## Original Research

# IMPLICATIONS OF BODY IMMUNITY OF PREGNANT WOMEN AFTER INTAKE OF MIXED MICRONUTRIENT-INFUSED WATER 

Dianita Rifqi P, Inna Sholicha F *, Aida Ratna W<br>Faculty of Health Sciences, University of Muhammadiyah Ponorogo, East Java, Indonesia<br>* Corresponding author: innasholicha@umpo.ac.id


#### Abstract

Introduction: Pregnant women are susceptible to infection due to changes in body physiology, the immune response mechanism must be maintained by maintaining body immunity through optimal nutritional fulfillment to prevent exposure to Covid-19 and certain diseases, one of which is infused water Lemon (Citrus Limon) Date Mix Method ( Phoenix Dactylifera). Methods: The research design used pre-experiments with the form of one group pre and post-tests took Purposive sampling with treatment with 40 respondents, age range 21 years old - 35 years old and age range over 35 years old conducted in August 2022 in Ponorogo Regency East Java Indonesia, with saphiro-wilk \& Wilcoxon test data for normality test and T-test data analysis. Result: From paired t-test with sig value. (2 tails) 0.037 is smaller than the p -value $(0.005)$ so it means that there is a difference between before and after giving infused water Lemon (Citrus Limon) Mixed Dates (Phoenix Dactylifera) Conclusion: There is a difference between before administration and after administration of infused water Lemon (Citrus Limon) Mixed Dates (Phoenix Dactylifera). Lemon contains water and a mix of dates that are rarely consumed by pregnant women which in fact after consumption can ward off various diseases that are proven to increase body immunity.


Keywords: Body Immunity, Micronutrient, Infused Water, Pregnant

## Introduction:

Pregnant women are prone to infections caused by changes in body physiology and immune response mechanisms (Wu, 2020). In pregnancy, fetal growth, as well as the maintenance of maternal, and fetal health, require a balance of immune responses(Burwick et al., 2021). Infused water is a piece of some fruits that will be mixed with cooked water and then allowed to stand for a while in the refrigerator (6-12 hours) to be able to remove the juice. Three important nutritional elements such as water, minerals, and vitamins can overcome pregnant women who are dehydrated while in pregnant women (Kaban et al., 2021)

In the 2021 period, many regions reported an increase in cases of deaths of pregnant women due to Corona. One of them, as happened at Dr. Soetomo Hospital, Surabaya, East Java, as many as 28 pregnant women due to exposure to Covid-19 died in the period July-August 2021 (Refrizal, n.d., 2021). Then since February 2022, Ponorogo entered level II PPKM (Enforcement of Restrictions on Community Activities) based on the assessment of the Indonesian Ministry of Health. Covid-19 cases in Ponorogo continue to decline.

The need for nutrients for pregnant women requires a variety of foods for the maintenance, growth, and development of the fetus and as a breastfeeding reserve, therefore adequate micronutrients and macronutrients are needed such as rice, vegetables, fish, meat, and fruit, including vitamins from foodstuffs. (Damayanti et al., 2017). Infused lemon water is believed to contain vitamin C which is beneficial for the body. Vitamin $C$ is a type of water-soluble vitamin and plays a role in warding off various diseases (Munir \& Munir, 2020). According to the USDA Nutrient Database, lemons are richer in vitamin C and folic acid than lime, which is 39 mg of vitamin C and $20 \mu \mathrm{~g}$ of folic acid in 100 grams of lemon juice, while in 100 grams of lime there are 30 mg of vitamin C and $10 \mu \mathrm{~g}$ of folic acid, which functions as an antioxidant, helps the development of blood cells, blood as well as neutralizing free radicals(Kadhim Hindi \& Ghani Chabuck, 2014). Date palm water has a vitamin C content of $2.64 \mathrm{mg} / \mathrm{ml}$, it is necessary to consume date palm water as much as $28-34 \mathrm{ml}$, dates have an energy of as much as 277 kcal, with carbohydrates of 74.97 g , protein $1,81 \mathrm{~g}$, vitamin A with 149 IU , folic acid 15 mcg , potassium 696 mg , magnesium 54 mg , calcium 64 mg , and beta carotene 89 mg (Putri et al., 2020). Reviewing the special background of pregnant women by implementing health protocols and maintaining the body's immunity by fulfilling optimal nutrition will reduce the risk of exposure to COVID19 and susceptibility to certain diseases.

## Methods

The research design used pre-experiments with the form of one group pre and post-test taken purposive sampling with treatment with 40 respondents from a population target of 60 respondents, with inclusion criteria age range 21 years - 35 years and age range over 35 years and attended pregnant class activities and has entered trimester 2 and 3. This research is August 2022 in Ponorogo Regency. East Java Indonesia. Before the research took place, it had been tested ethically and declared to have passed ethics Muhammadiyah University with no "Ethical Exemption" No.167/ER/KEPK/2022, This research procedure used this research material, namely 1000 ml bottled water, 1000 ml boiled water, Khalas dates, Lemon. Each ingredient is soaked in boiled water for 6 hours with the composition of dates per 1000 ml is 7 grains with 1 lemon size medium weight $\pm 100$ grams cut into pieces. The research procedure was treatment consuming infused water with the ingredients mentioned. The procedure for all treatments and without observed for 14 days and monitored using a video call. On the last day of the study, the respondents were given questionnaires to evaluate the results of treatment. The resulting data were analyzed using the $T$-test $(\alpha=5 \%)$. Before the T-test is carried out, the result data is tested first the ability norm of data distribution will be shapiro-wilk, if the data is not normally distributed then use the Wilcoxon n test with statistical program SPSS version 22.

## Results

Based on the results of research conducted in August 2022 on the Implications of Body Immunity Based on Infused Water Lemon (Citrus Limon) Mix Dates (Phoenix Dactylifera) for Pregnant Women the results :
Table 1: Socio-demographic Characteristics of Respondent

|  | Characteristics | Frequenc <br> $\mathbf{y}$ | Percent | SD |
| :---: | :--- | :---: | :---: | :---: |
| Periods of <br> Pregnant | Trimester 2 | 40 | 100.0 | 0.00000 |
| Age of <br> Respondent | $21-30$ years old | 34 | 85.0 | 0.044650 |
|  | $31-35$ Years Old | 5 | 12.5 |  |
|  | 36 years Old and <br> more | 1 | 2.5 |  |
| Parity | Primipara | 24 | 60.0 | 0.496140 |
|  | Multipara | 16 | 40.0 |  |

The respondent's gestational age category entering TM 2 gestational age, namely the age range of 16 weeks - 28 weeks with the age range of respondents 21 years old, parity with primipara 24 respondents and over to 35 years old a total of 39 respondents with the age of 41 years old 1 person, then the following results were obtained:

Table 2. Characteristics of Respondent Frequency Distribution Based on Health Complaints Experienced Before Treatment and After Treatment in the Treatment Group

|  | Before <br> Treatment |  |  | After <br> Treatment |  |  |  | P Value |
| :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\mathbf{N}$ |  | $\%$ | Average <br> Value | $\mathbf{N}$ | $\%$ | Averag <br> e Value | Differen <br> ce |
| Flu | 10 | 50.0 | 1.4 | 5 | 30 | 1.25 | 0.15 | $<0.001$ |
| Cough | 6 | 30.0 | 1.7 | 1 | 5.0 | 1,59 | 0,11 | 0.034 |
| Tired | 8 | 40.0 | 1.6 | 8 | 40.0 | 1.6 | 0.00 | $<0.001$ |
| Diarrhea | 0 | 0.00 | 0 | 2 | 10.0 | 1.95 | -1.95 | 0.421 |
| Nausea | 0 | 0.00 | 0 | 2 | 10.0 | 1.95 | -1.95 | 0.330 |

Based on the data obtained from the results of the study, it is stated in the table above that some respondents experienced complaints before treatment, the most were flu cough and fatigue, while after treatment flu cough complaints decreased with a difference in the average value before treatment 1.4 and after treatment 0.15 then for cough from the average value before treatment 1.7 and after treatment the average value was 1.95 .

Table 3. Characteristics of Frequency Distribution of Respondents Based on Discomfort during Pregnancy (Complaints) Factors Experienced Before Treatment and After Treatment

|  | Before Treatment |  | Mean | After Treatment |  | Mean | P-Value |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | N | \% |  | N | \% |  |  |
| Severe Complaints | 4 | 10. | 2.1000 | 3 | 7.5 |  | . 037 |
| Moderate Complaints | 12 | 30. |  | 0 | 0 | 2.650 |  |
| Healthy and no complaints | 24 | $\begin{gathered} 60 . \\ 0 \end{gathered}$ |  | 37 | 92.5 |  |  |

based on the data, there is a difference in the average value of the pre-test results of 2.1 which means that the average has a moderate level of immunity where the general condition has moderate complaints, then the post-test results are known to have a change in the mean value of 2.65 which can be concluded that the general condition level of the condition is good, no complaints and healthy. it can be seen that the paired t pre and post-test results obtained a sig value (2tailed) of 0.037 with a $p$-value of 0.05 . from the test value of $p$-value OF $0.037<0.05$. so it is concluded that h0 is rejected, meaning that there is a difference between before giving and after giving infused water lemon (citrus limon) mixed dates (phoenix dactylifera).

## Discussion

The gestational age category of respondents entering TM 2 gestational age, namely the age range of 16 weeks - 28 weeks with maternal age is a productive age that is not included in the high risk of pregnancy. Pregnancy is divided into 3 trimesters, The first trimester of pregnancy starts from 0-14 weeks, the second trimester starts from weeks 14-28 weeks, and the third trimester of pregnancy starts from weeks 28-42 weeks The thing that pregnant women will experience the many symptoms of hormonal changes, one of which is hormones in the early days of pregnancy, where these changes cause many physiological reactions that can occur in the body (Paninsari et al., 2021). It must be recognized that a successful pregnancy consists of three specific stages of trimesters 1,2 , and 3 , each of which is faced with different immunological challenges (Chen et al., 2020). The immune system is the body's protective system from diseases caused by various microorganisms with the principle of maintaining a balance of conditions inside and outside the body. Then in terms of physicality, the mother herself has a relatively productive age that does not have a high risk, this is very supportive of the health of the mother and fetus during pregnancy.

In terms of the immune system, it has the potential to store memory of specific antigens that have infected the body so that it does not require a long recovery time (Susilawati et al., 2019). Characteristics of the mother's immune system during pregnancy are important for understanding how the mother's immune system maintains fetal allogeneic tolerance (Morelli et al., 2015). It can also provide strategic information in efforts to prevent the death of pregnant women due to the effects of infection, in addition to seeking optimal protection due to maternal vaccination for maternal and fetal protection after birth (Abu-Raya et al., 2020). Some respondents experienced complaints before treatment, most of which were flu cough, and fatigue, while after treatment cough flu complaints decreased with a difference in average values before treatment 1.4 and after treatment 0.15 then for a cough from the average value before treatment 1.7 and after treatment average value 1.95 . The mother's immune system plays an important role in the formation, maintenance, and completion of a healthy pregnancy. However, the specific mechanisms used to achieve this goal are not well understood. Various cells and molecules of the immune system are key players in the development and function of the placenta and fetus.

In addition, from the results of the study, there was a difference between before giving and after giving Infused Water Lemon (Citrus Limon) Mixed Dates (Phoenix Dactylifera. The pre-post test result of 2,100 then the post-test result value of $2,65,0$ which can be concluded to have a positive difference with a good general incidence rate. Infused water is drinking water that is included with additional pieces of fruit, vegetables, or even spices, so that juices from fruits or vegetables and spices, soaked in ordinary water will come out, which gives flavor, and has various benefits for those who drink the infused water (Munir, 2020). The potential of water infusion as a natural antioxidant that has a good taste and is one of the micronutrient particles containing antioxidants that have refreshing and delicious characteristics has been presented to the public who can take alternatives to minimize the increase in mortality which is the effect of degenerative diseases caused by exposure to free radicals. (Fibonacci, 2020). Infused lemon water is believed to contain vitamin C which is beneficial to the body. Infused water is not added with sugar and other additives so that the aroma and taste come from the fruit soaked in it (Pratiwi, 2020). Vitamin C is a type of vitamin that is soluble in water and plays a role in warding off various diseases (Munir \&; Munir, 2020). Half a cup (106 grams) of lemon (without skin) can provide 56.2 milligrams ( mg ) of vitamin C - an essential nutrient for both mother and baby (Jablonski, 2019). This is supported by the results of Ayu's research (2020) that lime (Citrus aurantiifolia) is one of the fruits rich in vitamin $C$ with a content of up to $27 \mathrm{mg} / 100 \mathrm{~g}$. Lime juice is usually used as a flavoring for dishes, drinks, drinks, or citric acid-making ingredients. In addition, lime as a natural herb also has properties as a cough medicine, phlegm decay (mucolytic), urine decay (diuretic), and sweat, and helps the digestive process (Ayu et al., 2020). Lemons or citrus fruits are the largest source of powerful vitamins B and C (thiamine, pyridoxine, niacin, riboflavin, pantothenic acid, and folate). They are also the cause of phytochemicals, such as flavonoids, limonoids, and carotenoids. The phytochemicals of this lemon or grapefruit have antifungal, anti-thrombotic, and antiinflammatory agents. Previously they have shown that lemon products are a rich source of vitamins, minerals, and dietary fibre. However, bioactive and non-nutritional compounds in oranges are considered to minimize the risk of various types of chronic diseases (Ahmed, 2021). The results of the study of vitamin C levels in infused water of oranges ajwa dates amounted to $31 \mathrm{mg} / 100 \mathrm{~g}$ (Amaliyyah, 2021). The immune system response has two parts, namely innate immunity and adaptive immunity (da Silveira et al., 2021). Lemon water is rich in magnesium and calcium which are very good for bone health (Coal, 2017). Not only the mother's bone health but also the fetus. The potassium content in lemon is very good for the baby's nerve cells. As long as you don't have stomach problems, drinking lemon water during pregnancy is still allowed at a dose of about one glass per day (Kundaryanti \&; Leniyana, 2021). There are no studies showing that lemons themselves boost immunity and are beneficial for fetal development, but some top-rated nutritionists contain vitamin C that can boost immunity. The advantage of infused water is that the nutritional content is maintained because there is no crushing process like juice made. Water infusion is made by putting pieces of fruit in water and soaking them in a cooler or room temperature for several hours.

During pregnancy, great adaptations occur to the mother's immune system to protect the future mother and her baby from pathogens while avoiding an adverse immune response to the allogeneic fetus. The human body has an immune system to fight foreign objects (pathogens) that will enter the body, commonly called body immunity. Body immunity is the defense of the human body in dispelling pathogens such as bacteria, viruses, and other pathogens. If the pathogen manages to enter, the body will detect if the pathogen comes from outside the body, so the body will react in a coordinated manner with cells and compounds in the body and will react to the pathogen (Adijaya \&; Bakti, 2021). The data from this study is also almost the same as this study conducted by Ula (2018) on pregnant women in the third trimester to carry out alternative medicine by utilizing ajwa date meat extract (Phoenix dactilyfera L.), because date meat extract can improve the immune system by counting the types of leukocytes so that it can be used in handling various diseases, especially in embryos during pregnancy (Ula, 2018). Date fruit is a food that contains high energy with ideal composition, it contains carbohydrates, tryptophan, omega-3, vitamin C, vitamin B6, Ca2 +, Zn, and Mg. Date fruit contains very high fiber, besides that, it also contains potassium, manganese, phosphorus, sulfur iron, sulfur, calcium, and magnesium which are very good for consumption (Widowati et al., 2019). Based on Romadloniyah research that has been conducted on 56 pregnant women and those who have given birth, there are $60 \%$ of women consume dates during pregnancy stating that dates can strengthen the womb and speed up the treatment process from the estimated date. And another $15 \%$ of women stated that them had experienced a miscarriage before consuming dates (Romadloniyah et al., 2020). Phoenix dactylifera L (Date) belonging to the family of Arecaceae, called 'Nakhla' and 'Tree of Life' by the Arabs, is considered one of the oldest cultivated fruit trees. Various parts of this plant are traditionally claimed to be used for the treatment of a wide spectrum of diseases including memory impairment, fever, loss of consciousness, and nervous disorders. There is tremendous interest in this plant as evidenced by considerable work in recent decades (Nurhikmah, 2016). Scientific research on the immunostimulant effects of date palm fruit has also been conducted. In vitro, the administration of date water extract is proven to increase immune system activity characterized by an increase in the number of IFN- $\gamma^{+}$CD4+ cells, one type of white blood cell that is important in protecting the body against infection (Karasawa et al., 2011). Another study showed the activity of ajwa date water extract which is known to increase the number of natural killer (NK) cells in test animals. NK cells are known to include innate immune cells, which are important for the body's resistance to viral infections and (Priani, 2021).

## Conclusion

There is a difference between before the study and after the study infused water Lemon (Citrus Limon) Mix Dates ( Phoenix Dactylifera). Lemon contains water and a mix of dates that are rarely consumed by pregnant women which in fact after consumption can ward off various diseases that are proven to increase body immunity.

## ACKNOWLEDGMENT

thanks to all midwives (health center siman in ponorogo east java Indonesia) for helping the researcher with observations of respondents, and also for all respondents with participation.

## Conflicts of Interest

The author declares no conflicts of interest.

## References

- Abu-Raya, B., Michalski, C., Sadarangani, M., \& Lavoie, P. M. (2020). Maternal Immunological Adaptation During Normal Pregnancy. Frontiers in Immunology, 11(October), 1-18. https://doi.org/10.3389/fimmu.2020.575197
- Adijaya, O., \& Bakti, A. P. (2021). Improving the body's immune system in the face of the COVID-19 pandemic. Jurnal Kesehatan Olahraga, 51-60.
- Ahmed, A. S. and M. (2021, November). Citrus Fruits_ Nutritive Value and Value-Added Products _ IntechOpen. Intochpent.
- Amaliyyah, R. (2021). Analisa Kadar Vitamin C Pada Infused Water Kurma Ajwa Jeruk Nipis dan Kurma Ajwa Nanas Madu. Stikes Insan Cendikia Jombang.
- Ayu, D. F., Sormin, D. S., \& Rahmayuni. (2020). Study of Making InfusedWater from Bauh Dates (Phoniex Dactylifera) with the Addition of Lime ( Citrus Aurantiifolia ). JTIP Indonesia, 12(02), 10-16.
- Batubara, N. A. (2017). (Citrus limon ) Against Flow Rate, Salivary Ph Value And Colony Number Of Taphylococcus Aureus (In Vivo) University Of North Sumatra.
- Burwick, R. M., Lokki, A. I., Fleming, S. D., \& Regal, J. F. (2021). Editorial: Innate Immunity in Normal and Adverse Pregnancy. Frontiers in Immunology, 12(February), 10-13. https://doi.org/10.3389/fimmu.2021.646596
- Chen, M., Zeng, J., Liu, X., Sun, G., Gao, Y., Liao, J., Yu, J., Luo, X., \& Qi, H. (2020). Changes in physiology and immune system during pregnancy and coronavirus infection: A review. European Journal of Obstetrics and Gynecology and Reproductive Biology, 255, 124-128. https://doi.org/10.1016/j.ejogrb.2020.10.035
- da Silveira, M. P., da Silva Fagundes, K. K., Bizuti, M. R., Starck, É., Rossi, R. C., \& de Resende e Silva, D. T. (2021). Physical exercise as a tool to help the immune system against COVID-19: an integrative review of the current literature. Clinical and Experimental Medicine, 21(1), 15-28. https://doi.org/10.1007/s10238-020-00650-3
- Damayanti, D., Pritasari, \& L, N. T. (2017). Gizi Dalam Daur Kehidupan. KEMENKES RI.
- Fibonacci, A. (2020). Antioxidant Activity of Nabeez Water from Ajwa Palm Date Fruits (Phoenix dactylifera L) as a Favourite Drink of the Prophet Muhammad SAW. Journal of Physics: Conference Series, 1594(1). https://doi.org/10.1088/1742-6596/1594/1/012001
- Jablonski, N. (2019). Is Lemon Good for Pregnancy Plus, Recipes for Nausea and More. Health Line. https://www.healthline.com/health/pregnancy/is-lemon-good-for-pregnancy
- Kaban, F. Y., Vetriyasa, B., Khairani, D., \& Ginting, C. N. (2021). The Effect Of Infused Water Lemon (Citrus Limon) And Red Ginger (Zingiber Officinale Rubrum Variety) To Reduce Nausea-Vomiting In First Trimester Pregnant Women At Pratama Mariana Medan Clinic In 2020. Jurnal IImiah Kebidanan Imelda,7(1),1-5.https://doi.org/10.52943/jikebi.v1i2.451
- Kadhim Hindi, N. K., \& Ghani Chabuck, Z. A. (2013). Antimicrobial activity of different aqueous lemon extracts. Journal of Applied Pharmaceutical Science, 3(6), 74-78. https://doi.org/10.7324/JAPS.2013.3611
- Kundaryanti, R., \& Leniyana. (2021). Efficiency of Ginger and Lemon Water Decoction in Hyperemesis Gravidarum. National University.
- Morelli, S., Mandal, M., Goldsmith, L. T., Kashani, B. N., \& Ponzio, N. M. (2015). The maternal immune system during pregnancy and its influence on fetal development. Research and Reports in Biology, 171. https://doi.org/10.2147/rrb.s80652
- Munir, N. F., \& Munir, N. W. (2020). Infused Water Jeruk Lemon (Citrus Limon) Dan Jahe Merah (Zingiber officinale Roxb.var. Rubrum). Jurnal Ilmiah Kesehatan Iqra, 8(2), 94-99.
- Paninsari, D., Sandi, H., Yani, R., Sari, L. M., \& Damaiyanti, P. (2021). Description Of Knowledge Of Pregnant Women In Trimester III About The Impact Of Fatimah Grass

Consumption In The Mariana Clinic Medan City. JurnalKesehatan LLDIKTI Wilayah, 1(2), 1923.

- Pratiwi, S. W. (2020). PThe effect of giving infused water dates to changes in potassium levels in Poltekkes students of the Ministry of Health Yogyakarta with prehypertension. Poltekkes Kemenkes Yogyakarta, 16(3), 1-21http://eprints.poltekkesjogja.ac.id/1134/4/4. Chapter 2.pdf
- Priani, S. E. (2021). The immunostimulant activity of Tibb an-Nabawi natural products: a literature review Kajian beberapa bahan alam berbasis thibbun nabawi yang memiliki aktivitas peningkat imunitas. Jurnal Ilmiah Farmasi (Scientific Journal of Pharmacy), 17(1), 46-55. http://journal.uii.ac.id/index.php/JIF46
- Putri, E. B. P., Putri, F. K., \& Sulaiha, S. (2020). Comparison Of Flavonoid And Vitamin C Levels In Goji Berry Infused Water (Lycium Barbarum) And Date Nabeez Water (Phoenix Dactylifera L.). Medical Technology and Public Health Journal, 4(1), 32-37. https://doi.org/10.33086/mtphj.v4i1.1458
- Refrizal. (n.d.). Reduce the mortality rate of pregnant women due to Covid-19. In DPR.Go.id. DPR.Go.id.
http://www.dpr.go.id/berita/detail/id/28730/t/Perubahan+APBN+2020\%2C+Pemerintah+Tak+ Mudah+Hadapi+Tantangan
- Romadloniyah, N. S., Oktaviani, F. N., \& Arifin, I. (2020). Dates (Ruthab) To Prevent Miscarriage And Smooth Labor. An-Nadaa: Jurnal Kesehatan Masyarakat, 7(1), 55. https://doi.org/10.31602/ann.v7i1.2976
- Susilawati, Y., Moektiwardoyo, M., Halimah, E., Wicaksono, I. A., Ramadhania, Z. M., \& Prastiw, S. S. (2019). Immunomodulatory Activity of Papaya Leaf Ethanol Extract (Carica papaya L.) by Bacterial Induction Method and CBC-Diff. Jurnal Sains Dan Kesehatan, 2(4), 303-310.
- Ula, anis mukaromatul. (2018). Effect Of Ajwa Date Flesh Extract (Phoenix Dactylifera L.) Against Hemoglobin Levels In Pregnant Mice (Mus musculus). Diss. UIN Sunan Ampel Surabaya, 27.
- Widowati, R., Kundaryanti, R., \& Lestari, P. P. (2019). The Effect Of Giving Date Juice On The Increase In Hemoglobin Levels In Pregnant Women. Al-Azhar Indonesia Seri Sains Dan Teknologi, 5(2), 60-65.
- Wu, Y. T. (2020). Re: Novel Coronavirus COVID-19 in late pregnancy: Outcomes of first nine cases in an inner city London hospital. European Journal of Obstetrics \& Gynecology and Reproductive Biology, 251(January), 266-284.

