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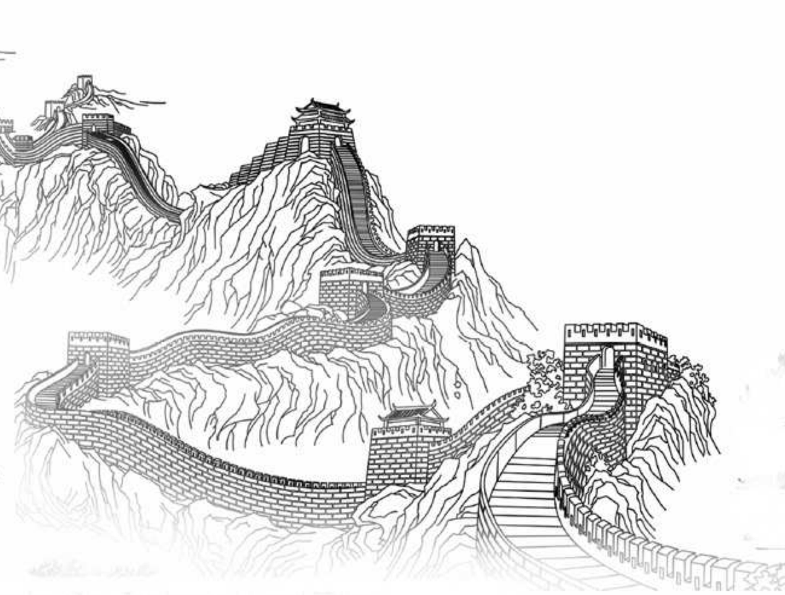

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# RECENT TRENDS IN RABBIT DOES REPRODUCTIVE MANAGEMENT: SPECIAL REFERENCE TO HOT REGIONS

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## ABSTRACT

Enhancing reproductive performance is an important factor in rabbit production management. Rabbits are considered induced ovulatory animals, and when artificial insemination (AI) is applied, the ovulation has to be induced by exogenous hormones (GnRH). Different synthetic GnRH analogues (gonadorelin, buserelin, triptorelin, leuprorelin) have been successfully utilized. In addition, some studies have demonstrated that ovulation can be induced successfully in rabbit females by the vaginal absorption of different GnRH analogues, which are included in the seminal plasma, avoiding intramuscular injection.

Recently, using hormones in rabbit reproduction technology management becomes unfavorable from the welfare point of view. Bio-stimulation methods are natural and are an alternative to hormonal treatments. These methods include doe-litter separation (DLS), lighting control and male proximity. The temporary separation of the rabbit doe from litters before AI is an alternative approach for improving sexual receptivity, fertility and prolificacy of doe rabbit farms. Daily lighting period control favorably affects doe reproduction performance.

Heat stress, occurring in hot regions, alters several aspects of reproductive functions in female rabbits such as hormonal secretions of the hypothalamo-pituitary-gonadal axis leading to infertility. It also depresses appetite resulting in negative energy balance

Better understanding for negative effect of heat stress on rabbit performance, requires good, technically practical, and economically feasible corrective measures. The most commonly used heat load indices are Temperature Humidity Index (THI) and Heat Stress Index (HSI). The responses following elimination of the stress after night cooling are referred as compensatory responses and have not been addressed by rabbit researchers.

Studies for how to make appropriate decision on strategies to ameliorate thermal heat load included physical and biological strategies and represent a challenge to rabbit scientists. Responding to the challenge of future addition of heat stress from climate change in hot regions of the world, it is apparent that there are many remaining research waves to be carried out to help increase rabbit productivity in hot regions.

## I. -INTRODUCTION

The mushrooming demand for animal proteins by the soaring World population coupled with income growth and fast urbanization is more evident in the developing countries. This is expected to continue at a faster rate in future years. In these countries more people have been able to afford the more protein diets provided by livestock products (**Steinfeld et al., 1997**). For example global meat production is projected to be more than double from 229 million tons in 1999/01 to 465 million tons in 2050 (**Steinfeld et al., 2006**). To meet such demand other alternative for the traditional meat sources for production is mandated. Rabbit is a good potential source as a solution to fulfill demand for animal proteins.

Rabbits are known to be 2.5-4.0 times more efficient in extracting proteins from forages than sheep, and beef animals (Rastogi, 2000). In the present view of no religious taboo against consuming rabbit meat and in light of the need to save feed grains, badly needed for fight against hunger, raising rabbits is an excellent choice. Furthermore, rabbit meat as compared to chicken, beef and pork meat is high in protein and low in fat (Nistor et al., 2013; McNitt et al., 2013)

Increasing rabbit productivity as a solution to improve quality of diet and income growth for farmers is touted by the Chinese say" if a family has several rabbits, it will not lack in oil, salt and vinegar, if a family has hundred rabbits it will not lack clothes and pants, if a family has some hundreds of rabbits, it will not lack a building".

Enhancing reproductive performance is significant factor in rabbit productivity (number of youngs per doe /unit of time). It is well documented that reproductive efficiency is "fine –tuned" by clues of various environmental factors, improving management techniques and providing adequate feeding quality and quantity. These factors have been well addressed and studied primarily by the scientists in developing countries of the temperate zone of the World. However, limited and spare data are available to form a good foundation for promoting reproductive performance in the lesser developing countries which are mostly located in arid, semi-arid and tropical regions of the World. In these hot regions, environmental (physical and biological) factors are one of the primary constraints to sustainable, efficient and profitable livestock production. These detrimental effects must be considered in a new wave of research for the rabbit.

The objectives of this paper, due to the limited time and space, are: (I) providing a review of the available data on recent trends on reproductive management of the female rabbit (II)minimizing potential detrimental impact of heat stress on productivity, and (III) identifying areas in hot regions where future research could make a contribution to promoting rabbit production

## II. REPRODUCTIVE MANAGEMENT TRENDS IN FEMALE RABBITS

Reproductive activity of does is under the control of neuro-endocrine axes and can be modified by genetic, feeding and management factors. In rabbit does, ovulation is induced by coitus (Ramirez and Bayer, 1988) and the female could be inseminated independently on their sexual receptivity (SR) which, in turn, is irregular with the only exception being on the day of partum (Harned and Casida, 1969) and immediately after weaning (Castellini et al., 2003). Naturally, when AI is used, the induction of ovulation is achieved by exogenous synthetic analogues of GnRH (Castellini, 1996).

Gestation period is 31-33 days and following this period, rabbit does give births in a nest in early morning. The lactation period is about 4-5 weeks. Commercial producers seeking a high intensive production, generally inseminating does during lactation, a time where the sexual receptivity is low (Gonzalez- Mariscal et al., 2007).This fact negatively impacts reproductive performance, since low sexual receptivity hinder pregnancy. Consequently it is important that does are receptive at the time of AI and estrous synchronization is needed to obtain high fertility response. Ubilla and Rebollar, (1995) observed high plasma estradiol 17β concentration that reflects maturity of ovarian follicles on days 1, 5-7 and 23-30 of the post-partum period. When does were inseminated, conception rates were generally higher.

### II.1. Reproductive rhythm and sexual receptivity

Reproductive rhythms (RR) can be categorized as intensive (AI post –partum or within 4 days from kindling; 35 days RR), semi-intensive (AI at 11days post-partum; 42 days RR) and extensive (AI after 3weeks of lactation or after weaning; 49 days RR). Intensive RR has major problems due to severe impacts on litter size, fertility rate and the length of reproductive activity (Maertens and Okerman, 1988; Cervera et al., 1993). Rebollar et al., (2009) showed that rabbit does managed with intensive RR needed a higher number of inseminations to become pregnant compared to females in semi-intensive RR

Semi-intensive RR is widely used but does not take into consideration the physiology of lactating rabbit does (Castellini et al., 2003). In addition, it leads to high replacement of does, high mortality and culling rate; (Guerder, 2002). Cardinali et al., (2008) reported low sexual receptivity, poor body condition score and low fertility rates associated with semi-intensive RR. With these limitations, this farm system is surprisingly the most observed in Europe.

Extensive rhythm seems to be better suited to the reproductive physiology of rabbit and maintains a more sustainable equilibrium of body weight and fat deposit (Feugier, et al., 2005) Also, it eliminates the hormonal and energetic antagonism between lactation and pregnancy. A study on the economic evaluation of RR showed a favorable impact of extensive RR on the economic performance of the enterprise and a low level of economic risk (Bertazzoli and Rivaroli, 2007).

Sexual receptivity (SR), parity, lactation status, and pseudo pregnancy at the time of insemination influence reproductive performance (Theau-Clément et al., 2012). Rabbit does do not show sexual cycles with regular heat periods during which ovulation occurs spontaneously. There are alternate periods of acceptance (oestrus) and of refusal of mating (diestrus), (Theau-Clément et al., 2011).. Sexual receptivity is determined at the day of AI using three methods: colour of vulva, (presence of red or pink indicates receptive rabbit, and purple or white indicates non receptive rabbit); rectal temperature and vagina cytology (the percentage of keratinized cells according to Ola and Oyegbade, (2012).A rectal temperature >38°C and a percentage of keratinized vagina cells >50% indicate receptive does. Colour of vulva is the best method to predict receptivity.

Sexual receptivity is associated with a better fertility (Theau-Clément et al., 2015); possessing a higher number of preovulatory follicles in the ovaries (Kermabon et al., 1994) and higher plasma estrogen concentrations (Rebollar et al., 1992). Also, itis associated with high prolificacy, higher ovulation intensity, fertilization rate, and higher embryo survival (Hoffman et al., 2010).

**II.2. Oestrus synchronization methods**

***II.2.1. Hormonal treatments:***

Pregnant Mare Serum Gonadotropin (PMSG) or (eCG) have been used for about 15 years to synchronize rabbit doe estrus. However, it could have an immunogenic response since it is an exogenous protein with high molecular weight. For this reason, its efficacy may decrease when used over a long period. An injection of PMSG before insemination generally increases fertility of does, but its efficacy could depend on the treatment conditions (dosage, interval between injections and insemination, etc.). The optimal interval between PMSG injection and AI has been little studied. Only Alvariño, (2005) concluded that fertility decreases when the interval reaches 96 hours, without any significant differences of fertility from 24 to 72 hours. It must be mentioned that some authors found a positive effect of PMSG only during the first four injections (Lebas and Fortun-Lamothe, 1996; Rebollar et al., 2006). It is commonly accepted that a dose of 20-25 IU of PMSG at 48 hours before insemination of lactating does at 11 days post-partum increases the percent of receptive does at insemination.

***II.2.2. Bio-stimulation methods**:*

Bio-stimulation methods are natural and less expensive alternative to hormonal treatments (Lorenzo et al., 2014). Some of the methods that have been tried include doe – litter separation, lightening control, male proximity and others.

*a/ Doe litter separation (DLS)*

It is well known that shortly after weaning (2-3 days), high percentage of does enter estrus (Theau-Clément and Roustan 1992). Nevertheless, regular post-weaning insemination with no competition

between pregnancy and lactation is likely to be cost-effective. Dam-litter separation (DLS) has been shown to potentially induce estrus.The DLS before AI is an alternative approach for improving sexual receptivity, fertility and prolificacy of doe rabbit farms, (Theau-Clément et al., 1998).
The DLS is easy to use, inexpensive, compatible with the animal welfare and well adapted to cyclic production (Boiti, 1998; Theau-Clément et al., 1998). Also, DLS on specific days of lactation before insemination was effective as eCG treatments in promoting growth of follicular waves and high steroidogensis activity (Ubilla et al., 2000; Rebollar et al., 2008). The DLS can be performed during 24-48h in lactation or nursing with a short controlled (Bonanno et al.,2002; 2004) Another method is applying a 2-day controlled nursing before insemination by allowing for a10 min. nursing of the litter at 24h of separation (Rebollar et al., 2008)

The DLS, applied before the 11day post-partum and lasting 48h was found to increase fertility rate of free nursing does by almost 20% (Bonannoet al., 2000; 20002), but reduces the growth rate of litters (Theau-Clément, 2000). In a study carried out by Bonanno et al., (2004) they found splitting the 48h DLS into two successive 24h periods, improved fertility similar to 48h DLS, and avoided a reduction in litter growth rate caused by a lower milk intake. Therefore, the short interruption in the continuous DLS lasting 48h, resulting from the controlled suckling might be considered a valid alternative strategy for avoiding the slowing down of the litter growth rate, and limiting the possible negative effects on rabbit welfare, without reducing fertility (Bonanno et al., 2004). It has been mentioned (Lorenzo et al., 2014) that different treatments should be used along the reproductive life of the does taking into account their reproductive rhythm and age.

*b/. Lighting regime*

Light, as an environmental factor was found to have pronounced effect on rabbit reproductive performance. A certain level of light intensity makes a signal to the pineal gland to start or stop melatonin synthesis and secretion. Stopping melatonin triggers a release of the hypothalamic hormones (Malpaux et al., 1999), which regulate secretion of pituitary hormones responsible of ovulation (Udala and Blaszezyk, 1999).

In temperate climates, where day length in spring is longer, fecundity is improved; on the contrary, during winter it is reduced (Matics et al., 2012). In arid and semi-arid climates, where the high environmental temperature may interact with light, the situation is different. In these regions female rabbit productive performance is better in winter (short day length) than spring and summer (long day length).

In large rabbit farms, in temperate climates, in order to moderate seasonality effects, 16h lighting schedule is applied during the whole year. Increasing the daily lighting schedule period from 8h to 16h prior to AI improves the does reproductive performance (Theau-Clément et al., 1990; Gerencser et al., 2010; Matics et al., 2012). Szendro et al., (2004), found that reproductive performance of does kept under 16L: 8D or 8L: 4D; 8L: 4D lighting regimes was not different. According to Hoy and Selzer, (2003), the 6L:6D:6L:6D lighting schedule increases the frequency of twice-A-day nursing, while (Gerenscer et al., 2007) noted that 8L:4D:8L:4D lighting schedule disturbs the does nursing behaviour.

The effect of light schedules on does reproductive performance is summarized in Table (1). The light schedule is used as a bio-stimulation method for estrus induction of doe rabbits. A definite trend is not clear, with the exception of 16L: 8D lighting schedule which was recommended by some authors (Theau-Clément and Mercier, 2004). This general supposition was supported by Marai et al., (2004) who mentioned that the feasibility of certain light regime used in commercial rabbit production, has no definite response. Regarding the contradiction observed in the results mentioned in the literature, it is suggested to standardize the conditions under which the light regime experiments are carried out, since day light is interrelated with other factors of climate as temperature and humidity… etc, which differ from region to another and even within the same region (Marai et al., 2004). It is worth mentioning also that in a study under the sub-tropical environment of Egypt, with its shining sun all the year, exposure of mature rabbits to different light regime showed adverse effect on most of the traits studied, when compared to natural day light, probably to that lamps radiation during application of the light regime techniques increase the feeling of warmth and such perception is aggravated during the hot climatic conditions (Marai et al., 2004). Surprisingly, under heat stress conditions in summer and red light colour, Kalaba and Abdel-Khalek, (2011) recorded the highest level of melatonin, kindling rate and litter size in comparison with natural and fluorescent lights, although reproductive activity of does starts in the absence of melatonin, as stated by Malpaux et al., (1999) and not under this high level of melatonin.

**Table 1:** Effect of different light schedules on does reproductive performances

| Light regime | result | authors |
|---|---|---|
| 14h continuous light | Maximizing doe reproduction | Uzcategui and Johnston, (1992) |
| 8h artificially light day | 5% more live born pups | Schuddemage et al., (2000) |
| Increasing daily light from 8h to 16h | Increasing doe reproductive performance | Theau- Clément t et al., 1990 Mirabito et al., (1994) Gerencser et al., (2010) |
| Intermitted lighting schedule | Improving kindling rate | Uzcategui and Johnston, (1992) Arveux and Troislouches, (1995) |
| | Increasing litter size | Arveux and Troislouches, (1995) |
| | Decrease suckling mortality | Arveux and Troislouches, (1995) |
| | Improving milk yield and litter weight at day 21. | Virag et al., (2000) |
| 16h:8D or 8L:4D; 8L:4D | No difference in reproductive performance | Szendero et al., (2004) |
| 6L:6D ; 6L:6D | Increasing frequency of twice –a- day nursing | Hoy and Selazer, (2003) |
| 8L:4D; 8L:4D | Disturbs does and nursing behavior | Gerencser et al., (2007) |
| 16L:8D | Is recommended to increase receptivity and young growth | Theau-Clément and Mercier, (2004) |
| 16L:8D and 12L:6D | No different results of reproductive performance | Matics et al., (2012) |
| **Light colour** | | |
| Natural fluorescent and red colour | higher kindling rate and litter size for red colour than other colours | Kalaba and Abdel-Khalek, (2011) |
| LED lighting and LED dual photostimulation | Positive effect on oestrous and kindling rate | Eiben et al., (2016) |

## II. 2. Ovulation induction

Artificial insemination has become a common practice in large rabbit farms of numerous countries due to its vast benefits in maximizing rabbit reproductive management. For successful AI practice it is necessary to induce ovulation due to the absence of the stimuli evoked by natural mating. Hormonal treatments have been widely used to induce ovulation of female rabbits artificially inseminated. Hormonal administration is carried out either by intramuscular injection or through intravaginal administration.

*II.2.1. Hormonal muscular GnRH injection*

The first attempts at inducing ovulation in rabbits using GnRH synthetic analogues occurred about 20 years ago (Rodriguez and Ubilla, 1988). Since then, AI has been progressively incorporated into use on many large and medium size farms. Different GnRH analogues (gonadorelin, buserelin, triptorelin, leuprorelin) have been successfully used, and the standard AI technique includes an intramuscular (i.m.) injection at different doses depending on the strength of the synthetic GnRH analogue (Rebollar et al., 1997).

Theau-Clément et al., (1990) compared the efficacy of two synthetic GnRH analogues, (0.8µg of buserelin and 20µg gonadorelin) administered i.m. immediately before AI in receptive and nonreceptive rabbits.In both rabbit groups, ovulation rate increased from 72 to 88%. Rodriguez and Ubilla, (1988) injected i.m. 20 or 40µg of gonadorelin in receptive and non-receptive rabbit does and observed that the higher dose only increased ovulation rate. Mehaisen et al., (2005) compared the effectiveness of buserelin acetate (2µg, i.m.) and hCG (75 IU, i.v.),both hormones increased the number of ovulating follicles (17.3 vs. 13.8), the recovery rate of embryos (48.7% vs. 34.8%), and number of embryos per doe (7.5 vs. 6.2).

*II.2.2. Hormonal intra-vaginal treatment*

To avoid i.m injection, several researchers have succeeded to induce ovulation via vaginal absorption of GnRH analogues included in semen prepared for AI. (Daader et al., 2002; Quintela et al., 2004; Viudes de Castro et al., 2007; Dal Bosco et al., 2012). Recent work hypothesized that in sexual receptive does, estrogens increased vascularization of the genital tract and increased permeability of the mucosa, which may increase the speed of absorption. Indeed, Quintela et al., (2004) hypothesized that GnRH is absorbed only by the vaginal mucosa and it does not enter into the uterus. Therefore, an unknown proportion of added analogous may have been lost due to seminal backflow of the high volume inseminated. Thus, the intra- vaginal absorption of GnRH may be negatively correlated with insemination dose. Dal Bosco et al., (2012) andViudes de Castro et al., (2007) concluded that introducing buserelin and triptorelin to the seminal dose as a method to induce ovulation, increased ovulation, fertility and prolificacy rates at a comparable rate to those obtained with the use of intramuscular treatments. Variations in dose response of GnRH analogues are probably attributed to a number of factors like vaginal mucosa state, extender composition and probably sperm concentration (Viudes de Castro et al., 2007). It may be possible that when more sperm concentration is used more quantities of hormones might be added to seminal dose to obtain normal reproductive results (Viudes de Castro et al., 2007). Several authors (Dal Bosco et al., 2012; Quintela et al., 2012 and Zhang and Qin Yinghe, 2012) continued conducting researches on adding different GnRH analogues to seminal doses. Zhang and Qin Yinghe, (2012) confirmed that adding leuprorelin (15 µg) to the semen could be used to obtain fertility comparable to those with the general intramuscular injection of buserelin for the ovulation induction in rabbit does.

Quintela et al., (2012) went further when used MRT-bit extender that incorporated GnRH analogues to induce ovulation in rabbits and leads to similar efficiency with that intramuscular hormone administration. The same authors mentioned that, in most rabbit farms, the GnRH administration is usually done by the farmer himself, with some risk of misuse, and increasing the time needed for each AI. Using a semen extender directly incorporating GnRH in its composition, and moreover prepared in the AI centers, would be beneficial for the farmer.

*II.2.3. Ovulation –Inducing Factors*

In the last few years, using hormones becomes unfavorable from the welfare point of view, in addition to their somehow high costs. Recently, researchers started to direct their attention towards other solutions to meet consumer demands for cleaner and greener approaches to farming. The story started in 1985, when a group of Chinese researchers found that when camel seminal fluid was injected into female camels, they ovulated, even when no sexual activity had occurred. The researchers claimed that there was chemical compound in the fluid that stimulated ovulation. For 20 years their claim was ignored, (Waldron, 2012).In 2005, Adams et al., successfully repeated the Chinese experiment in llama and documented the existence of a potent factor; ovulation-inducing factor (OIF) in the seminal plasma of llama that elicited a surge in circulating concentration of LH and induced an ovulatory and luteotropic responses. The stimulatory chemical compound is a protein called beta nerve growth factor (β-NGF). This protein was found to be abundant in alpaca seminal plasma and induced ovulation in 80% of female alpacas following administration of 1mg, i.m. (Kershaw Young et al., 2012). It is suggested thatβ-NGF induces its effects at the level of the hypothalamo- pituitary axis (Salas et al., 2006).

Dissen et al., (1996b) implicated β-NGF in the control of ovarian function, and its receptor trkA is present in the follicle of the rat (Dissen et al.,1996a). Furthermore, β-NGF acts through this receptor on human granulosa cells to stimulate the expression of FSH receptors and the secretion of oestradiol (Salas et al., 2006). Alpaca seminal plasma has been reported to induce the release of LH from mice pituitary cells in a dose-dependent manner and the use of an anti-GnRH antibody did not hinder this response (Paolicchi et al., 1999). Consequently, it is likely that the mode of action of seminal plasma β-NGF is at the level of the hypothalamo–pituitary axis, inducing ovulation by stimulating the secretion of LH.

The source of seminal plasma β-NGF in camelids is unknown. However, it has been reported that β-NGF mRNA is expressed predominantly in the vas deferens of the mouse and rat reproductive tract (MacGrogan et al., 1991), whereas in the guinea-pig (Harper et al., 1979; MacGrogan et al., 1991), bull and rabbit (Harper and Theonen, 1980) β-NGF is mostly expressed in the prostate. Both β-NGF protein and mRNA are expressed in the testis of the alpaca and are thought to be involved in spermatogenesis (Wang et al., 2011)

Silva et al., (2015) mentioned that β-NGF from llama seminal plasma origin elicits a preovulatory LH surge followed by ovulation and the development of functional corpora lutea (CL), regardless of the route of administration. It was concluded (Kershaw Young et al., 2012) that β -NGF may provide an alternative mechanism for the induction of ovulation in alpacas and; reduces the need for synthetic hormones and partially improves fertility in combination with AI.

Silva et al., (2011) through their results strongly support the presence of an OIF in the seminal plasma of rabbit, as evidenced that intramuscular administration in llamas (1) induces preovulatory LH surge (2)induces ovulation and consequently (3) induces the development of a normal CL. The results also confirmed that semen factors play a pivotal role in the mechanism of ovulation in llamas, while the same factors don't seem to have a relevant importance in the rabbit induction of ovulation. Similarly, Masdeua et al., (2014) failed to demonstrate the effect of different dosages of OIF of rabbit seminal plasma on ovulation induction in does.

As this is the case regarding the disagreement of using seminal plasma inducing ovulation in rabbit doe,it is of great importance for researchers to continue doing the necessary efforts to realize the hopeful progress in respect with using seminal plasma in inducing ovulation in rabbit as alternative method.

## III. PRODUCTIVITY OF FEMALE RABBITS IN HOT REGIONS

In hot regions of the world, heat stress is considered one of the primary constraints facing sustainable progressive rabbit production(Lebas et al., 1986; El-Raffa, 2004; McNitt et al., 2013; Kumar et al., 2013; Marco-Jimenez et al., 2013).

Mammals respond physiologically, biochemically and behaviorally to maintain homothermy and thus minimize adverse consequences. To regulate body temperature (Tb), livestock animals balance, heat production and heat loss mechanisms, (Yousef, 1985). Therefore, defining the thermoneutral zone (TNZ) or the comfort zone for a given species or breed is of economic importance for livestock producers to aid them select appropriate managerial practices to enhance performance, efficiency, well-being of animals and /or help them to ameliorate the stressful environmental conditions. Data on livestock production under heat stress have been well reviewed and analyzed recently (Aggarwal and Upadhyay, 2013; Collier and Collier, 2012 and De Shazer, 2009).

### III .1.Heat stress: measures and effects

To fully understand the constraints of heat stress on efficient and sustainable productive performance of livestock in general requires: (1) a good measure of environmental heat load, i.e. feeling of warmth; (2) to develop interventions to resolve constraints by providing a technically practical and economically feasible corrective measures. The estimation of how "comfortable" or stressful an environment is complicated (**Yousef, 1990**; **Hahn et al., 2009**; **Gaughan et al., 2012**).

Scientists for decades have been trying to develop a universally acceptable benchmark to measure environmental heat load. The elements of the physical thermal environment are combined to form one number reflecting a measure of heat load (Figure 1).

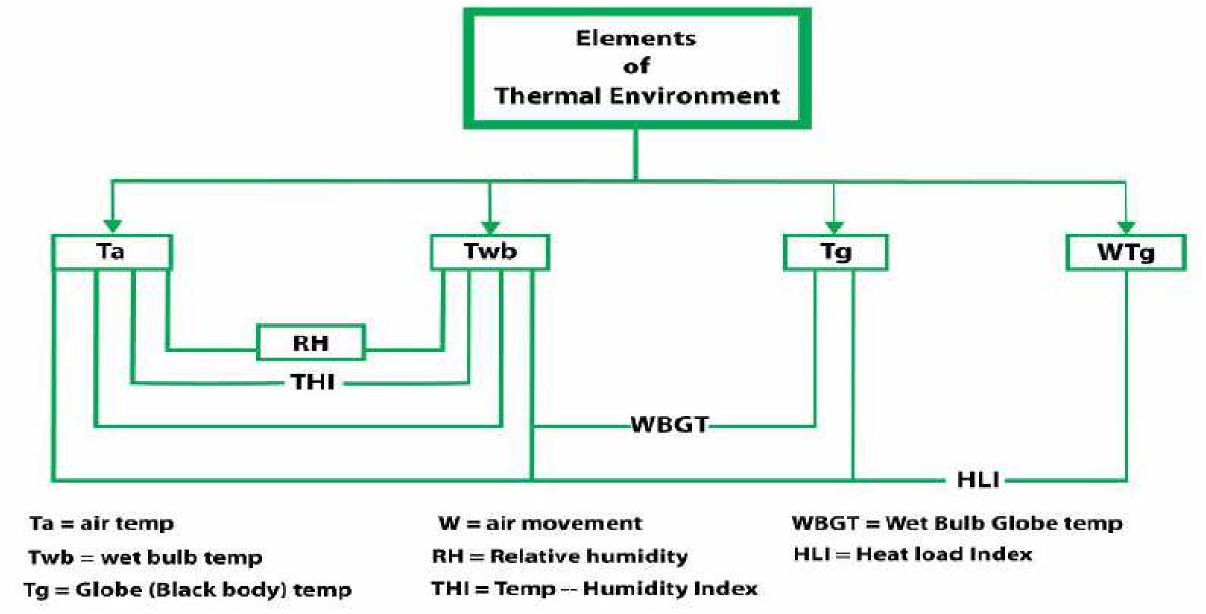


**Figure 1** : Indices of heat stress

No single meteorological element (Ta: air temperature;Twb: wet bulb temperature;Tg: global (black) body temperature and RH: relative humidity) can adequately express environmental warmth. While Ta measures air temperature only, the animal body reacts with feelings of heat to virtually all climatic factors. Thus a combination of two or more climatic elements is necessary to ideally measure environmental heat load. Several attempts have been made to develop empirical mathematical equations to combine the thermal environmental elements in different proportions as a benchmark for environmental heat load (Gaughan et al., 2012). Each of the indices presented in Fig. (1) has its advantages and limitations. The most commonly used index for livestock production is THI. THI=dbf-(0.55-0.55RH)(dbf-58) where, dbf, dry bulb temp,( °F) RH, relative humidity ( livestock and poultry heat stress indices, Agricultural Engineering Technology Guide, Clemson University, SC 29634, USA; cited by Abdel-Samee, 1995).The US-National Weather Service, uses the THI index to warn animal producers in the MINK states (Missouri; Indiana; Nebraska and Kansas) of the expected heat severity as shown inTable 2 (Hahn et al., 2009).

**Table 2:** THI as an advisory warning to animal producers in the MINK states of the USA.

| THI* | Heat load assessment | Advice |
|---|---|---|
| ≤ 74 | Normal | No safety problems |
| 75-78 | Alert | Expect some decrease in production |
| 79-81 | Danger | Expect significant ** decrease in production |
| ≥84 | Emergency | Animal**Mortality can occur |

* THI values in $^{O}$F
** Management intervention is required.

It should be emphasized here, that heat severity is determined by duration and intensity of exposure. For example, two environments may have the same THI despite different Ta. Additionally 3 days of a heat event in which exposure to heat, a few hours each day, will not have as a great an impact as another 3 days even in which exposure to the same heat load lasts many hours every day. Most published studies on rabbits have not considered measuring environmental heat load using any of these indices except for the few which used the THI (Marai et al., 2006 Daader et al., 2003). Most reported investigations used only Ta and may be also, RH as a measure of environmental warmth. Such poor measure of environmental heat load has lead to obvious conflict, discrepancy, and confusion among findings reported by investigators. Heat stresses possess serious limitations for fertility in breeding rabbits. It adversely impacts puberty, ovarian functions, oogenesis, oocyte maturation, fertilization development, implantation, number of kits born alive, litter size, litter weight, milk production and pre-post weaning mortality (Lebas et al., 1986 Marai et al., 2006, 2002, 2001 Daader et al., 2003 Fernandez-Carmona et al., 2003 Kumar et al., 2013 McNitt et al., 2013 and Abdel-Samee et al., 2012). In general, as environmental heat load exceeds the adaptive limit of rabbits, overall productive and reproductive traits fail to adjust and minimize adverse effects as described in figure 2.

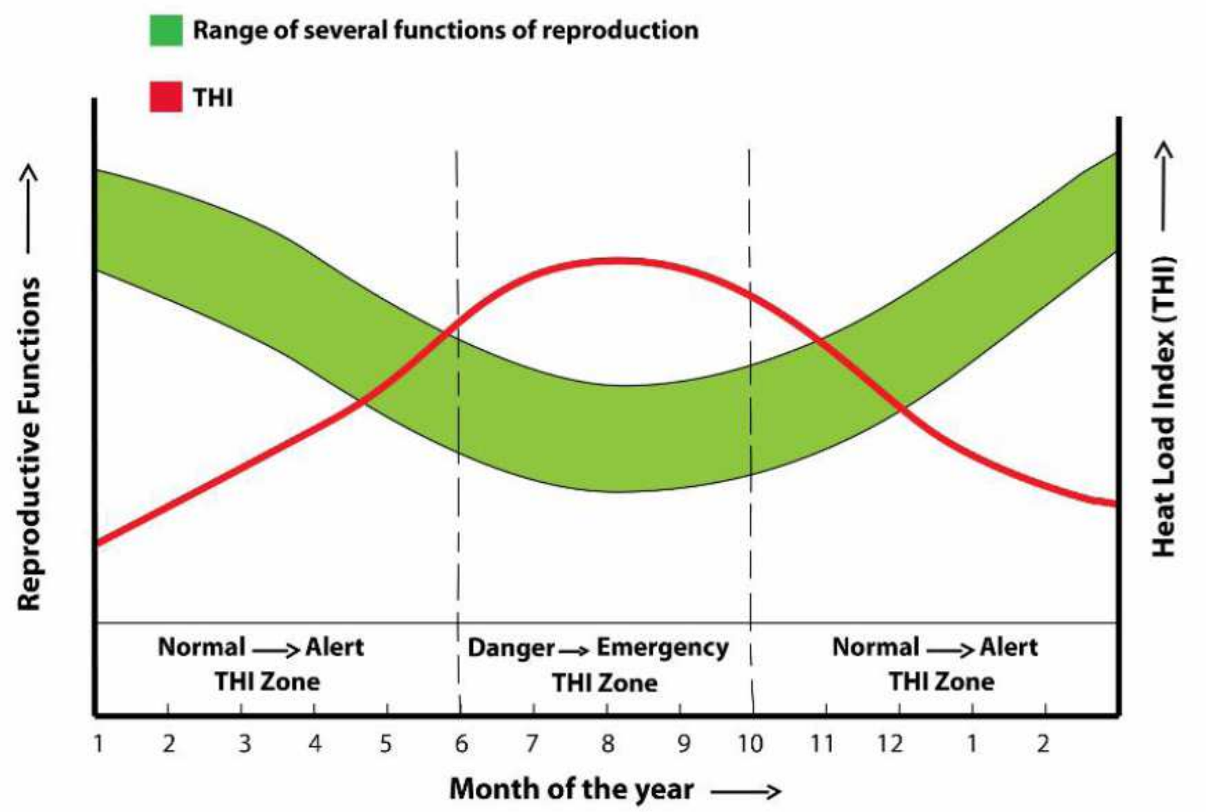


**Figure 2** : Animal response to heat load index (THI)

The zone which rabbit heat production equals heat loss is named thermoneutral zone (TNZ) and available values are summarized in Table (3). The discrepancy among these authors is probably related to their different measurement of heat load and to the evaluation of the physiological responses of the animals. Traditionally and until recently, measuring one or more of the response such as, heat production (rate of O2 consumption); body or rectal temperature, respiration rate, heart rate are used to identify TNZ or develop what is known as Heat Stress Index (HSI). For example, Fadare (2015) using four different breeds of rabbits developed HSI using only pulse and respiration rates. This approach, measuring one or more physiological response to evaluate HSI had beenpreviously criticized by Moberg, (1985) who stated "scientists should de-emphasize the traditional approach of measuring discrete physiological responses to stress and instead examine the effects of stress on parameters such as reproduction, production… etc, which would serve as indicators of animal well-being".

**Table 3:** Measurements of thermoneutral zone (TNZ) on breeding rabbits.

| Range of TNZ, $^{O}$C | Authors |
|---|---|
| 18-22 | Marai and Habeeb, )1994( |
| 18-22 | Piles et al., (2012) |
| 15-25 | Cerveraand Carmona (1998) |
| 15-24 | Animalwelfare@ecodev.vic.gov.au, Dec2015 |
| 9-19 | McNittand Lukefahr (1996( |
| 20-25 | Abdel-Nour et al., (2013) in growing Giza White rabbits |
| 22-25 | Abdel-Nour et al., (2013) in growing New Zealand White rabbits |

As mentioned above TNZ is considered as HSI and represents the zone atwhich the animals are in comfort condition and do not suffer from any thermal stress. The wider range of TNZ (Table3) for growing Giza White rabbits than that of New Zealand White rabbits (Abdel-Nour et al., 2013) indicates that the former breed is more adaptive than NZW, and is probably attributed to genetic variability

The Moberg alternative is certainly worthy of consideration and should be tested. A criterion such as animal performance, i.e. growth rate, production and reproductive levels, constitutes multiple endpoints to better measure stress severity. Furthermore, most published studies to-date have focused on the acute and chronic biologic responses to thermal stress and have failed to consider the effect of night cooling system cycle on productive traits . In addition, most of these reports did not measure the responses following elimination of the stress. These responses are referred to as "compensatory responses" (Hahn, 1982). In some cases, when stress is removed, animal performance could exceed the normal level "Over-shoot" rather than by a return to normal level Fig.(3). Thus if one considers the entire spectrum of animal responses, stress may have minimal or no effect or loss over a productive cycle (Figure 3).

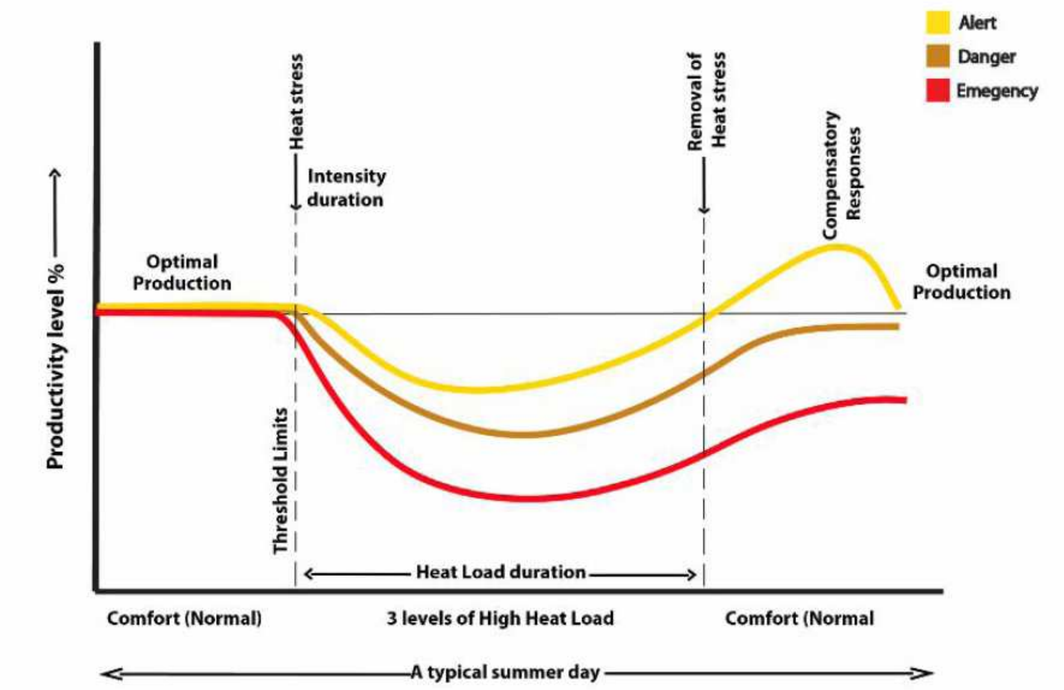


**Figure 3** Effects of various heat load intensity on productive functions, before, during and after exposure

The general concept of compensatory responses has not been addressed by rabbit researchers. Further studies should be designed to develop the threshold limits for compensatory responses as shown in Figure 3. Determining the threshold limits should provide better understanding of how far it is necessary to modify adverse environment to guard maximum animal performance, animal health, safety and well-being.

The threshold limits is defined as the maximum heat load level, intensity and duration that result in compensatory responses leading to minimal or no loss in productivity during a given cycle of animal performance. This will allow for improvement of management strategies that may be used to ameliorate heat stress.

It is widely accepted that heat stress alters several aspects of reproductive functions in female rabbits leading to infertility (Lebas et al., 1986) and thus represent a major source of economic loss. However, the underling mechanisms of the deleterious effect of heat stress on rabbit reproductive performance remains poorly understood and an open question for future research. The outlined mechanism herewith comes from studies using farm and laboratory animals (Aggarwal and Upadhyay, 2013 Takahashi, 2012 Hansen, 2009 and Dobson et al., 2003). Based on available data, we summarized the possible mechanisms for the female rabbit in Figure 4.

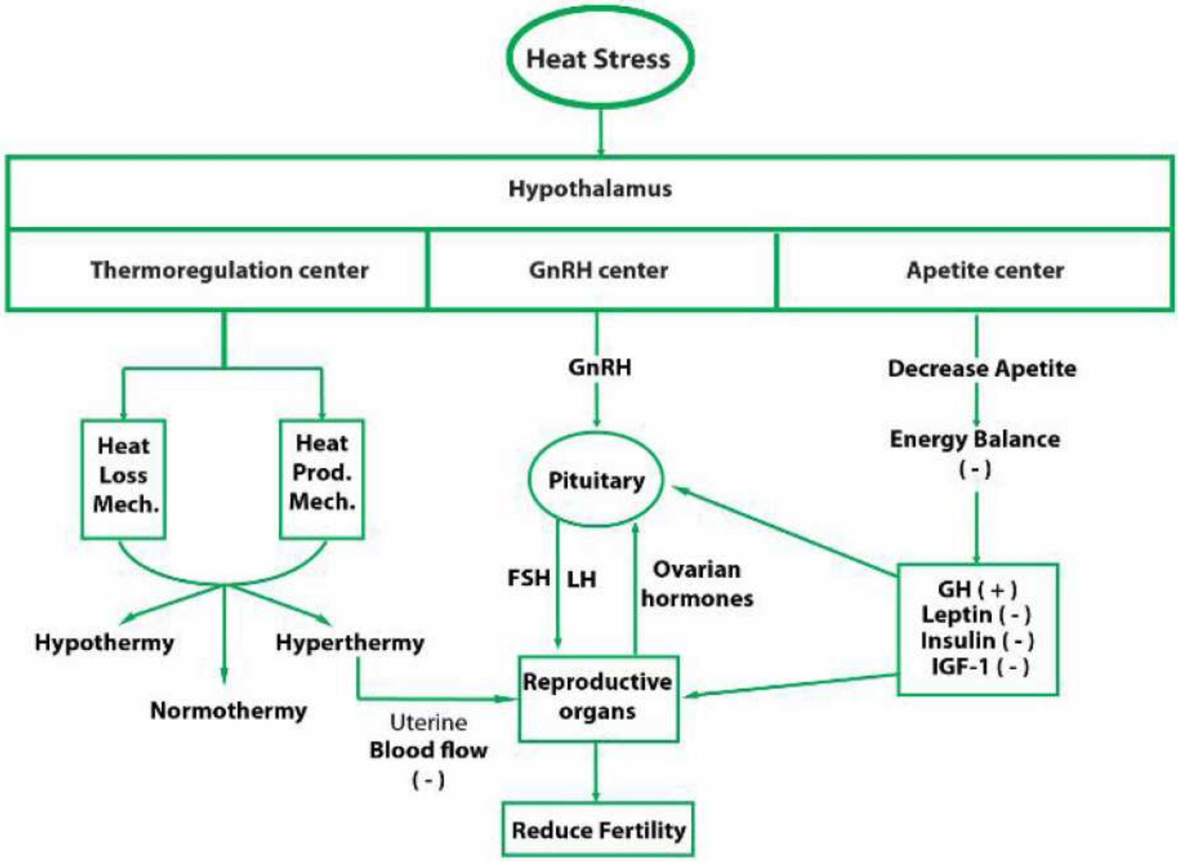


**Figure 4** : Mechanisms of heat stress respnses on reproductive performance

As presented in Figure 4, heat stress alters the hormonal secretions of the hypothalamo – pituitarygonadal axis. These hormones control several processes that span from follicle development to parturition and lactation. In addition, hyperthermia shifts blood circulation to the periphery to enhance heat dissipation resulting in reduced uterine blood flow, i.e. nutrients and hormones, affecting reproductive activity (Lublin and Wolfenson, 1996). Furthermore, heat stress depresses appetite resulting in negative energy balance. These in turn, increase growth hormone (GH) and decrease insulin and leptin (a 16.5KDa cytokine) which is secreted by adipocytes cells. Leptin may act as metabolic signal to switch on and off reproductive activity. Insulin is found to stimulate follicular growth and increase oocyte quality. The increased GH level is coupled with "GH resistance" i.e. GH receptors are down regulated. All of these hormonal and metabolic changes cause" decrease in GnRH leading to a decrease in LH resulting in decrease of follicular estradiol (Aggarwal and Upadhyay, 2013).These suggested mechanisms for the rabbit are an area where we need younger brains to be put to good use. Improving reproductive performance constitutes a major challenge for rabbit production in the hot regions and is dependent on revealing these mechanisms.

### III.2. Heat stress: mitigation measures

Responses of rabbits to an adverse heat load are well investigated and continue to be of future interest, however, studies for how to cope with heat stress (intensity and duration) remains a challenge. The development of mitigation measures to reduce thermal heat load are necessary to make appropriate decisions on strategies and tacts to reduce productive and economic losses during hot weather. Any amelioration measures must be technically practical in face of the limited resources available to farmers in hot regions, and economically feasible to provide maximum economic benefits. For many decades, counter measures for reducing thermal heat load presented a challenge to livestock scientists. Many excellent reviews examining available data have been recently published (Sejian et al., 2012 Rhoads et al., 2013 Yassein et al., 2008 and Hahn, 1985). A summary of available information is outlined in Fig. (5). The mitigation schemes fall into two categories:

**1) Physical strategies**: These mitigation measures aim to modification of animals housing and surrounding micro-environment. These include:

**a)** Providing either natural shade for animals *i.e.* tree shades or artificial shade made from straw. Shade should be designed to maximize ventilation and protection from solar and ground heat radiation.

**b)** For totally housed animals, design of the structures must consider increasing natural ventilation by achieving air flow without fans (Meat and livestock Australia, 2002). Furthermore, to use maximal density in each cage to allow normal rabbit behavior, the European Food and Safety Authority (2005) recommended 14-23 kits/m², whereas under heat stress conditions, Morales (2012) recommended a maximum density of 18 rabbits/m².

**(c)** Cooling the animals microenvironment using one or more of the following tested methods with varied success in farm animals (Davis et al., 2003)

i. Forced ventilation and wetting using a combination of water sprinkles with high speed of air movement via a fan will increase total heat loss from animals. Sprinkling maximizes the amount of evaporative cooling from animals.

ii. Forced ventilation, when natural ventilation is inadequate, the increased air movement using fans enhances convective heat loss.

**2) Biological strategies:** This counter measures aim to alleviate the negative consequences of heat stress using managerial techniques suitable and available to farmers in hot regions. The measures are divided into four groups (Figure 5).

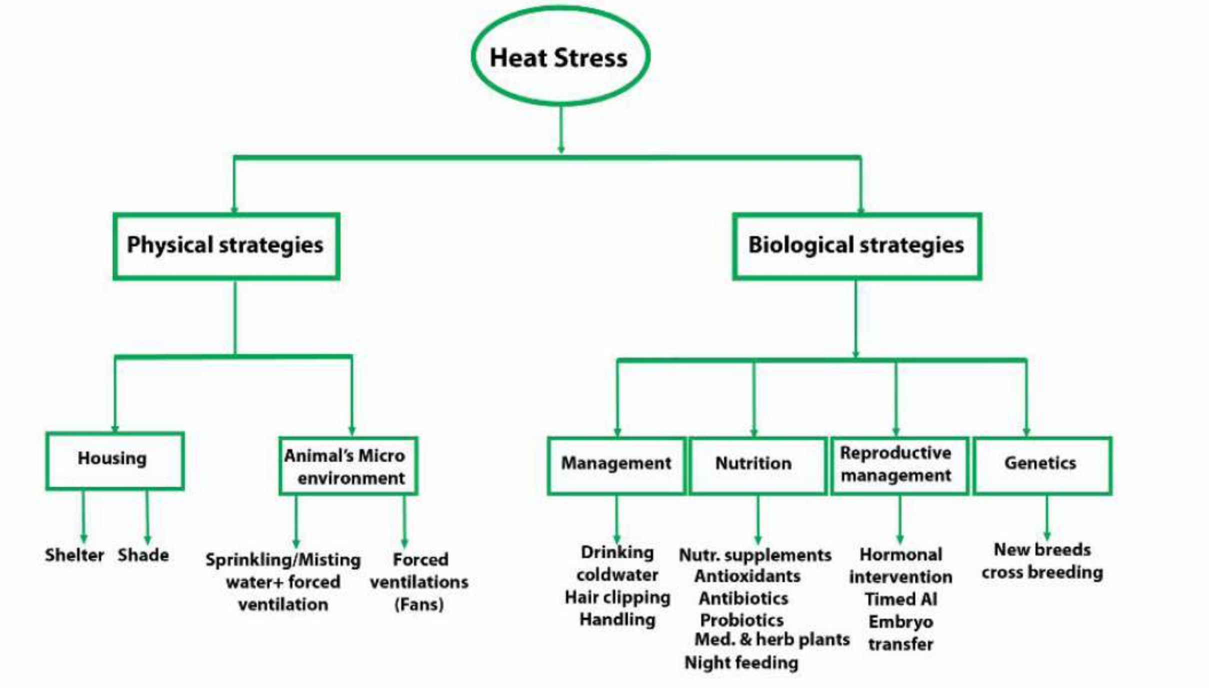


**Figure 5** : Corrective Measures to cope with heat stress

**a) Management modification**: based on available near-term adverse weather forecasting information, farm manager must make tactical decisions to reduce losses. Some of the possible tactical counter measures include:

i. Using a good quality drinking water at a temperature of 10-15 ºC (Yassein et al., 2008; Abdel-Samee et al., 2012; El-Tarabany, 2008; Asker and Ismail, 2012).

ii. Hair /Fur clipping: shortening the long and thick skin coverage of rabbits was reported to improve productivity under heat stress (Lukefar and Ruiz-Feria, 2003; El-Tarabany, 2008; Askar and Ismail, 2012).

iii. Handling animals: avoiding handling of rabbits during the hour of high heat load was helpful in alleviating the deleterious effect of heat stress. This will decrease metabolic heat production associated with muscular activity.

**b) Nutritional Strategies:**
Nutrition is a potential avenue to aid animal's adaptation in hot climates (Rhoads et al., 2013Baungard and Rhoads, 2012 Cervera and Fernandez Carmona, 2010). Heat stress shifts energy metabolism toward carbohydrates use and decrease lipids oxidation. Therefore, nutritional supplementation promoting glucose utilization may be beneficial. Several studies on rabbit show that various diet supplements improved many productive and reproductive performance in heat stressed animals (Table 4). Moreover, changing time of feeding and/or quantity and quality enhanced animal comfort (Davis et al., 2003). Further research uses various concentrations and duration of supplements should be conducted to further identify the ability of these supplements to alleviate the deleterious effect of heat stress.

**c) Reproductive managementtechniques**: such as hormonal intervention or therapy, AI and embryo transfer are considered useful techniques to avoid the unfavorable effects of heat stress on reproductive performance and improving fertility in hot seasons (Al-Katanani et al., 2002; Daader et al.,1997a,b )

**Table 4:** Nutritional strategies to alleviate the negative consequences of heat stress in rabbits

| Nutritional supplementation | References |
|---|---|
| Antioxidants | |
| Vitamin A | Daader et al., (1999); Daader et al., (2016) |
| Vitamin C | Iyeghe-Erakpotobor et al., (2013) |
| Vitamins E | AL-Zafry and Medan (2012) |
| Selenium | Kamel, (2011) |
| Antibiotics and Probiotics | |
| (Avoparcin;Flavomysin)(Baspro; lacto-sacc) | Abdel-Samee, (1995) |
| Medicinal, herb plants and oils extracts. | Abdel-Samee et al., (2012); Daader et al., (2016) |

**3) Genetic Manipulation**

a) Genetic development of heat tolerant livestock breeds has been a long sought offer solution to reduce productive and economic losses in animal industry. In rabbits, there are only few old studies, conducted mostly in Egypt and limited to estimation of heritability of heat tolerance characters such as, body temperature and respiration rates (Obeidah, 1975 Toson, 1993). Rabbits should be an excellent choice to develop a new thermo-tolerant line, since they have short generation interval, high reproductive potential, rapid growth rate and great genetic diversity (Rastogi, 2000).

ii. Cross-breeding: This is one of the most developed intervention measure to resolve constraints of heat stress in livestock industry. Breeding the available local breeds of rabbits "Baladi breeds" which are heat and diseases tolerant with the various highly productive breeds of the temperate zone (exotic breeds) should yield generation superior to the local ones in productivity performance. Recently, a crossing research projects between Spain(heat tolerant high prolific breed) and Egypt (local Baladi breeds)wereconducted and successful results were obtained (Iraqi et al., 2010; El-Raffa, 2010).

## IV . PERSPECTIVES OF FUTURE RESEARCH

Responding to the challenge of future additional heat stress from climate change in hot regions of the World, it is apparent that a new wave of research is mandated to address the global needs for food security. Much work has been done to document the detrimental effects of that stress on rabbits and other farm animals. However, there are many remaining open questions that need to be addressed to help increase animal productivity in hot regions. These gaps in our knowledge include, but not limited to the following:

1.Thermoregulation in newborn rabbit. There is considerable research evidence showing significant mortality rate in pre-weaned newborn rabbits. What are the contributing factors to mortality in newborn rabbit? Hull and Hull in 1982 concluded that each day passes for new born rabbits, preferred environmental temperature fell. This finding suggests that poor thermoregulatory responses may contribute to the high mortality rate. Mechanisms of heat production and heat loss avenues need to be studied in the newborn of various breeds of rabbits.

2.Development of a heat stress early warning system. In each of the developing countries, considerable research effect is needed to help animal producers to predict intensity and duration of heat stress. Such effort requires full cooperation between scientists at academic institutions, Ministry of Agriculture, and appropriate NGO_ S to collect required data to develop a Livestock Weather Safety Index (LWSI). It is not unusual to develop more than one index for a country with various climatic Zones. This has been done and these indices are reported as a part of weather forecast in some developing countries. An example, is the heat stress forecast maps for cattle described on the USDA website (WWW.are.usde.gov/main/dos.htm) Also, the University of Missouri developed the thermal Aid which is a smart phone app that combines information on both weathers and respiration rate that allow producers to make crucial decision regarding heat stress mitigations (http://thermalnet.missouti.edu/thermalAid/index.html).

Furthermore, during a tropical summer day, LWSI moves from one category to another depending on time of the day. Assessment of available thermal indices was reviewed by De Shazer, (2009).

3. What are the consequences of heat stress removal? Most reported scientific information has not addressed animal responses following removal of heat stress. These responses are termed compensatory responses Fig. (3). For a given heat load intensity and duration, the response may over shoot and thus compensatefor most, if not all, of the productive losses during the heat stress duration. With all this said, what can we do? Research should emphasize a good measure of the “Threshold Temperature Critical Limits” above which the compensatory responses fail to prevent productive losses. Identifying the threshold for productive traits losses (TTCL) will help rabbit producers to recognize the potential threat of heat stress and to make proactive plans for mitigations. It is always better to do a plan ahead time rather than reacting after heat stress starts, i.e. know when to interfere. Prevention is the key to manage heat stress. What are the mechanism underlying heat stress responses? Responses (physiological, biochemical, and behavioural) of rabbits to heat stress are well documented. However, the mechanisms underlying these responses are poorly understood (Figure 4). Future research should reveal the how and why a given response is displayed. Achieving better understanding of these mechanisms is fundamental to provide better mitigations measure to prevent or lessen decline in productivity.

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