play an important role in blood pressure regulation, since it does so in normal man[10] as well as in various disease states.[11] However, our study clearly shows that renin is not responsible for the hypertension seen when ketamine is administered.

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Lymphocyte Transformation during Operations with Spinal Anesthesia

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Cellular immunity as tested by in-vitro techniques is depressed postoperatively. Both lymphocyte transformation and the incorporation of radioactively labeled thymidine into DNA with phytohemagglutinin (PHA) stimulation have been shown to be impaired following surgical operations.[1,2] Since general anesthesia was used in previous studies, this study was undertaken to determine whether operations in conjunction with spinal anesthesia also affect lymphocyte responsiveness to PHA.

PATIENTS AND METHODS

Seven patients were selected for this study. All underwent elective operations, their ages and surgical procedures being listed in table 1. For spinal anesthesia, tetracaine, 8-10 mg, was instilled. Patient 6 had two transurethral resections of his prostate, separated by a three-month interval. Results from both operations are reported, but only the values from the second operation are included in the statistical analysis, since at the time of the first operation, ^{3}H-thymidine incorporation studies were not being done. Premedica-

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TABLE 1. Effects of Operation and Spinal Anesthesia on Results of *In-vitro* Tests of Cellular Immunity

| | Age (years) | Operation | Test* | Lymphocyte Response to PHA | | | | |
				Pre-operative	2 days	4–7 days	12–14 days	Other
Patient 1	76	Transurethral resection	LT% ³H-thy%	61 4.47		33 1.67		
Patient 2	69	Transurethral resection	LT% ³H-thy%	61 4.14		43 2.48		63 (33 days) 4.42
Patient 3	72	Fulgeration of anal carcinoma	LT% ³H-thy%	61 5.04		46 2.77		
Patient 4	31	Hemorrhoidectomy	LT% ³H-thy%	67 7.82	59 4.08	55 3.66		
Patient 5	77	Transurethral resection	LT% ³H-thy%	58 —		49 —		60 (100 days) 4.76
Patient 6	65	First transurethral resection	LT% ³H-thy%	66 —		50 —		65 (84 days) 7.16
		Second transurethral resection (3 months after first)	LT% ³H-thy%	65 7.16	50 3.41			60 (30 days) 4.36
Patient 7	40	Anal fistulectomy	LT% ³H-thy%	65 6.40		59 3.99	60 6.74	

* LT% = percentage of lymphocytes transformed; ³H-thy% = percentage of ³H-thymidine incorporated into DNA/10^6 cells.

tions used were: meperidine, 50–75 mg; hydroxyzine hydrocholoride, 50–75 mg; atropine, 0.5 mg. None of the patients received any immunosuppressive drug before or after operation, and none received blood transfusions.

Blood was collected in heparinized syringes, with lymphocytes being harvested by the method of Avery *et al.*[3] Lymphocytes were cultured in Eagle's Minimum Essential Medium (MEM); medium containing L-glutamine, 29.2 mg/100 ml; 10 per cent human AB+ serum; and medium containing 5,000 U penicillin + 5,000 mg streptomycin/100 ml. PHA-P (Difco), 20 mg/ml, was added to each tube. After 72 hours of incubation at 37 C with 5 per cent CO_2, 1,000 lymphocytes were counted from each of the duplicate cultures and the percentage of transformed cells (LT) determined microscopically. The percentages of cells transformed in the duplicate cultures agreed to within 20 per cent. ³H-thymidine incorporation studies were done by the method of Humphrey *et al.*[4]

Following three days of incubation with PHA, 0.5 μCi of ³H-thymidine (New England Nuclear Corp., 6.7 Ci/mM) was added and samples were pulsed for 5½ hours. Sample preparation for counting was done as described.[2] Samples were counted on a Nuclear Chicago liquid scintillation counter at 50 per cent efficiency for tritium. Results are reported as the percentages of the added ³H-thymidine/10^6 cells incorporated into DNA. The standard deviation of the difference of duplicate samples from their mean was 8.9 per cent.

Patients were studied one to three days prior to operation. Postoperative samples were studied as indicated in table 1.

In each run, freshly obtained lymphocytes from one to two healthy individuals were included to assess the inter-assay variability of the techniques. There was consistent close agreement in the responses to PHA in successive weekly assays of lymphocytes from these two subjects (table 2). The constancy of the lymphocyte responses when tested on

separate occasions is also reflected in results of tests of lymphocytes from two patients from the surgical wards who did not undergo surgery (table 2).

RESULTS

Lymphocyte transformation decreased during the postoperative week in each of the seven patients in this group. The preoperative mean of 62.6 per cent decreased to a mean of 47.8 per cent. The changes are highly significant by the t test for paired data (t = 5.47, $P < 0.01$). Lymphocyte transformation in the four patients from whom follow-up specimens were obtained returned to 62 per cent.

The preoperative mean of 5.23 per cent incorporation of ^{3}H-thymidine into DNA decreased to 2.98 per cent. Again, the postoperative decrease was highly significant, using the t test for paired data (t = 7.46, $P < 0.01$). The mean level in "recovery" samples obtained from three patients was 5.18 per cent.

Results in two patients were especially interesting. In Patient 3 (table 1), both lymphocyte transformation and ^{3}H-thymidine incorporation decreased following fulguration of an anal carcinoma under spinal anesthesia. Twelve days after the initial operation, a second operation (colostomy) was done under general anesthesia. This second operation is not included in the tables. Thirteen days after the second operation lymphocyte transformation and ^{3}H-thymidine incorporation were suppressed to 51 per cent and 3.52 per cent, respectively. These values are very similar to those found after the first operation. There was partial recovery by the 34th day after the second operation (lymphocyte transformation, 56 per cent; ^{3}H-thymidine incorporation 4.39 per cent).

Patient 6 (table 1) is noteworthy since he had two transurethral prostatic resections for benign prostatic hypertrophy three months apart. The decreases in lymphocyte transformation after the two operations were very similar, although postoperative sampling times differed (fifth day after the first operation and second day after the second operation).

TABLE 2. Variability of Lymphocyte Responses to Phytohemagglutinin

Age (years), Diagnosis	Test*	Lymphocyte Response, Weekly Assay Number														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Subject 1 42, normal	LT%	69	67	69	68	67	68	65	66	65	66	66	65	64	63	68
	^{3}H-thy%	—	—	—	—	4.73	4.57	4.81	4.76	4.78	4.88	4.66	—	4.83	4.88	4.88
Subject 2 43, normal	LT%	62	63	68	62	62	65									
	^{3}H-thy%					4.25	4.55	5.14								
Subject 3 54, cholecystitis	LT%	61	63	64												
	^{3}H-thy%	4.40		4.59												
Subject 4 52, anal fistula	LT%	64	63													
	^{3}H-thy%															

* LT% = percentage of lymphocytes transformed; ^{3}H-thy% = percentage of ^{3}H-thymidine incorporated into DNA/10^6 cells.

DISCUSSION

The suppressive effects of surgical procedures upon the immune system as evaluated by *in-vitro* tests of lymphocyte responsiveness to PHA are supported by this study. In the study of Park *et al.*,[1] utilizing ^{3}H-thymidine incorporation, lowering of the lymphocytic response to PHA was noted to occur within two hours after operation. Operation appeared to have a direct suppressive action upon the lympocyte's responsiveness to PHA. Additionally, postoperative sera had an inhibitory action upon ^{3}H-thymidine incorporation. General anesthesia was implicated in the latter study as an important factor contributing to the postoperative decrease in the lymphocytic response. Riddle and Berenbaum[2] reasoned that general anesthesia was not likely to be important in the postoperative impairment of lymphocyte transformation that they found, since the extent of suppression of lymphocyte transformation was independent of both duration of operation and general anesthesia. The results of the present investigation support the conclusion that surgery, not general anesthesia, is responsible for the postoperative suppression of lymphocytic immunocompetence, since this inhibition also occurs with spinal anesthesia. It remains to be determined whether spinal anesthesia alone may contribute to the postoperative inhibition of lymphocytic responsiveness.

The mechanism underlying the inhibitory effect of surgery upon the *in-vitro* response of lymphocytes remains speculative, as does any conclusion about the implications of such suppression in relation to clinical problems such as postoperative infection and tumor dissemination.

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The Use of Haloperidol for Treatment of Postoperative Nausea and Vomiting—A Double-blind Placebo-controlled Trial

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Previous reports have established the antiemetic properties of haloperidol.§[1–6] Tornetta[1] demonstrated that the incidence of postoperative nausea and vomiting was significantly decreased by preoperative administration of low doses of haloperidol. However, a United States government report asserts that evidence of prophylactic effectiveness of an antiemetic agent cannot be used to imply that it is effective therapeutically.[7]

This study was undertaken to assess the ability of haloperidol, administered intramuscularly, to control nausea and vomiting in postoperative patients after these symptoms had appeared.

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§ Supplied as Haldol (haloperidol) by McNeil Laboratories, Inc., Fort Washington, Pennsylvania 19034.

METHODS AND MATERIALS

All patients who had not received drugs with antiemetic activity prior to or during