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Muscular Subaortic Stenosis:

The Initial Left Ventricular Inflow Tract Pressure as Evidence of Outflow Tract Obstruction

E. DOUGLAS WIGLE, M.D., F.R.C.P.[C], F.A.C.P.,*
PIERRE AUGER, M.D.† and YVES MARQUIS, M.D.,† *Toronto*

Two types of intraventricular pressure differences within the left ventricle of man are described. The first is encountered in cases of muscular (or fibrous) subaortic stenosis, in which the outflow tract pressure distal to the stenosis (and proximal to the aortic valve) is low, whereas all pressures recorded in the left ventricle proximal to the stenosis, including that just inside the mitral valve (the initial inflow tract pressure) are high.

The second type of intraventricular pressure difference may be recorded in patients without muscular subaortic stenosis when a heart catheter is advanced to the left ventricular wall in such a manner that it becomes imbedded or entrapped by cardiac muscle in systole. Such an entrapped catheter records a high intraventricular pressure that is believed to reflect intramyocardial tissue pressure, which normally exceeds intracavitary pressure. In such cases the initial inflow tract pressure is not high and is precisely equal to the outflow tract systolic pressure, i.e. both are recording intracavity pressure. This type of intramyocardial to intracavitary pressure difference may also be encountered in the left ventricle of dogs.

The recent suggestion that intraventricular pressure differences in the left ventricle of cases of muscular subaortic stenosis are due to catheter entrapment by cardiac muscle is refuted by using the initial inflow tract pressure as the means of differentiation between the two types of intraventricular pressure differences outlined.

Les auteurs décrivent deux types distincts de différence de pression intraventriculaire au sein du ventricule gauche. Le premier s'observe dans les cas de sténose sous-aortique musculaire (ou fibreuse), dans laquelle la pression enregistrée dans la chambre de chasse (outflow tract) du ventricule gauche, soit la pression distale à la sténose (et proximale à la valve aortique), est basse, alors que toutes les pressions proximales à la sténose, y compris celle qui est enregistrée juste à l'intérieur de la valve mitrale (pression initiale de la chambre de remplissage) (inflow tract) sont élevées.

Le second type de différence de pression intraventriculaire peut être noté chez des malades qui ne présentent pas de sténose musculaire sous-aortique lorsqu'un cathéter cardiaque est avancé jusqu'à la paroi du ventricule gauche de façon telle qu'il est enfoui dans ou enserré par le muscle cardiaque durant la systole. Un tel cathéter enfoui ou enserré enregistre une pression intraventriculaire élevée que l'on croit être le reflet de la pression intramyocardique laquelle normalement dépasse la pression intracavitaire. Dans ces cas, la pression initiale de la chambre de remplissage n'est pas élevée et est précisement égale à la pression de la chambre de chasse, c'est-à-dire qu'elles réflètent toutes deux la pression intracavitaire. Ce type de différence entre les pressions intramyocardique et intracavitaire peut aussi s'observer dans le ventricule gauche du chien.

Il a récemment été suggéré que les différences de pression intraventriculaire gauche, dans les cas de sténose musculaire sous-aortique, sont attribuables au fait que le cathéter est enfoui dans ou enserré par le muscle cardiaque durant la systole. La mesure de la pression initiale de la chambre de remplissage a permis de refuter cette hypothèse et de distinguer entre les deux types de différence de pression qu'on vient de signaler.

SINCE Brock[1] first described muscular subaortic stenosis in 1957 this entity has been the subject of intense clinical,[2-7] pathological,[2, 4, 7, 8] genetic,[2-4, 6, 9, 10] hemodynamic,[2-5, 7] pharmacologic[9-11] and surgical[2, 12-14] interest. Although initially considered an uncommon condition, it is becoming increasingly obvious that such is not the case. During the past six years we have encountered some 50 patients with this disorder, the majority of whom have had the diagnosis confirmed by heart catheterization.[15] More than 20 of these patients have undergone surgery for relief of the outflow tract obstruction.[13, 14] As the result of this experience it has been suggested by others[9] that this con-

From the Department of Medicine, University of Toronto, and the Cardiovascular Unit, Toronto General Hospital.
*Director, Cardiovascular Unit, Toronto General Hospital; Assistant Professor, Department of Medicine, University of Toronto.
†Ontario Heart Foundation Research Fellow, Cardiovascular Unit, Toronto General Hospital.
Supported by the Ontario Heart Foundation.
Address reprint requests to: Dr. E. D. Wigle, Director, Cardiovascular Unit, Toronto General Hospital, 101 College Street, Toronto 2, Ontario.

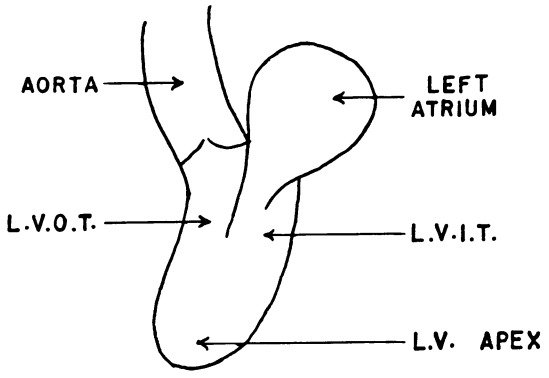

Fig. 1.—Diagram of the left heart chambers viewed from the left side of the body. The left ventricular outflow tract (L.V.O.T.) is that area of the left ventricle below the aortic valve whose lateral boundaries are the ventricular septum (anteromedially) and the anterior leaflet of the mitral valve (posterolaterally). The left ventricular inflow tract (L.V.I.T.) is that area of the left ventricle below the mitral valve. One may further divide the left ventricular cavity into a third area, the left ventricular apex (L.V. apex). The terms inflow and outflow refer to the direction of blood flow relative to the left ventricle.

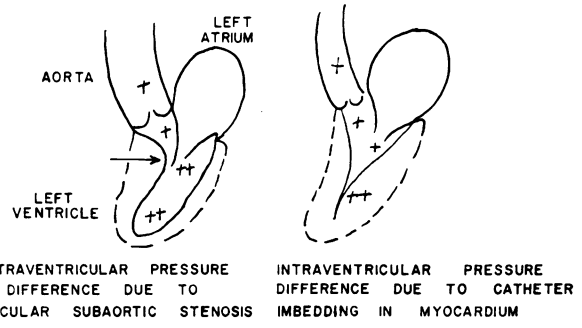

Fig. 2.—*Left.* In muscular subaortic stenosis the systolic obstruction (arrow) is in the left ventricular outflow tract, hence the intraventricular systolic pressure distal to the obstruction (and proximal to the aortic valve) is low (+) whereas the systolic pressure in all areas of the left ventricle proximal to the obstruction (including the initial inflow tract pressure) is high (++).

Right. When an intraventricular pressure difference is present owing to one catheter being imbedded or entrapped by cardiac muscle, only the area in which the catheter is imbedded in muscle records a high intraventricular pressure (++). The intraventricular systolic pressure in all other areas of the left ventricle including the inflow tract pressure is low and equal to aortic systolic pressure (+). This type of intraventricular pressure difference, which is really an intramyocardial to intracavitary pressure difference, is most frequently encountered when the left ventricle rapidly ejects its content of blood in early systole.[16, 18, 20] This may at times result in obliteration of the apical portion of the left ventricular cavity as is shown in this diagram.

dition may be more common in Canada than elsewhere.

In discussing this condition, the terms left ventricular outflow tract and left ventricular inflow tract are frequently used. A definition of these terms suitable to the ensuing discussion is shown in Fig. 1. It is our belief that the obstruction to left ventricular outflow occurs by apposition of the ventricular septum and the anterior leaflet of the mitral valve during systole (Fig. 2, left). This obstruction results in the occurrence of an intraventricular pressure difference, i.e. left ventricular systolic pressure proximal to the obstruction exceeds the systolic pressure in the left ventricular outflow tract distal to the obstruction and proximal to the aortic valve (Fig. 2, left).

Recently, Criley *et al.*[16] from the Johns Hopkins Hospital have challenged the very existence of muscular subaortic stenosis. These authors have suggested that the high intraventricular pressure recorded in these patients is not due to obstruction to left ventricular outflow, but instead is consequent upon the heart catheter becoming entrapped in cardiac muscle following early and rapid evacuation of blood from the left ventricle (Fig. 2, right). These authors believe that the intraventricular pressure differences encountered both in man and in dogs are due to this same phenomenon, i.e. catheter entrapment by left ventricular muscle.[16, 17]

This report summarizes work directed to a solution of the problem as to the nature of intraventricular pressure differences, as revealed by pressure recordings within the left ventricle, in man and dogs. The work in humans was carried out in patients with and without muscular subaortic stenosis.

Studies carried out in dogs in conjunction with Blundell *et al.*[18] indicated that intraventricular pressure differences provoked by noradrenaline infusion were due to the catheter (recording the high intraventricular pressure) becoming entrapped or imbedded in cardiac muscle. This conclusion was based on the belief that if muscular obstruction to left ventricular outflow was the cause of these pressure differences, then all areas within the left ventricle proximal to the obstruction, including the left ventricular inflow tract, would have a high systolic pressure, as depicted in Fig. 2, left. In the dog studies,[18] the intraventricular pressure was high at the apex of the left ventricle but the intraventricular pressure just inside the mitral valve was low and equal to left ventricular outflow tract pressure (Fig. 2, right). This latter hemodynamic situation is incompatible with outflow tract obstruction. The non-obstructive nature of these intraventricular pressure differences in dogs is in agreement with the work of other authors.[16, 19, 20]

Utilizing this information from animal experimentation, we directed our attention to the cause of intraventricular pressure differences in patients diagnosed clinically to have muscular subaortic stenosis. It was our belief that if these pressure differences were due to muscular obstruction to left ventricular outflow, then all pressures proximal to the obstruction would be elevated, including the pressure just inside the mitral valve (Fig. 2, left). In order to obtain the initial pressure within the left ventricular inflow tract, special transseptal left heart catheters with only an end hole were used. (The usual transseptal catheter has an end hole plus four side holes located in the centimetre proximal to the distal end of the catheter.) By entering the left ventricle via the mitral valve with such an end-hole catheter it was our belief that there would be a well-defined and sharp change from atrial to ventricular pressure and that if there were obstruction to left ventricular outflow, this initial inflow tract pressure would be higher than the outflow tract pressure. The anatomy of the

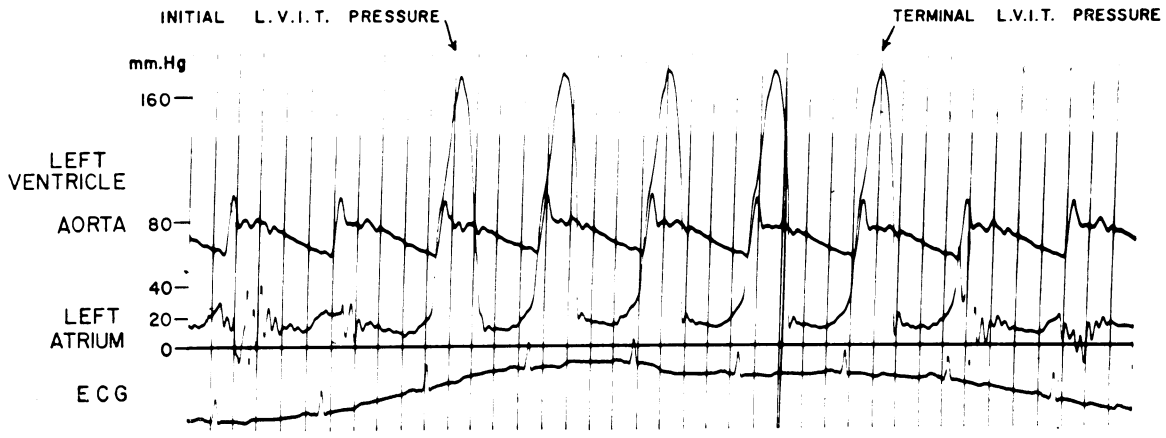

Fig. 3.—Left heart pressure recordings from a case of muscular subaortic stenosis. Aortic pressure recording is continuous. The end-hole transseptal catheter records left atrial pressure at the left and on entering the left ventricle via the mitral valve (centre) the initial left ventricular inflow tract (L.V.I.T.) pressure is high, exceeding aortic systolic pressure, the latter equalling the systolic pressure in the left ventricular outflow tract distal to the obstruction (Fig. 2, left). Similarly, on withdrawing the transseptal catheter back into left atrium from the left ventricle (right), the terminal left ventricular inflow tract (L.V.I.T.) pressure is high. With the use of this technique in which it is considered impossible for the catheter to become imbedded in cardiac muscle, the high intraventricular pressure just inside the mitral valve provides evidence of the presence of outflow tract obstruction. Note that intraventricular pressure declines before the dicrotic notch in the aortic pressure (see text).

mitral valve is such that it is considered impossible for an end-hole transseptal catheter to become entrapped in cardiac muscle when recording the initial inflow tract pressure at a time when the transseptal catheter tip is but a few millimetres inside the ventricle.

Fig. 3 demonstrates a continuous recording of aortic pressure in one case of muscular subaortic stenosis when the end-hole transseptal catheter was moved back and forth across the mitral valve from left atrium to left ventricle and vice versa. In this particular case the catheter was advanced from left atrium to left ventricle and withdrawn from left ventricle to left atrium more than 10 times in either direction. In every instance the first recorded pressure on entering the left ventricle and the last recorded pressure on withdrawing from the left ventricle was higher than the aortic systolic pressure (which was identical with that recorded in the left ventricular outflow tract distal to the stenosis, Fig. 2, left). Furthermore, the transseptal catheter could be moved about within the left ventricular inflow tract and to the cardiac apex without altering the pressure recorded by this catheter. The findings depicted in Fig. 3 are representative of the findings in seven consecutive cases of muscular subaortic stenosis investigated in this manner in the past year. Thus, in muscular subaortic stenosis (Fig. 3), the finding of a high intraventricular pressure just inside the mitral valve (the initial inflow tract pressure) (Fig. 2, left) is a hemodynamic situation different from that found in dogs with an intraventricular pressure difference induced by noradrenaline infusion, where the intraventricular pressure inside the mitral valve was low (Fig. 2, right). The hemodynamic situation in muscular subaortic stenosis is entirely compatible with there being outflow tract obstruction (Fig. 2, left), whereas the hemodynamic situation in the dog studies is incompatible with the presence of outflow tract obstruction (Fig. 2, right).

Subsequent to discerning that two different hemodynamic situations may exist in the presence of an intraventricular pressure difference (muscular subaortic stenosis in man and catheter entrapment by heart muscle in dogs) we have advanced heart catheters into the left ventricular cavity, until they came into contact with the wall of the left ventricle, while investigating patients with generalized heart muscle disease (without outflow tract obstruction). On a number of occasions it has been possible to produce intraventricular pressure differences by wedging or imbedding the heart catheter in cardiac muscle in these patients (Fig. 4). When the imbedded or entrapped catheter was withdrawn to the left ventricular inflow tract just beneath the mitral valve, the intraventricular pressure difference disappeared, i.e. obstruction to left ventricular outflow was not present (Fig. 2, right; Fig. 4). This latter hemodynamic situation in man is identical to that seen in dogs when the intraventricular pressure difference was induced by pharmacological means and is indicative of catheter entrapment by left ventricular muscle. That the catheter was imbedded in muscle during systole in this situation was indicated by the fact that blood could not be withdrawn from the proximal end of this catheter in systole (because the distal end was entrapped in muscle). On the other hand, in muscular subaortic stenosis, not only could blood be withdrawn from the proximal end of the catheter in systole (and diastole), but if the proximal end was left open, a jet of blood shot out in systole. These latter observations are believed to indicate that in muscular subaortic stenosis the distal end of the catheter recording the high intraventricular pressure was surrounded by blood (not muscle), and the high pressure was the result of outflow tract obstruction.

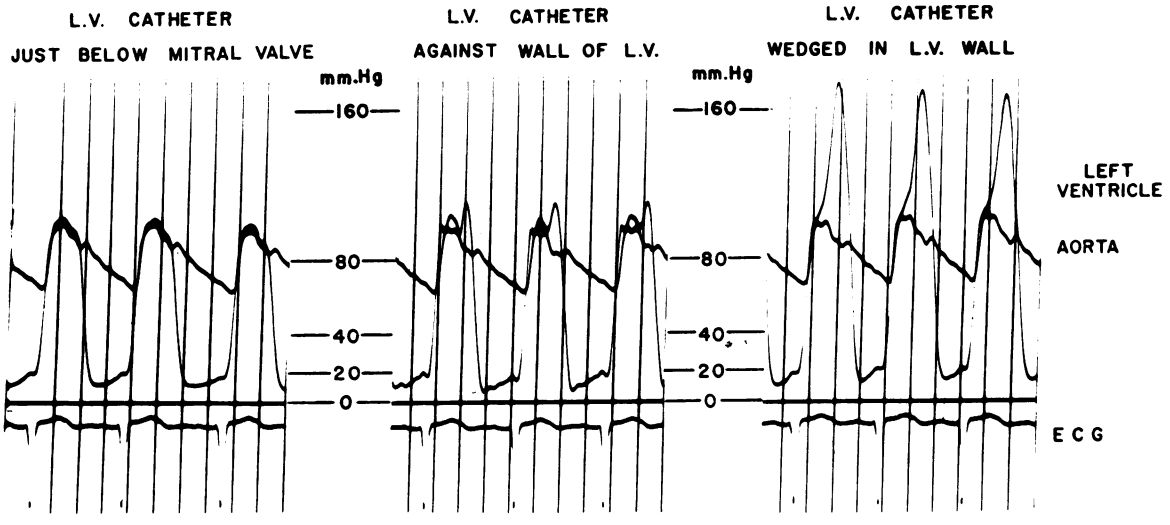

Fig. 4.—Intraventricular pressure difference due to imbedding of catheter in left ventricular myocardium. In the panel at the left, the left ventricular inflow tract pressure, below the mitral valve, is equal to aortic systolic pressure. As the catheter is advanced toward the left ventricular wall (centre), a small systolic pressure difference between the left ventricle and aorta appears in late systole. At the right the catheter is pushed further toward the wall and a large systolic pressure difference exists between the left ventricle and aorta, i.e. the catheter has become imbedded in the left ventricular muscle during systole and reflects to a variable extent intramyocardial pressure, which is known to exceed left ventricular cavity pressure(21, 22) and to decline after the dicrotic notch in the aortic pressure(23) (see text).

Also of importance in differentiating between these types of intraventricular pressure differences is the fact that the high intraventricular pressure in muscular subaortic stenosis fell at or before the time of the dicrotic notch in the aortic pressure (Fig. 3). Frequently, when a high intraventricular pressure was recorded by a heart catheter entrapped or imbedded in muscle the ventricular pressure fell after the dicrotic notch in the aortic pressure (Fig. 4) or after left ventricular cavity pressure. Several investigators[21-23] have demonstrated that intramyocardial tissue pressure declines after left ventricular cavity pressure or after the dicrotic notch in the aortic pressure. These same workers[21, 22] have demonstrated that intramyocardial tissue pressure increases from epicardium to endocardium, where it may be as much as two and a half times left ventricular cavity pressure.[21] It is believed that the high intraventricular pressure recorded by a cardiac catheter entrapped or imbedded in left ventricular muscle is to a variable extent a reflection of intramyocardial pressure.

SUMMARY AND CONCLUSIONS

As the result of the studies described herein, we have concluded that there are two types of intraventricular pressure differences that may be encountered in the left ventricle of man. One type is encountered in muscular (or fibrous) subaortic stenosis (Fig. 2, left). In this condition the outflow tract pressure distal to the stenosis (and proximal to the aortic valve) is low, whereas all pressures recorded in the left ventricle proximal to the stenosis, including the pressure just inside the mitral valve (the initial inflow tract pressure), are high. The high intraventricular pressure falls simultaneously with the dicrotic notch in the aortic tracing (Fig. 3) or with the left ventricular cavity pressure distal to the stenosis. Blood may be withdrawn in systole from the proximal end of the catheter recording the high intraventricular pressure, providing evidence that the distal end, situated in the high-pressure area, is surrounded by blood.

The second type of intraventricular pressure difference may be seen when a heart catheter is advanced to the wall of the left ventricle in such a manner that it becomes entrapped or imbedded in muscle in systole. The high pressure recorded by such a catheter is believed to reflect intramyocardial tissue pressure, which is normally higher than intracavity pressure.[21-23] In this type of intraventricular pressure difference the left ventricular pressure just inside the mitral valve (the initial inflow tract pressure) is low and equal to the systolic pressure in the left ventricular outflow tract and aorta (Fig. 2, right). In this situation the high intraventricular pressure frequently falls after the dicrotic notch in the aortic pressure or after left ventricular cavity pressure (Fig. 4). Blood cannot be withdrawn from the proximal end of the catheter in systole because the distal end is surrounded by muscle in these circumstances.

By making careful observation of the initial inflow tract pressure it is believed that the intraventricular pressure difference due to muscular subaortic stenosis may be differentiated from that seen when such a pressure difference is due to a catheter being imbedded or entrapped by cardiac muscle. These studies are believed to refute the suggestion that the intraventricular pressure difference in cases of muscular subaortic stenosis is due to entrapment of the catheter (recording the high intraventricular pressure) by cardiac muscle.

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The Incidence and Prevention of Folate Deficiency in a Pregnant Clinic Population

LOUIS LOWENSTEIN, M.D., GEORGE CANTLIE, M.D.,
OSCAR RAMOS, M.D. and LAUDER BRUNTON, M.D., *Montreal*

Non-anemic women attending a public antenatal clinic were given, daily, a multivitamin tablet containing 78 mg. of elemental iron. The follow-up studies included an analysis of their diets. A total of 311 patients were included, of which one group received a supplement of 0.5 mg. folic acid and 0.005 mg. vitamin B_{12}. The incidence of megaloblastic bone marrow change in the unsupplemented group was 26% and of low blood folates approximately 50%. The incidence of megaloblastic changes was sharply reduced in the supplemented group and the blood folates were elevated to supranormal levels, indicating that the dose of folic acid used may have been above the minimal requirement. Formiminoglutamic acid (FIGLU) excretion could not be correlated with other parameters of folate deficiency. Neutrophil lobe counts did not relate to megaloblastic changes or low folate levels unless there was more than 5% hypersegmentation. The dietary intake was suboptimal in total calories, iron and food folate.

A des femmes non anémiques qui fréquentaient une clinique prénatale publique, on a donné tous les jours un comprimé polyvitaminique renfermant 78 mg. de fer élément. L'étude post-thérapeutique comprenait une analyse de leur régime alimentaire. Cette étude portait sur 311 femmes, dont un certain groupe recevait un supplément de 0.5 mg. d'acide folique et 0.005 mg. de vitamine B_{12}. Parmi les patientes qui ne recevaient pas ce supplément, la fréquence des changements mégaloblastiques de la moëlle osseuse était de 26% et la fréquence de l'hypofolatémie de 50% environ. La fréquence des modification mégaloblastiques était par contre fortement réduite parmi le groupe recevant le supplément et les concentrations sériques de folate étaient supérieures à la normale, signe que la dose d'acide folique administrée pouvait avoir dépassé les besoins minima. Il n'a pas été possible d'établir de corrélation entre l'excrétion de l'acide formiminoglutamique (FIGLU) et les autres paramètres de l'insuffisance en folate. La numération des neutrophiles n'avait pas de rapport avec les changements mégaloblastiques ni avec l'hypofolatémie, à moins que la proportion de neutrophiles segmentés ne dépassât de 5% au moins la valeur normale. La ration diététique était sous la normale aux points de vue calorique, fer et folate d'origine alimentaire.

A RECENT report[1] has dealt with the incidence of megaloblastic marrow changes and of low blood folate and vitamin B_{12} values in an *anemic* pregnant population in Montreal. Although the determining factor of the anemia in these patients was iron deficiency, a 25% incidence of early megaloblastosis was observed. Furthermore, while 80% of the megaloblastic cases possessed low serum folate values, over 30% of the normoblastic cases also had microbiological evidence of folate deficiency. In all patients the incidence of low folates was 48%. The response of most patients to small daily doses of folic acid suggested that such low values may occur as a manifestation of an early and pre-megaloblastic state of folate deficiency. Ten per cent of the megaloblastic cases had low serum vitamin B_{12} values only.

From the Division of Hematology, Department of Medicine, Royal Victoria Hospital and McGill University Clinic, and the Department of Obstetrics and Gynecology, Royal Victoria Hospital, Montreal, Que.
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Address reprint requests to: Dr. Louis Lowenstein, Division of Hematology, Royal Victoria Hospital, Montreal 2, Quebec.

It may be possible to prevent development of low blood folate and B_{12} values and of megaloblastosis by prophylactic administration of small daily doses of folic acid and vitamin B_{12} during the latter half of pregnancy. As reported previously, the variable bone marrow response to graded doses of folic acid in some patients raises the question of the amount necessary for this purpose. Accordingly, it was decided to investigate in detail the hematologic and nutritional status of a large group of *normal* women from a comparable population. At the same time, the opportunity was taken to assess the role of a single supplementary daily dose of folic acid and vitamin B_{12} on the incidence of megaloblastosis and microbiological deficiencies of these vitamins. To ensure adequate dosage for this purpose, the one selected was thought to be larger than the probable minimal daily requirement, but was still in the small dose range.