

Figure 1. Parkinson's Disease in a 70-Year-Old Man.

Panel A shows a magnified CT scout image of the patient's right forearm. The bar represents one cycle (27 mm). Panel B shows an electrocardiogram of lead I with arrows pointing to pseudoflutter waves. The bar represents 5 mm.

mated to be 3 and 4 Hz by means of CT and electrocardiography, respectively — findings ultimately confirmed by direct visual observation.

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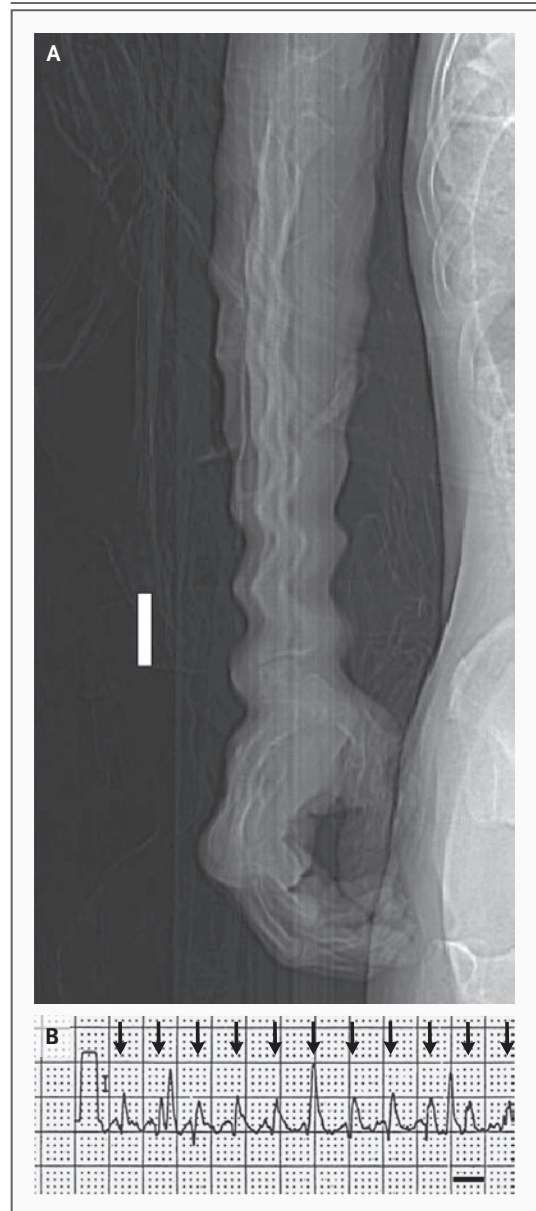
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1. Handwerker J, Raptopoulos VD. A medical mystery: dilated bowel. *N Engl J Med* 2007;356:503.

Editor's note: We received 1475 responses to this medical mystery — 53% from physicians in practice, 26% from physicians in training, 16% from medical students, and 5% from other readers. Responses were received from 82 countries. Many of the responses reflect pathophysiological thinking as well as a team effort — such as the results of a discussion of the case during a teaching conference.

Ten percent of the respondents correctly diagnosed Parkinson's disease, with tremor-induced changes in the right arm (on the scout film) and on the electrocardiogram, and the dilated bowel. Thirty-four percent diagnosed Chagas' disease, which was probably due to the dilated bowel and presumed cardiac dysfunction. Twenty-one percent of the responses suggested a toxic metabolic cause, such as hypokalemia, hypomagnesemia, or adverse effects of medication (e.g., from digitalis or calcium-channel blockers); 11% suggested atrial fibrillation with mesenteric ischemia due to an embolic event; 5% diagnosed Ogilvie's syndrome; and the remaining 19% diagnosed a variety of other conditions, such as toxic megacolon, amyloidosis, and Hirschsprung's disease.



Ovarian Transplantation in a Series of Monozygotic Twins Discordant for Ovarian Failure

TO THE EDITOR: We previously reported in the *Journal* a case of a successful ovarian transplantation between 25-year-old monozygotic twins. One had undergone menopause at the age of 14 years, whereas the other was still fertile.¹ After receiving a graft of ovarian tissue from her sibling, the

previously menopausal twin conceived spontaneously during the second menstrual cycle and delivered a healthy full-term baby. Subsequently, 10 other pairs of monozygotic twins who were discordant for ovarian failure sought consultation at our center for ovarian transplantation. Four women

had previously failed to conceive after receiving donor eggs through in vitro fertilization (IVF), two also required surgery for fibroids or cysts, and all preferred the possibility of natural conception, the option to cryopreserve spare tissue for future use, and the advantage of undergoing a single procedure. We report on the outcomes of the seven twins who have already undergone ovarian transplantation.

All recipients had high follicle-stimulating hormone (FSH) levels and had had amenorrhea for 2 to 26 years (Table 1). In all cases of transplantation, ovarian graft tissue was obtained by unilateral oophorectomy, trimmed to approximately the same dimensions as the resected surface of the recipient ovarian medulla, and shaved to a thickness of approximately 1 mm to facilitate early revascularization. The medullary bed was

sutured to the undersurface of the cortical graft with 9-0 sutures to maintain tight tissue approximation. All seven recipients resumed menses (range, 65 to 93 days after surgery), and by day 140 after transplantation, all had regular cycling, with a normal serum FSH level on day 3 of the menstrual cycle. There have been five pregnancies thus far (four were spontaneous and one was achieved through natural-cycle IVF), and the other women continue to have regular menstrual cycles, although after 2 years the FSH levels began to rise.

Genetically discordant premature ovarian failure in monozygotic twins is not as rare as we had previously assumed.² Ten of the 11 cases that we have seen were apparently the result of congenital germ-cell deficiency, since histologic analysis verified the absence of primordial follicles and

Table 1. Initiation of Menstrual Cycles and Establishment of Pregnancy in Recipients of Ovarian Transplants.

Recipient No.	Age at Menopause	Pretransplantation FSH Level	Age at Transplantation	Time to First Menses	Post-Transplantation FSH Level on Day 3 of Menses	Intermenstrual Interval*	Detection of Pregnancy	
							No. of Days after Transplantation	Cycle No.
	<i>yr</i>	<i>mIU/ml</i>	<i>yr</i>	<i>days</i>	<i>mIU/ml</i>	<i>days</i>		
1	13	74.6	24	80	7.1 (after delivery)	62	167	2
					7.0 (after return of menses)		23, 18, 27, 36, 26, 32, 35	765
2	22	96.4	38	93	5.2	42, 24, 27, 25	250	5
3†	— (no menarche)	112.4	25	77	6.8	23, 30, 26, 25, 26, 21, 24, 27, 34, 25		
4	28	57.3	34	82	9.4	21, 48, 26, 21, 20, 27, 26	286	8
5	14	58.7	40	87	13.8	87, 29, 38, 34, 28, 28, 31, 35, 34		
6	24	101.0	26	65	9.7	20, 39, 40, 32, 29		
7	29 (bone marrow transplantation)	86.2	33	82	4.4	22, 29, 29	195	3

* The intermenstrual interval is shown for all cycles after transplantation until pregnancy or until the time of reporting.

† This recipient has no ovaries or fallopian tubes; she will require in vitro fertilization.

there were no other antecedent diseases or exposures associated with ovarian failure.³ Identical twins, like animal clones, are not actually identical, owing to epigenetic variations such as DNA methylation. Recipient 7 had had acute lymphoblastic leukemia more than 4 years before ovarian transplantation and had also received a bone marrow transplant (which is what caused her ovarian failure) from her sister, who has not had cancer. Unlike her sister, she also had a large nevus on her face. Recipient 5 had type 1 diabetes, whereas her twin had normal glucose levels but had a history of Graves' disease. These are all diseases for which there is a recognized genetic predisposition⁴ and that were discordant in these monozygotic sisters.

The type of twinning was known for six of the pairs of monozygotic twins. Three of the six were monozygotic and monoamniotic (incidence, 50%), which is normally rare among twin pregnancies (incidence, 1 to 3%; $P < 0.005$).⁵ This suggests that late splitting of embryos may be associated with discordant ovarian function, which could be due to either misallocation of early germ-cell precursors or increased epigenetic instability of genes regulating oogenesis.⁶

Our transplantation results should encourage continued efforts to bank ovarian tissue for patients with cancer, in anticipation of reimplantation after remission. More speculatively, these procedures could enable healthy women to extend their reproductive life span.

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