EFFECT OF CALCIUM AND VITAMINS A AND D ON INCIDENCE OF PREGNANCY TOXÆMIA

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The following experiment, carried out at St. Mary Abbots Hospital,* London, during 1936, was devised to determine whether the mere addition of calcium and vitamins A and D to the dietaries of patients attending the antenatal clinic would have any effect on the incidence of toxæmic symptoms.

Apparently healthy women, not more than twenty-four weeks' pregnant, were divided by the sister into two groups when they first attended at the clinic, no attention being paid to their previous obstetric histories. They were divided at random in the following manner:

An equal number of blue and white beads were placed in a box. Each woman accepted for the experiment was asked to draw a bead from the box. Those who drew blue beads were placed in Group A while those who drew white beads were placed in Group B. The beads drawn out were placed in a separate container.

The patients in Group A were requested to take daily, for the remainder of their pregnancies, calcium lactate 20 grains, vitamin A (11,000 International units) and naturally occurring vitamin D (450 units); while those in Group B served as controls. The oil containing the vitamins was supplied in capsules, of which four were to be taken every day, while the calcium lactate was distributed in the form of tablets.

No advice concerning diet was given to either group of patients.

Each group contained 50 women. In Group A 25, and in Group B 25, were primigravidae. The symptoms were recorded by independent antenatal officers who had no knowledge as to which patients were receiving the additional substances. All patients developing albuminuria, showing hypertension, or suffering from excessive vomiting, or oedema were admitted into the antenatal ward. Those suffering from insomnia or severe headaches were also advised to go into hospital.

RESULTS

The results obtained are shown in Tables I and II. The symptoms of the patients admitted for albuminuria and hypertension are not included, so that the heading "symptoms" refers to patients

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(References continued from previous column)

Komasarvitch (1930) Russ. oftal. J. 12, 327.
Magiato A. (1912a) Arch. d'Ophth. 32, 175.
— (1912b) Ann. Ocul. 147, 44.
— (1912c) J. Amer. med. Ass. 59, 18.
Samolov and Braunstein (1932) Kharbon Biomediz. 1, 424.
Savvatotz (1939) Sovetsk. vestnik oftal. 6, 29.
Yaroubov, A. G. (1933) Sovetsk. vestnik oftal. 6, 29.

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ward her urine became protein-free and her blood pressure returned to normal limits before she was delivered. She had suffered from eclampsia, and during her second pregnancy she was admitted for albuminuria in St. Mary Abbots Hospital. In her first pregnancy she had been twice previously confined—on both occasions impossible to take previous obstetric histories into consideration unless all the confinements had taken place in comparable institutions. One woman in Group A, admitted for albuminuria and hypertension, had been twice previously confined—on both occasions in St. Mary Abbots Hospital. In her first pregnancy she had suffered from eclampsia, and during her second pregnancy she was admitted for albuminuria and hypertension. As the result of treatment in the ward her urine became protein-free and her blood pressure returned to normal limits before she was delivered of her third child.

### Table I

Incidence of Toxic Symptoms in Treated (A) and Untreated (B) Women

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Group A (50)</th>
<th>Group B (50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases.</td>
<td>Primigravidae</td>
</tr>
<tr>
<td>Albuminuria and hypertension</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>13</td>
<td>6</td>
</tr>
</tbody>
</table>

### Table II

Analysis of "Other Symptoms"

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperemesis</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Edema</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Headaches</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Cramps</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Insomnia</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>10</td>
<td>21</td>
</tr>
</tbody>
</table>

Not included in the above two categories. A systolic blood pressure of, or exceeding, 140 mm. Hg was considered evidence of hypertension. The numbers suffering from "other symptoms" are shown in Table II, most patients complaining of more than one symptom.

### Comment on the Findings

Prof. E. S. Pearson, of the department of statistics at University College, London, has been kind enough to study these figures and has expressed the opinion that the difference in incidence of "complications" between the two groups is very unlikely to have arisen by chance. It is therefore desirable to consider factors, other than the diet, which may have contributed to this difference.

Of the 100 patients, 76 were between twenty and thirty years of age. Of the primigravidae 4 (2 in each group) were under the age of twenty, each being nineteen years of age. The number of women over thirty was 20, including 2 primigravidae in each group: 9 of these were in Group A and 11 in Group B. It is thus evident that the ages of the women in the two groups were strictly comparable.

It has already been stated that no regard was paid to the previous obstetric histories of the multigravidae. There are arguments in favour of confining future experiments to primigravidae, but it would have been impossible to take previous obstetric histories into consideration unless all the confinements had taken place in comparable institutions. One woman in Group A, admitted for albuminuria and hypertension, had been twice previously confined—on both occasions in St. Mary Abbots Hospital. In her first pregnancy she had suffered from eclampsia, and during her second pregnancy she was admitted for albuminuria and hypertension. As the result of treatment in the ward her urine became protein-free and her blood pressure returned to normal limits before she was delivered of her third child. The previous obstetric histories of many of the patients were unobtainable, but it is significant that the same difference in incidence of "complications" between the two groups is observed among the primigravidae as among the multigravidae.

All the patients in the experiment were observed equally often over approximately the same period of time. No woman was included who was not in the position to take the "protective substances" for sixteen weeks before delivery, and no one took them for more than twenty weeks. The social status of all the patients was, so far as could be judged, strictly similar. There was no room for variation in the "standards" adopted by the antenatal officers, for the criteria were well defined. If albumin was found in the urine a catheter specimen was subsequently obtained and tested. No patient was recorded as suffering from albuminuria unless albumin was detected in a catheter specimen. Similarly, no patient was admitted for hypertension unless, after rest, the systolic pressure equalled or exceeded 140 mm. Hg. A symptom, such as headache, was accepted only if it persisted and was severe. Moreover, it may be argued that every patient who was admitted to the antenatal ward and confirmed the findings of the antenatal officers.

It therefore seems logical to assume that the difference in the incidence of "complications" between the two groups must, if due to chance, be attributed to the substances given. This assumption is strengthened by the results of the dietetic treatment of these patients in the antenatal ward. The symptoms cleared up in every case. A slight degree of albuminuria, not exceeding 0·05 per cent., persisted in 3 of the 13 patients admitted for this condition, while the blood pressure returned to the normal in 13 of the 16 patients admitted for hypertension. These results strongly suggest that the other main factor in the prevention of the toxemias of pregnancy is the vitamin-B complex.

It is somewhat disappointing that, after waiting so long for the opportunity of conducting this experiment, the number of women included should be so small. This is due to the fact that only a small proportion of the patients booked sufficiently early and attended the hospital antenatal clinic throughout their pregnancies. These results, however, point in the same direction as those obtained by Mendenhall and Drake, and are published in the hope that further experiments on a larger scale will be conducted elsewhere. There is no proof that all the patients in Group A took their capsules and tablets regularly, and it might be expedient to incorporate a trace of methylene-blue in each tablet.

Experiments conducted on these lines would show to what degree, if any, the different protective substances are associated with toxemic symptoms. It is my belief, for instance, that vitamin A is of more importance in preventing senile changes in the placenta, and consequent death of the fetus, than in preventing toxemic symptoms. Then, too, experiments conducted on different parts of the country might show that the degree of deficiency of any given protective substance varied from area to area. On the other hand, all the protective substances could be incorporated in a pill and a capsule and be distributed at a cost not greatly exceeding that of a daily pint of milk.

There is one further and still more important reason why such investigations should be under-

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The antrum, the flange lies just outside the nose, flush and acute streptococcal tonsillitis. The intubation cannula is of such a length that when it is inserted into occasions. Patients shrink from this repeated condition which is more frequently overlooked (except by rhinologists) than any other disease.

When the presence of an empyema of the antrum is confirmed by the lavage, it may be necessary to repeat the puncture and lavage on subsequent occasions. Patients shrink from this repeated puncture under local anaesthesia and consequently I always (where possible) perform antral puncture under a short nitrous oxide and oxygen anaesthesia. The patient is permitted to regain complete consciousness before the lavage is commenced.

Antral drainage (antrostomy) is called for in the case that fails to respond to repeated antral puncture and lavage. This operation is not devoid of complications, of which the most frequent are otitis media and acute streptococcal tonsillitis.

**METHOD**

Repeated antral punctures and even an antrostomy can be avoided by the following procedure, which I term intubation of the antrum.

The intubation cannula (see Figure) is short, straight, and of wide bore. The flange is perforated by a slot on each side, to which a strong thread is applied. The cannula is of such a length that when it is inserted into the antrum, the flange lies just outside the nose, flush with the upper lip. It is retained in situ by strapping the threads to the cheeks.

Using this special retanable antrum cannula, the antrum is punctured with the trocar and cannula through the inferior meatus. The trocar is withdrawn and the cannula left in situ. The antrum is perfused with saline. A loose pad of gauze is also strapped over the nose.

The patient is confined indoors or to bed, and every 3 hours the first day, every 4 hours the next day, and subsequently three times daily the antrum is irrigated, about a pint of sterile tepid saline being used. The cannula is left in for up to a week, when it is withdrawn, cleaned, sterilised, and re-inserted.

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**ILLUSTRATIVE CASES**

I originally devised intubation for use in the first of the following cases, where a plastic operation on the cheek, on the same side as the empyema of the antrum, was contemplated. A pedicle graft from the abdomen was grafted on to the forearm, preliminarily transplanting it on to the cheek to cover a scarred area left after the treatment of an extensive facial nevus.

**CASE I.**—Acute empyema of antrum cured by intubation of the antrum.

A girl of 20 complained of a right nasal discharge with severe pain over the antrum, due to an acute empyema of the antrum. An enormous amount of conching pus was removed by antral lavage following the antral puncture. The cannula was left in situ and antral lavage was then performed every four hours during the day for two weeks, the cannula being changed every five days. For the first 10 days pus was irrigated from the antrum, but within 3 weeks the infection cleared up completely.

*The cannula is made to my design by Messrs. Mayer and Phelps, London.*