicting the "unpredictable" vaccine reactions. Proceedings of North American Veterinary Conference. Ithaca: International Veterinary Information Service.

Pandey, M.R., Singh, N.D. and Yadav, R.S. 1987. Effect of vaccination against hemorrhagic septicaemia on milk yield body temperature and feed intake of Tharparkar cross-bred cow and Murrah buffaloes: A note. *Indian J. Anim. Sci.*, **3:** 35-6.

Pankaj, P.K., Raina, V.S., Roy, B., Mohanty, T.K. and Mishra, A. 2007. Studies on effect of vaccination on seminal characteristics of riverine buffaloes (*Bubalus bubalis*). *Buffalo Bull.,* **26**(3): 91-103.

Perumal, P., Khate, K. and Rajkhowa, C. 2013. Effect of foot and mouth disease vaccination on seminal and biochemical profiles of mithun (*Bos frontalis*) semen. *Asian Pac. J. Reprod.*, **2**(3): 178-184.

Radhakrishnan, R., Venkataswami, V. and Pattabiraman, S.R. 1975. Further report on the effect of protective vaccination on semen quality of breeding bulls. *Indian Vet. J.*, **52**: 620-625.

Rao, A.R. 1976. Sperm akinesia in a Hallikar bull. *Indian Vet. J.,* **53**: 414-418.

Rao, A.R., Bane, A. and Gustafasson, B.K. 1980. Changes in the morphology of spermatozoa during their passage through the genital tract in dairy bulls with normal and impaired spermatogenesis. *Theriogenology*, **14**(1): 10-12.

Rao Narsimha, A.V. 1974. Vaccination stress in crossbred bulls. *Indian Vet. J.,* **51**: 74-75.

Rao, T.K.S., Mohanty, T.K. and Bhakat, M. 2017a. Effect of Vitamin E supplementation on semen and blood profile of vaccinated bulls. *Indian J. Anim. Sci.,* **87**(4): 456-460.

Rao, T.K.S., Mohanty, T.K. and Bhakat, M. 2017b. Levamisole as an immunomodulator to ameliorate vaccination stress in cross bred bulls. *Indian J. Anim. Sci.,* **87**(7): 840-843.

Rao, V.J. and Venkataswami, V. 1974. Histo-pathology of testicular tissue of crossbred bulls in Foot and Mouth disease vaccination. II. *Indian Vet. J.*, **48**: 1101.

Rathore, A.K. 1970. Acrosomal abnormality in ram spermatozoa due to heat stress. *Br. Vet. J.,* **126**: 440-443.

Roberts, S.J. 1956. Veterinary Obstetrics and Genital diseases. Ithaca, New York.

Rolf, C., Cooper, T.G., Yeung, C.H. and Nieschlag, E. 1999. Antioxidant treatment of patients with asthenozoospermia or moderate oligoasthenozoospermia with high dose vitamin C and vitamin E: a randomized, placebo-controlled, double –blind study. *Hum Reprod.*, **14**(4): 1028-33.

Saha, S., Mishra, G.K., Singh, R.B., Shukla, M.K., Tiwari, R. and Saxena, S.K. 2011. Effect of FMD vaccination on semen characteristics in Holstein Friesian bulls. *Indian J. Anim. Reprod.,* **32**(2): 49-51.

Saxena, V.B. and Tripathi, S.S. 1977. Effect of foot and mouth disease vaccination on semen quantity,

quality and preservability in Jersey bulls. *Indian Vet. J.*, **54**: 959-964.

Schurmeyer, T. and Nieschlag, E. 1984. Effect of ketoconazole and other imidazole fungicides on testosterone biosynthesis. *Acta Endocrinol.,* **105**(2): 275-80.

Setchell, B.P. 1978. The scrotum and thermoregulation. In: Setchell BP, ed. The mammalian testis. Ithaca: Cornell University Press, pp. 90-108.

Setchell, B.P., Voglmayr, J.K. and Hinks, N.T. 1971. The effect of local heating on the flow and composition of rete testis fluid in the conscious ram. *J. Reprod. Fertil.*, **24**: 81-89.

Shah, N.H. 1998. Haemorrhagic septicaemia in dairy buffaloes in Pakistan: pathogenesis and prevention. PhD Thesis submitted to Amsterdam: Vrije University of Amsterdam.

Singh, R., Verma, H.K. and Kumar, S. 2003. Effect of the foot-and-mouth disease vaccination on the semen quality of buffalo bulls. *Indian J. Anim. Sci.,* **73**(11): 1319-1323.

Singleton.1968. *Indian Vet. J.,* **45**: 885 (Abstr.)

Smith, H.B. and Klose, J.B. 1980. Response of goats to clostridial vaccines. *Victorian Veterinary Proceedings,* **38**: 46.

Smith, L.D.S. 1957. Clostridial disease of animals. In: Brandly C A, Jungher EL, Editors. Advances in Veterinary Science. New York: Academic Press.

Steinberger, E. and Dixon, W.J. 1959. Some observations on the effect of heat on testicular germinal epithelium. *Fertil. Steril.,* **10:** 578.

Venkatareddy, J., Venkatamunichetty, A., Ramachandran, S.V. and Sreeraman. 1991. Effect of foot and mouth disease vaccination on semen quality. *Indian J. Anim. Prod.,* **12**: 13-14.

Venkataswami, V. and Rao, V.J. 1970. Preliminary report on the effect of foot and mouth disease vaccination on semen quality of crossbred bulls-1. *Indian Vet. J.*, **47**: 23-29.

Tanyildizi, S. and Bozkurt, T. 2003. Effect of acetylsalicylic acid and metamizol on hyaluronidase activity and sperm characteristics in rams. *Anim. Reprod. Sci.*, **76**: 195-204.

Tilakaratne, A. and Soory, M. 2000. Effect of the anti-androgen finasteride on 5 alpha-reduction of androgens in the presence of presence of human gingival fibroblasts: modulatory action of the alkaline phosphtase inhibitor levamisole. *J Periodontal Res.,* **35**(4): 179-85.

Tizard, I.R. 2013. In: The use of vaccine: Veterinary Immonology, 9th Edition, pp. 273. Elsevier Inc.

Tripathi, S.S. and Saxena, V.B. 1976. A note on the foot-and-mouth vaccination stress on quantity, quality and preservability of semen of Murrah buffalo bulls. *Indian J. Anim. Sci.,* **46**: 44-47.

van Oirschot, J.T., Rziha, H.J., Moonen, P.J., Pol, J.M., van Zaane, D. 1986. Differentiation of serum antibodies from pigs vaccinated or infected with Aujeszky's disease virus by a competitive enzyme immunoassay. *J. Gen. Virol.,* **67**(6): 1179-1182.

Velasquez-Pereira, J., Chenoweth, P.J., McDowell, L.R., Risco, C.A., Staples, C.A., Prichard, D., Martin, F.G., Calhoun, M.C., Williams, S.N. and Wilkinson, N.S. 1998. Reproductive effect of feeding Gossypol and Vitamin E to Bulls. *J. Dairy Sc.* **76**: 2894-2904.

Venkataswami, V., Pattabi Raman, S.R., Daniel, J. and Sundaravadanam, V.K. 1972. Effect of vaccination on spermatozoa resistance and on their metabolic activity. *Indian Vet. J.,* **49:** 1012-1016.

Venkataswami, V. and Rao, V.J. 1970. Preliminary report on the effects of foot and mouth vaccination on semen quality of crossbred bulls-I. *Indian Vet. J.,* **47:** 25-29.

Vezina, D., Mauffette, F. Roberts, K.D. and Bleau, G. 1996. Selenium-vitamin E supplementation in infertile men. Effect on semen parameters and micronutrient level and distribution. *Biol. Trace Elem. Res.*, **53**: 65-83. [ISI][Medline]

Vogler, C.J., Saacke, R.G., Bame, J.H., DeJarnette, J.M. and McGilliard, M.L. 1991. Effects of scrotal insulation on viability characteristics of cryopreserved bovine semen. *J. Dairy Sci.,* **74**: 3827-3835.

Vogler, C.J., Bame, J.H., DeJarnette, J.M., McGilliard, M.L. and Saacke, R.G. 1993. Effects of elevated testicular temperature on morphology characteristics of ejaculated spermatozoa in the bovine. *Theriogenology,* **40**: 1207-1219.

Waites, G.M.H. and Setchell, B.P. 1990. Physiology of the Mammalian Testis. In: Lamming GE ed. Marshall's Physiology of Reproduction, 4th Edn., Vol. 2, Reproduction in the Male. Edinburgh: Churchill Livingstone, pp. 1-105.

Wildeus, S. and Entwistle, K.W. 1983. Spermiogram and sperm reserves in hybrid *Bos indicus* × *Bos taurus* bulls after scrotal insulation. *J. Reprod. Fertil.*, **69**: 711-716.

Yeruham, I., Yadin, H., Haymovich, M. and Perl, S. 2001. Adverse reaction to FMD vaccine. *Vet. Dermatol.,* **12**(4): 197-201.

Zepp, F. 2016. Principle of Vaccination. *Methods Mol Biol.,* **1403**: 57-84.