PISUM SATIVUM (LINN):
m-XYLOHYDROQUINONE AS AN ORAL CONTRACEPTIVE
A CRITICAL EVALUATION

By
S. N. Sanyal

It has been reported previously that Pisum Sativum (the common field pea) acts as a contraceptive. A series of animal experiments on white rats were performed and the results published (Sanyal, 1950–55) demonstrating its contraceptive effect due to the inhibition of the peripheral action of progesterone and consequent prevention of nidation of a fertilized ovum. Subsequently the active substance was located in the oil of the seeds, isolated in the pure state and its chemical nature determined. The synthesis of the active principle was also effected. The results of animal experiment on white rats with the synthetic active principle, m-xylohydroquinone, corroborated the previous experimental results. Further spectrophotometric studies in vitro as well, demonstrated that m-xylohydroquinone alone, and not its isomers, can interfere with progesterone. But in the language of Professor Swyer of the University College Hospital, London (England), to argue from rats to human beings is rather a risky procedure. After 25 months of trial on a large number (727) of human female subjects, this claim has been fully substantiated. This field trial was initiated at the instance of Dr. Clarence J. Gamble, of Boston, Mass., U.S.A., at the Baldeodas Maternity Hospital, Calcutta under the supervision of Dr. (Mrs.) S. Ghosh in June 1953. The results of first 12 months’ trial was published in November, 1954. Now the results of 25 months’ trial have been published.

SUMMARY OF THE RESULTS OF THE TRIAL

According to the report, the trial was divided into two series. The first series dealt with patients attending the out-patients clinic. Here the initial dose was administered by the health visitor herself, the second dose being handed over to the patient to be taken on a specified day. There was no certainty as to the
actual use of the second dose. The patient often failed to turn up on the appointed dates, leading to a lowering of the value of the trial. In the second series the health visitor went over to the respective homes of the patients on specified days and made them swallow the capsules in her immediate presence. Both the groups came from low-income strata of people, largely made up of lower middle class.

THE RESULTS

In the first series there were 473 patients with a preclinic rate of 65. Out of these 473 patients 46 were subsequently found out to have been pregnant before the use of the medicine and eliminated from the computation. The remaining 427 patients had a total of 2,167 patient months excluding a total of 236 months of omission. The clinic rate when all calculated was 31 and when two months of use were eliminated from the calculation, it was 27. In the second series there were 254 patients with a preclinic rate of 65. Here the trial lasted for 15 months. Out of 254 patients, 22 were detected pregnant before use and were eliminated from the calculation. The remaining 232 patients had a total of 1,465 patient months. The total clinic rate was 20 and when two months of use were eliminated the rate is 11. The average of the two series showed a total clinic rate of 26 and when two months of use were eliminated it was 20. Questions were raised from different quarters that this success might be due to protection from lactation. For this the results were recalculated eliminating the lactation months. In the first series, 336 patients had a total of 1,567 patient months, eliminating amenorrhoea months, and the rate became 37 when all calculated and 32 when two months of use were eliminated. Ninety-one patients with no menstruation were eliminated. In the second series 254 patients with a total 934 patient months had a pregnancy rate of 27 and eliminating two months of use it was 12. Forty-seven patients with no menstruation were eliminated. The average of two series gives a rate of 32 and 22. This conclusively shows a significant reduction in pregnancy rate as compared to the existing rate. As expected, the reduction was greater where better individual attention was given, as in the second series, to ensure that both the capsules were administered in near about the specified days – namely 16th and 21st days of the cycle in normal cases, or 7 and 12 days before the next expected date of menstruation. It may be surmised, however, that still better result might have been achieved if there were greater supervision and if only a smaller number of patients, say about 50, kept in charge of one health visitor. It will be found from the report that most of the patients were illiterate and could not properly and timely intimate through post cards, their dates of menstruation.

A number of significant and important facts are, however, available from
the report. It is definitely proved that the medicine is not an abortifacient. Sixty-eight patients used the medicine, over a number of months during the period of conception, which started prior to the beginning of method, but none of them aborted. The report also sets at rest any possible misgivings about permanent sterility. Fourteen patients conceived during their absence of one month or consecutively for two months. Out of 33 of the patients who dropped, it was found, during a short follow-up before the compilation of the result, that 8 patients conceived within three months of discontinuance of the treatment and 25 patients did not conceive during the observed period of six months. According to an available report (Guttmacher and Tistze, 1949) 30 per cent may conceive within the next ovulation and 30 per cent of the rest may conceive within the next three months or so. No further proof is needed to show that this medicine cannot bring about permanent sterility or any derangement in the reproductive mechanism. The report also clearly signifies that there is no damaging effect on babies born in cases of failure after the use of the medicine. Thirty-two failure cases attended the hospital for confinement. Out of these 27 gave birth to normal babies with weights varying from 5 to 8 pounds. There were 2 still-births and three miscarriages. This proportion is quite normal amongst similar subjects of low economic level. As regards its toxic effect nothing could have been detected, either acute or chronic (Sanyal, 1955).

**Comparison with Other Methods**

According to Finkelstein et al. (1952), in the unweighted mean pregnancy rate of 10 studies with jelly or cream alone as contraceptive, the actual pregnancy rate was 22.3. The median rate is 17 to 20. According to Whelpton et al. (1953), in a study in Indianapolis of relatively fecund protestant couples, the pregnancy rate varied as follows:

- Diaphragm and Jelly ................. 4
- Condom .................................. 7
- Withdrawal ............................... 10
- Jelly alone ............................... 11
- Suppository .............................. 16
- Douche .................................. 21
- Safe period ............................... 26

According to Tistze (1954), the pregnancy rate varied from 4 to 38 using different methods as contraceptives. A comparison of the above figures shows that this oral contraceptive, m-xylohydroquinone, can reasonably and favourably reduce the pregnancy rate.

**Further Statistical Data and Biometric Information**

Questions had been raised from different quarters as to whether this oral contraceptive will be equally effective in cases of young subjects where the fertility
Table 1 – Age grouping.

(1) 15 to 20 Years of Age:
<table>
<thead>
<tr>
<th>Total No. of patients</th>
<th>57</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinic Rate</td>
<td>97</td>
</tr>
<tr>
<td>Clinic Rate 35 (All calculated)</td>
<td>56 (2 months eliminated)</td>
</tr>
</tbody>
</table>

Average of Live birth per patient
- Still birth » » 2.43 ± 0.280
- Miscarrige » » 0.05 ± 0.095
- Child living » » 2.14 ± 0.089
Percentage of death of child 11.76 %

(2) 21 to 25 Years of Age:
<table>
<thead>
<tr>
<th>Total No. of patients</th>
<th>207</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinic Rate</td>
<td>74</td>
</tr>
<tr>
<td>Clinic Rate 24 (All calculated)</td>
<td>15 (2 months eliminated)</td>
</tr>
</tbody>
</table>

Average of Live birth per patient
- Still birth » » 3.57 ± 0.103
- Miscarrige » » 0.24 ± 0.055
- Child living » » 3.11 ± 0.100
Percentage of death of child 13 %

(3) 26 to 30 Years of Age:
<table>
<thead>
<tr>
<th>Total No. of patients</th>
<th>246</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinic Rate</td>
<td>65</td>
</tr>
<tr>
<td>Clinic Rate 33 (All calculated)</td>
<td>18 (2 months eliminated)</td>
</tr>
</tbody>
</table>

Average of Live birth per patient
- Still birth » » 5.18 ± 0.209
- Miscarrige » » 0.38 ± 0.089
- Child living » » 4.23 ± 0.170
Percentage of death of child 17.1 %

(4) 31 to 35 Years of Age:
<table>
<thead>
<tr>
<th>Total No. of patients</th>
<th>152</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinic Rate</td>
<td>63</td>
</tr>
<tr>
<td>Clinic Rate 31 (All calculated)</td>
<td>23 (2 months eliminated)</td>
</tr>
</tbody>
</table>

Average of Live birth per patient
- Still birth » » 6.88 ± 0.170
- Miscarrige » » 0.42 ± 0.063
- Child living » » 5.56 ± 0.151
Percentage of death of child 19.1 %
Table 1 – Age grouping (cont.).

(5) 36 and Above Years of Age:

<table>
<thead>
<tr>
<th>Total No. of patients</th>
<th>Preclinic Rate</th>
<th>Clinic Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>... 117</td>
<td>57</td>
<td>17 (All calculated)</td>
</tr>
<tr>
<td></td>
<td>16 (2 months eliminated)</td>
<td></td>
</tr>
</tbody>
</table>

Average of Live birth per patient .............. 8.77 ± 0.122
Still birth » » .............. 0.19 ± 0.055
Miscarriage » » .............. 0.87 ± 0.018
Child living » » .............. 6.84 ± 0.118
Percentage of death of child .............. 22.83 %

rate is high. The results were, therefore, differently tabulated according to age grouping, (vide Table 1) showing average parity in each group and also according to parity grouping (vide Table 2) showing the average age in each group. The pertinent biometric information has also been furnished. The results have also been represented in graphical forms.

In the evaluation of the pregnancy rates according to age-group it was noted that at the age-group between 15 to 20, the pregnancy rate is highest being 97. At the age-group 21 to 25 the rate is 74, at 26 to 30 it is 65, at 31 to 35 it is 63 and at 36 and above years of age it is 57. It is apparent that the pregnancy rate diminishes along with the progressing age. The clinic rate similarly for the corresponding age group 15 to 20 is 35, when all the months of use are calculated, and 56, when two months of use is eliminated. At the age-group 21 to 25 it is 24, at the age-group 26 to 30 it is 33 and 18, at 31 to 35 it is 31 and 23 and at 36 and above years of age the rates are 17 and 16. Also when the pregnancy rates were evaluated according to parity grouping, the rates

![Fig. 1. Bar Representations. X = With lactation months. Y = Without lactation months. 1 = Preclinic rate. 2 = Clinic rate, all calculated. 3 = Clinic rate, two months eliminated.](image-url)
**Table 2 – Parity grouping (according to live births).**

(1) *With 1 Live Birth:*
- Total No. of patients: 22
- Average Age: 23.45 ± 1.50
- Preclinic Rate: 34
- Clinic Rate: 18 (All calculated)

(2) *With 2 Live Births:*
- Total No. of patients: 72
- Average Age: 22.25 ± 1.47
- Preclinic Rate: 55
- Clinic Rate: 35 (All calculated)

(3) *With 3 Live Births:*
- Total No. of patients: 117
- Average Age: 24.30 ± 1.13
- Preclinic Rate: 52
- Clinic Rate: 12 (All calculated)

(4) *With 4 Live Births:*
- Total No. of patients: 120
- Average Age: 26.33 ± 1.01
- Preclinic Rate: 58
- Clinic Rate: 42 (All calculated)

(5) *With 5 and Above Live Births:*
- Total No. of patients: 448
- Average Age: 31.69 ± 0.95
- Preclinic Rate: 68
- Clinic Rate: 26 (All calculated)

Total No. of patients: 779 (Including 52 registered patients who did not use the medicine).

<table>
<thead>
<tr>
<th>Event</th>
<th>Average (± Standard Deviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Live birth per patient</td>
<td>5.15 ± 0.401</td>
</tr>
<tr>
<td>» Still birth</td>
<td>0.12 ± 0.063</td>
</tr>
<tr>
<td>» Miscarriage</td>
<td>0.40 ± 0.230</td>
</tr>
<tr>
<td>» Child living</td>
<td>4.32 ± 0.541</td>
</tr>
<tr>
<td>» Age</td>
<td>27.39 ± 0.98</td>
</tr>
</tbody>
</table>

were as follows: The pre-clinic pregnancy rate of patients with one live birth is 34, with two live births it is 55, with three live births it is 52, with four live births it is 58, with five and above live births the rate is 68. Here it is noted that the pregnancy rate rises along with the increase in number of live births. The clinic rates too, corresponding to the number of live births as noted, are
Age-Grouping Curve. 1 = Preclinic rate. 2 = Clinic rate, all calculated. 3 = Clinic rate, two months eliminated.

Parity Grouping curve. 1 = Preclinic rate. 2 = Clinic rate, all calculated.

18, 35, 12, 42, and 26, when all the months of use were calculated. This observation that the increase in pregnancy rate along with the increase in the number of live births, is in agreement with the statistical information already known. The clinic rates too in each group show reasonable reductions (Graphs 2 and 3).
Further in the age-group curve showing a progressive fall in the pregnancy rate along with the progressive age, there is a notch in the curve showing a comparative halt at the age group of 31 to 35. This may probably be due to some psychological factor. Some struggle might be going on between «to have or not to have» on the probable approach of menopause and the apprehension of cessation of conception. In the clinic rate too there is a rise which may be due to wilful neglect, and indicates perhaps the same motive.

Records of certain number of deaths out of live-births, is available. The percentage of death of children progressively rises along with the progressing age and increase in the number of child-births. This may be due to economic pressure and want of care on the part of the mothers consequent upon the increase in numbers.

**Different Methods of Calculations**

There is divergence of opinion as to the method of calculation of pregnancy rate and no statistical standard is available. This gives rise to unnecessary anomalies and criticisms. Common method of calculation of fertile years is to find out the difference between the present age and the age at consumption of marriage and to deduct 3/4th of a year for each full term and 7/8th of a year for each miscarriage. According to this method of calculation the pregnancy rate in India is 60 to 70 and in U. K. or U. S. A. it is 40 to 50. The rate calculated from the present survey is 65. This seems more reasonable and in conformity with general statistics. But there is a section who are inclined to consider the period of lactational amenorrhoea and the calculated pregnancy rate becomes unnecessarily high. It seems that big unknown variant is likely to be introduced in this method of calculation. According to Pearl Reymond, no consensus has been reached as to the best method of controlling the factor of lactation which is thought to be associated with infecundity (1937). Period of lactational amenorrhoea is very variable, ranging one month to one year or more. No standard can ever be set at, say 3 months or 6 months. Many subjects start menstruating on the month following delivery. In poorer classes where there is little possibility of stoppage of sex relationship by segregation or use of separate rooms, menstruation often starts early. This may be due to psychological stimulation. There is a common belief that so long as the baby is suckling there is no chance of conception and many mothers suckle their babies deliberately for two years or more with this idea in view. Physicians discourage this practice for fear of superinvolution of uterus. Actually this belief has no foundation on facts. In large number of subjects and even in the trial conducted at the Baldeodas Maternity Hospital, it has been noticed that pregnancy started within the lactation period without menstruation intervening even once. At any rate if it is desirable to eliminate some fraction of a year or the months of lactation amenorrhoea in determining the clinic rate, it is also
necessary to eliminate similar period for full term from the fertile years in the calculation of the preclinic rate. In this case the preclinic rate becomes unnecessarily high and the clinic rate too becomes high, the final ratio remaining almost the same.

Location of the Clinic
There have been criticisms regarding the location of the clinic in a maternity hospital. If the question of lactation amenorrhoea is not to be considered these objections can be ruled out. Such contraceptive clinics should rather be housed in a maternity hospital where female subjects are in known surroundings, than anywhere else. In India there are many subjects who fight shy of public advertising the fact that they are using a contraceptive measure. They attend the hospital under the pretext of periodic examination for some disorders. In addition there are ample facilities for periodic examinations for detection of pregnancy and duration of gestation. In fact The Family Planning Commission of the Government of India has recommended such locations.

Advantages of the Method
The advantages of this oral contraceptive is two-fold. Apart from the prevention of nidation of a fertilized ovum by preventing progesterone preparing the lining of the uterus for the reception of the fertilized ovum, it acts as a spermicidal by being excreted into the cervical secretion. It has recently been reported by Dr. von Kaula, M. D. of the University of Colorado, Medical Centre, Colorado, U. S. A., in a personal communication that xyloquinones and hydroquinones are excreted into the cervical secretion and the concentration over there is about three to five times stronger than that of the blood, and the substances have spermicidal activity. Moreover this oral form of contraceptive requires no preparation, no intelligence on the part of the user and there is no cause for repugnance even with the fastidious subjects. It is suitable for all classes of people irrespective of their faith and belief and at the same time it is suitable for all pockets. By the introduction of such simple method, the real suffers, whose necessity is greatest, can really be helped and in this way the society and ultimately the nation will be benefited in the long run.

Supporting Facts
Apart from the result of Professor Nag, published in 1937, independent corroborations have been received from Dr. Menachre, Gustav, Bailerr, Martin of the National Drug Co. of Philadelphia in 1953. In their experiments they have determined that when mice are fed on Pisum Sativum at 20 per cent level, litter formation is diminished and at 30 per cent level it is completely abolished. Apart from current experimental proofs, there was published in 1954 a demographic evidence about the population of Tibet which is constant for the last
200 years. The principal diet of the Tibetans is barely, peas (Pisum Sativum), meat and dairy products. Polyandry is not significant or even important factor, as we know from the publication of Swami Pranavanand. According to him in Tibet, there is monogamy, polygamy, child marriage and even widow remarriage.

**Future Possibilities**

It seems that in near future this oral contraceptive, m-xylohydroquinone, may be administered just after the cessation of menstruation, i.e., in the oestrogenic phase. This might help much by elimination of calculation of days especially in cases of illiterate subjects. Experiments are in progress in this laboratory and there is definite indication, both in the spectro-photometric studies and also in biological studies on rats, that m-xylohydroquinone can antagonize oestrogen as well. Further this may furnish a clue to the metabolism of oestrogen and progesterone by some such substance metabolized by an enzyme or enzyme system.

**SUMMARY**

1. From the detailed studies of the results of two years' trial on a large population sample, it is now possible to pronounce with certainty that this oral contraceptive, m-xylohydroquinone, the active principle of Pisum Sativum, can reasonably reduce the pregnancy rate from the usual level. It is effective for all age-groups and all parity-groups and is not attended with any risk of abortion, permanent sterility or deformity in the baby born in failure cases. It is not toxic to the human system. A cent percent success is not claimed.
2. Some relevant questions of protection from lactation, location of the clinic in maternity hospital, etc. have been discussed.
3. Detailed statistical verifications with graphs, etc. have been supplied and relevant biometric information given.
4. Some experimental and demographic proofs have been supplied.

**ACKNOWLEDGMENTS**

Thanks are due to Dr. Clarence J. Gamble of Milton, Mass, U. S. A., for sponsoring the trial, for his unfailing help and advice and to Asit Chaudhuri and Ajit Chakravarty of the Statistical Department, Writers Building, Government of West Bengal, for the statistical calculations.

**REFERENCES**