

such as dizzy spells, syncope, breathlessness, impaired exercise capacity, and postural hypotension. These symptoms may constitute the "pacemaker syndrome," which once recognised is readily treated.

The syndrome results from atrial contraction occurring during ventricular systole and is a consequence of ventricular pacing. The atria contract against closed atrioventricular valves and produce raised mean pressures in the right and left atria with reduced cardiac output and blood pressure.^{2,3} The pacemaker syndrome occurs when retrograde atrioventricular conduction is intact and conduction spreads from the paced ventricles to the atria generally through the atrioventricular node; this may happen even when antegrade conduction is blocked. Ventricular pacing competing with sinus rhythm may be similarly symptomatic.^{4,5} Dual chamber pacing, in which pacing and sensing occur in both the atrium and ventricle, is rarely associated with the pacemaker syndrome because the physiological relation of atrial contraction preceding ventricular contraction is maintained.⁶

Patients with pacemaker syndrome complain of syncope or near syncope, dizziness, chest pain, fatigue, breathlessness, palpitations, and neck pulsations or pressure. Examination may show cannon waves in the jugular venous pulse or palpable liver pulsations. The diagnosis is made by observing or reproducing the adverse haemodynamic effects, signs, and symptoms during ventricular pacing.^{4,5,7}

Though the incidence of this symptomatic pacemaker syndrome is low, many "asymptomatic" patients have felt better with dual chamber pacing when this has been compared with ventricular pacing by within patient randomised control studies.⁸⁻¹² This is mainly because sequential atrioventricular contraction is restored.

Up to a fifth of patients with preserved retrograde atrioventricular conduction develop symptoms suggestive of the pacemaker syndrome.⁵ Retrograde conduction is present in 40% of patients with complete antegrade atrioventricular block and 90% of patients with normal atrioventricular conduction who have the sick sinus or carotid sinus syndromes.¹³ Therefore atrial or dual chamber pacing is best for patients with the sick sinus syndrome¹¹ and dual chamber pacing for those with the carotid sinus syndrome.^{14,15}

Symptoms of the pacemaker syndrome may be reduced by reprogramming a ventricular pacemaker so that competition between paced and sinus rhythm is minimised by adding rate hysteresis such that pacing starts only after a pause substantially longer than the pacing interval.¹⁶ The antiarrhythmic agents flecainide and disopyramide are effective in blocking retrograde conduction in patients with pacemakers^{17,18} and may ameliorate pacemaker syndrome. Nevertheless, flecainide increases the pacing threshold and requires careful control of pacemaker output. Patients who do not respond to these measures must be upgraded to dual chamber pacing. In new patients who require pacing but retain antegrade conduction and have preserved retrograde conduction the syndrome may be prevented by implantation of a dual chamber pacemaker.

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Weight gain in pregnancy: eating for two or just getting fat?

What advice should a doctor give to a woman about her weight during pregnancy? Should he tell her to eat for two, or if she is gaining weight too fast should he advise her to diet? These are everyday questions, but, as so often happens, research has provided some conflicting answers.

The average woman gains 12.5 kg during pregnancy, though normal women may lose weight or gain over 20 kg.¹ Much of the increase is accounted for by the uterine contents, enlargement of maternal organs, and—particularly in the third trimester—increased body water.¹ The remainder, averaging about 3.5 kg, is fat. By a mechanism that is not fully understood² pregnancy alters carbohydrate metabolism,³ and subcutaneous fat is laid down over the abdomen, back, and upper thighs, mainly in the first and second trimesters.^{1,3} The fat is usually lost again afterwards—a process aided by lactation^{4,5}—and for most women long term weight gain is an effect of age rather than parity.^{1,3} Nevertheless, during pregnancy fat women tend to put on more weight than thin ones.³

Women who are overweight at the start of pregnancy face an increased risk of complications.^{3,6} Hypertensive disorders are more frequent,^{7,8} though the incidence in different reports varies widely—from 7%⁹ to 46%.^{3,10} Abnormal glucose tolerance is also more common, affecting 7-17% of obese women.⁷⁻¹⁰ Increased risks of urinary tract infections and possibly thrombophlebitis have been reported,⁸ but the risks of anaemia⁸ and preterm delivery¹¹ may be lower than in underweight women. Older studies found that perinatal mortality was higher among obese women,^{3,12} but more recent reports have not confirmed this^{7,9,10}; perinatal mortality may have been reduced in these patients because of recognition of the risks and consequent careful supervision.⁶ A recent American study concluded, however, that if

1 Feruglio GA, Steinbach K. Pacing in the world today. World survey on cardiac pacing for the years 1979 to 1981. In: Feruglio GA, ed. *Proceedings of the second European symposium on cardiac pacing*. Padua: Piccin Medical, 1982:953-67.

antenatal complications develop in an obese woman she is at greater risk of losing her baby than a woman of normal weight with the same complication, though if there are no antepartum complications maternal weight does not alter perinatal mortality.⁸

Obese women tend to have large babies.⁶⁻¹¹ They might therefore be expected to have increased risks of cephalopelvic disproportion, shoulder dystocia, and caesarean section, but the evidence on this question is not clear.¹¹ Some studies have reported increased rates of caesarean section,⁸⁻¹¹ but others have not.⁷⁻¹⁰ When operative intervention is required, however, there is increased morbidity and wound infection.⁷⁻¹¹ Among normal women the baby's birth weight is related both to the mother's weight before pregnancy¹³⁻¹⁴ and to her weight gain during pregnancy,¹³⁻¹⁵ but among severely overweight women the birth weight is related only to the weight before pregnancy and is not influenced by weight gain.¹³ The mother's weight also affects the baby's growth after birth: both normal⁷ and low birthweight¹⁶ babies put on weight more quickly if their mother is fat than if she is underweight. Whether this is due to genetic or intrauterine factors or to differences in later feeding patterns is unknown.

To what extent can obstetric risks be modified by dietary adjustment in pregnancy? Pregnant women are traditionally urged to eat for two, and concern has been expressed that enthusiasm for slimming may adversely affect fetal growth.¹⁷ Encouraging non-obese women to achieve an "appropriate" weight gain¹⁸ reduces the proportion of low birthweight babies,¹⁹ and in developing countries women may be given energy supplements for this purpose, though recently doubt has been cast on the need for such supplementation in the absence of obvious food shortages.²⁰⁻²¹ Nevertheless, there is little evidence that perinatal mortality can be improved by dietary measures aimed at increasing birth weight.

Recommendations for a minimum weight gain in pregnancy should take account of the weight before pregnancy: underweight women need to gain more than overweight women.²²⁻²⁴ If, then, there is no need to encourage fat women to gain weight in pregnancy¹³ should they be encouraged to lose weight? Dietary restriction for women who gain a lot of weight can reduce the birth weight of their babies, but once again there is no evidence that this reduces the risk of pregnancy complications.¹² A Scottish study¹² has concluded that "dietary restriction cannot be advocated even in the obese primigravida as it is possibly detrimental to the baby and of no benefit to the mother: it is probably better to try and reduce the obese woman's weight either before or after the pregnancy."

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Licensed to kill

About 5-10% of human peripheral white blood cells spontaneously and rapidly kill in vitro a wide range of cultured cell lines, tumour cells, and virus infected cells. These natural killer cells were described more than 10 years ago, and they are becoming of interest in several of the clinical medicine specialties. As well as being an important component of natural resistance to infection, they may also play a part in limiting the growth and metastatic spread of some tumours and in graft versus host disease. They may even prove to be useful in treating some tumours.

Natural killer cells are large, low density lymphocytes rich in azurophilic cytoplasmic granules, that can be isolated by density gradient centrifugation from peripheral blood. They are also found in lymphoid tissues and may be detected in inflammatory sites.¹ Natural killer cells isolated from peripheral blood lymphocytes are non-phagocytic, do not bear surface immunoglobulin, and, in contrast to T lymphocytes, do not require products of the HLA locus either for their activation or to recognise target cells. Although several pan natural killer markers have been described—(for example, those recognised by the monoclonal antibodies B73-1² and Leu 11a³—the operational definition of natural killer cells is still based on their cytotoxic activity. They are a heterogeneous population and therefore cannot yet be given a single phenotype relating to their function.

Although derived from bone marrow, the lineage of natural killer cells remains controversial. They can express phenotypic markers of myelomonocytic as well as of T cell origin.⁴ Most can form rosettes with sheep red blood cells and many of these can also express the M1 marker (monoclonal antibody defined monocyte-macrophage antigen). The CD3 antigen, which is associated with the antigen recognition site of T lymphocytes, is found on a subset of natural killer cells although they use a target recognition mechanism distinct from that used by cytotoxic T cells.⁵ The phenotypic heterogeneity may reflect differences in the stage of differentiation or ontogeny of natural killer cells. Natural killer effectors recognise glycosylated structures on target cell membranes by as yet undefined receptors.⁶ It was thought that developing techniques for culturing and cloning natural killer effector cells would allow them to be more