

Spontaneous Regression of Cancer: Preliminary Report

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SPONTANEOUS regression of cancer is a very intriguing and challenging phenomenon, which has been mentioned as a probability or fact by numerous writers in the field of oncology, but proof of its existence is difficult to obtain. Very few writers have ventured a statement relative to its frequency, but Bashford² has estimated it occurs once in 100,000 cases of cancer and Boyers,⁵ once in 80,000. Some authorities have expressed serious doubt that the phenomenon ever occurs.¹³

However, in recent years the publications of Dunphy,¹¹ Stewart,⁴⁰ and Morton and Morton,²⁹ in particular, have suggested that on extremely rare occasions neoplastic disease may not continue its inexorable progressive course, but may undergo temporary or permanent spontaneous regression. Since the last collective review of possible cases of spontaneous regression of cancer was made by Rohdenburg³⁵ in 1918 a comprehensive study of the incidence and nature of this phenomenon has been initiated by the authors with the support of the American Cancer Society.

We have defined spontaneous regression of cancer as the partial or complete disappearance of a malignant tumor in the absence of all treatment, or in the presence

of therapy which is considered inadequate to exert a significant influence on neoplastic disease. In general, this is the definition of spontaneous regression as proposed by Stewart. We do not imply that spontaneous regression need progress to complete disappearance of tumor, nor that spontaneous regression is synonymous with cure. In a few cases reported in this paper, tumor which underwent apparent spontaneous regression in one area flourished unchecked in other areas of the body or reappeared at a later time.

Although over 600 cases of tumor regression published or obtained by personal communication have been reviewed, to date only 47 cases have been considered by us to have adequate documentation (including histologic confirmation of the malignancy of the primary or metastatic tumor) to accept as probable examples of spontaneous regression. However, for this preliminary report certain categories have been arbitrarily excluded from consideration. These include publications prior to 1900, certain types of tumor in which the consistency of diagnosis of malignancy is highly controversial (chorionepithelioma, epithelioma of skin, and lymphomas), tumors conceivably totally removed by curettage or biopsy, metastases diagnosed only by roentgenograms without biopsy, long surviving cases without specific evidence of decrease or disappearance of tumor, some foreign articles in which interpretation of certain salient points is difficult, and certain cases obtained by personal communication in which more information has been requested. It is probable that some cases

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We wish to take this opportunity to thank numerous friends who have very generously contributed their time in sending abstracts of their cases, and given us consent to include them in this report.

TABLE I.—Collected Cases of "Spontaneous Regression"

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
BLADDER						
1. E. Davis ¹⁰	1948	56	M	Adenocarcinoma	Biopsy Ureterosigmoidostomy	Cystoscopic examination 50 days post-op. demonstrated normal bladder mucosa. Cystectomy done and no gross evidence of tumor found. However, cancer cells present in tissues underlying mucosa.
2. E. Davis	1948	60	M	Papillary Carcinoma	Biopsy Ureterosigmoidostomy	Cystoscopic examination 71 days post-op. demonstrated normal bladder mucosa. Cystectomy done and no gross evidence of tumor found. However, cancer cells present in tissues underlying mucosa.
3. R. Pearce ¹¹	1948	63	M	Papillary Carcinoma	Biopsy Ureterosigmoidostomy	Cystectomy done two months after ureterosigmoidostomy and normal bladder mucosa found with no gross evidence of tumor found. (Tumor 3 cm. in diameter and projecting 2 cm. into bladder before transplantation of ureters.) Histologic examination of removed bladder revealed carcinoma cells in muscle layer.
4. A. Trabucco ¹¹	1948	—	—	Papillary Carcinoma	Biopsy	No tumor found at time of cystectomy 6 months later.
5. L. G. Goldberg ¹⁷	1950	55	M	Transitional Cell Carcinoma	Biopsy Ureterosigmoidostomy	Complete regression in period of 3 weeks. (Histologic examination of bladder after cystectomy.)
6. C. D. Creevy ⁸	1953	34	M	Squamous Cell Carcinoma	Biopsy Ureterosigmoidostomy	No gross or histologic evidence of tumor after cystectomy 4 months later.
7. C. D. Creevy	1953	62	M	Transitional Cell Carcinoma	Biopsy Ureterosigmoidostomy	Complete regression present at autopsy 45 days after biopsy and 17 days after ureterosigmoidostomy. Histologic examination did not demonstrate tumor.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
8. Fort, Harlin and Atkinson ¹⁶	1951	55	M	Papillary Carcinoma	Biopsy Ureterosigmoidostomy	Complete regression present at autopsy 39 days after biopsy and 21 days after ureterosigmoidostomy. Histologic examination did not demonstrate tumor.
9. C. G. MacKay ²⁶	1907	37	F	Scirrhus Cancer	BREAST Mastectomy 1904	Large axillary and local masses disappeared.
10. E. Hodenpy ¹²¹	1910	37	F	Carcinoma	Radical mastectomy	Secondary growths in neck, scar, and liver disappeared or decreased.
11. H. Lilienthal ²⁶	1913	61	F	Scirrhus Cancer	Radical mastectomy 1907	Incomplete removal local recurrence (proved). Disappearance of local recurrence residual.
12. J. B. Scott ³⁷	1935	40	F	Carcinoma	Radical mastectomy	Nodules in scar and stony, hard hepatic enlargement disappeared.
13. J. O. Ferguson and B. M. Black ¹⁴	1954	45	M	Adenocarcinoma	COLON AND RECTUM Right transverse colostomy. Curettage of abdominal sinuses 300 roentgens of x-ray (inadequate for effect).	Tender, hard ill-defined mass of left lower quadrant, involving descending colon. Currtage material from 2 small sinuses draining pus diagnosed histologically as adenocarcinoma probably of intestinal origin. Fever was present. 2 years later patient returned and mass found to have disappeared. Abdominal exploration revealed no evidence of previous lesion but 6 cm. of descending colon absent. No tumor tissue found on microscopic examination of two blind ends of colon.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
14. E. H. Ellison ¹²	1955		M	Adenocarcinoma of rectum	Removal recurrent tumor on right side of colostomy.	Peritoneal nodules present especially along left pelvic brim and over sacrum and large nodes present in base of mesentery at time of removal of recurrence. Febrile episode for two weeks (virus pneumonia) 7 months after resection of recurrence. At emergency abdominal exploration 27 months after resection of recurrence no evidence of tumor found. Numerous peritoneal and lymph node biopsies reported histologically negative for tumor.
15. M. V. Rae ²⁴	1935	61	F	Hypernephroma of left kidney	KIDNEY Surgical removal of tumor.	Inspection of specimen revealed entire tumor mass calcified except for one small piece of tissue the size of a marble which was histologically diagnosed as hypernephroma.
16. F. J. Hall ²⁰	1908	45	F	Hypernephroma of left kidney	Surgical removal of tumor.	Tumor roughly spherical, measuring 6X4 cm. and completely separated from kidney substance lying free in cavity in upper pole of kidney. No vascular connection with kidney. Microscopic picture typical for hypernephroma although nuclei of cells took stain poorly and tumor tissue presumed to have been dead at time of removal. Microscopic examination of kidney itself was normal.
17. B. Blades and R. G. McCorkle, Jr. ³	1954		M	Bronchiogenic carcinoma	LUNG Thoracotomy and biopsy.	Temperature 38 to 38.5° C. for first three days post-op. Six months after exploratory thoracotomy clearing of pulmonary lesion apparent from roentgenograms. Chest roentgenogram more than 5 years after thoracotomy demonstrated almost complete disappearance of original lesion. Probable metastases to skull demonstrated by roentgenograms at this time.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
MALIGNANT MELANOMA						
18. F. S. Mathews ²⁷	1915	45	M	Melanosarcoma	Excision lesion of shoulder (skin) and grossly incomplete removal axillary mass the size of a fist. Microscopic diagnosis of axillary tissue same.	2 years after operation supraclavicular fulness previously present was gone and only mass the size of a hazelnut was present in axilla.
19. H. W. Meyer ²⁸	1955	36	F	Melanosarcoma	Excision of lesion of shoulder (skin). Partial excision of left axillary mass with drainage of abscess 6 months later. Microscopic diagnosis of axillary tissue same.	20 years after operation patient well and axillary mass completely disappeared.
20. G. T. Pack ²⁹	1955	32	F	Malignant Melanoma	Excision of lesion of groin (skin) and elective groin dissection. Metastatic skin nodules excised 2 years later. 14 injections rabies vaccine.	Several other similar skin nodules disappeared. Nine years later nodule noted over right ulnar styloid which was excised and diagnosed as metastatic melanoma. Patient subsequently died of generalized melanomatosis.
21. A. B. Vial and F. W. Collier ³⁵	1955	63	M	Malignant Melanoblastoma	Excision of lesion of thigh (skin) in 1950. 8 months later right groin mass excised. Mass recurred and 5 months later irradiated without effect. Portion of recurrent tumor removed in 1951. Several treatments of antibodies tagged with I-131.	Dozens of pigmented lesions (metastases), large liver, sloughing lesion in groin and several lesions in lungs. All lesions disappeared with a little pigment left in spots of skin. Biopsies of these pigmented areas showed no malignant cells whereas previously multiple biopsies demonstrated malignant melanoblastoma. Two years after treatment with antibodies 4 cm. nodule developed in scar of right groin. Mass excised and found to be malignant melanoblastoma.
22. T. B. Blocker, Jr. ⁴	1955	70	F	Melanoblastoma	Surgical excision of lesion of right malar area (skin) in 1946. Excision metastatic nodule right temporomandibular area in 1947. Regrowth of mass partially excised 7 months later (visible lesion excised).	Metastatic masses diagnosed histologically as metastatic melanoblastoma. Approximately 7 years later patient was found on physical examination to be free of tumor in the right parotid area.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
METASTATIC CARCINOMA—PRIMARY SITE UNKNOWN						
23. W. Levine and S. Weitner ²⁴	1945	34	F	Adenocarcinoma	Celiotomy and biopsy of peritoneal implants.	At time of celiotomy liver enlarged and nodular and multiple implants on peritoneum and omentum and large firm mass involving gastrosolic omentum and transverse colon. Temperature persistently elevated early postoperative period. Three years after celiotomy patient operated to terminate a pregnancy and no implants on peritoneum, omentum or viscera. Histologic study of uterus, tubes, ovaries and omentum revealed no evidence of tumor. Patient alive and well 4½ years after first operation.
24. W. A. Altemeier ¹	1955	42	F	Adenocarcinoma	Celiotomy and biopsy	Pelvic organs fixed by adhesions and many small cyst-like structures studding peritoneum. Gradual decrease in abdominal and pelvic mass until no longer present on examination 4 years after operation. Alive and well without evidence of tumor on examination 6 years after operation. Died suddenly probably of coronary thrombosis 1 year later. No autopsy.
NEUROBLASTOMA						
25. H. Cushing and S. B. Wolbach ⁹	1927	2	M	Sympathetic neuroblastoma	Biopsy of lesion Coley's toxin	10 years later lesion resected and histologic diagnosis of benign ganglioneuroma made. Original tumor reviewed and histologic diagnosis of neuroblastoma confirmed.
26. S. Van Creveld and R. Van Dam ²⁵	1947	18 months	F	Sympathoblastoma	Biopsy of tumor mass. Three x-ray treatments before surgery without effect.	Large tumor mass approximately 9 cm. X 6 cm. in right upper abdomen. 1½ years after biopsy mass size of tangerine palpable. 4 years after biopsy patient well and no mass felt. 5 years after biopsy no tumor felt on abdominal examination.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
27. D. Goldring ⁴⁸	1951	6 months	M	Neuroblastoma	Wedge biopsy of liver. 750 roentgen units of x-ray to right kidney area.	Age of 23 months no clinical evidence of tumor and marked proptosis of both eyes which had previously been present was gone. Rarefied areas in upper right humerus and skull no longer present.
28. F. W. Stewart ⁴⁹	1952	1 month	—	Neuroblastoma	Biopsy of subcutaneous nodules. Small amount of nitrogen mustard.	Biopsy of 2 of many subcutaneous nodules of abdomen, groins, back and head. Nitrogen mustard administered over 4 day period with no immediate effect over period of observation. Six weeks later abdominal mass began to shrink and cutaneous lesions began to disappear. Seven months after biopsy only two cutaneous nodules present and abdominal mass much smaller.
29. F. W. Stewart	1952	—	—	Neuroblastoma	Biopsy of lesion in femur. X-ray to femur. No treatment of primary (site unknown).	Patient first seen in infancy. Age of 14 years no evidence of metastatic or primary tumor.
30. F. W. Stewart	1952	Few months	M	Neuroblastoma	Biopsy of one subcutaneous nodule. Radium plaques applied to 1 or 2 nodules. Small amount of Coley's toxin.	Histologic diagnosis of neuroblastoma confirmed by several pathologists. Examination 5 years later revealed no evidence of nodules or tumor.
31. R. Phillips ³⁸	1953	4 months	F	Neuroblastoma	Celiotomy and biopsy large tumor of left adrenal gland. X-ray and chemotherapy.	Despite x-ray and chemotherapy rapidly developed proptosis of both eyes, profound anemia, sub-cutaneous and cranial metastases. Fatal termination appeared imminent at age of one year, then striking remission occurred. At age of 32 months patient reasonably well although characteristic ecchymosis of eyelids and frontal bossing still present.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
32. C. E. Koop, W. B. Kiesewetter, and R. C. Horn ²²	1955	17 months	M	Malignant Ganglioneuroma	Incomplete removal tumor mass. Biopsy mesenteric lymph nodes (malignant ganglioneuroma) but liver biopsy negative.	Tumor mass palpable to umbilicus 2 months after surgery. Two years and 4 months after surgery mass barely palpable at left costal margin. Patient well 2 years 11 months after surgery.
33. C. E. Koop, W. B. Kiesewetter, R. C. Horn	1955	2 months	M	Neuroblastoma	Incomplete removal of tumor involving area of both renal hili. Liver biopsy (hundreds of small white nodules present).	Patient developed subcutaneous nodules 6 weeks after operation. Abdominal mass decreasing in size 3 months after surgery.
34. C. M. Lee ²³	1955	6 months	M	Sympathicoblastoma	Biopsy liver metastases. 1.0 mg triethylene melamine for 3 days.	4 years after biopsy no evidence of adrenal tumor mass, right testicular mass or bony metastases to skull, scalp, long bones and mandible previously present. Patient well and strong.
35. S. Graves and J. W. Price ¹⁹	1917	18 years	F	Hemangioendothelioblastoma	ORAL Lesion partially removed with cautery.	After partial removal, tumor twice grew rapidly during pregnancy and subsided after delivery.
36. D. Roxburgh ²⁶	1935	60-70 years	F	Carcinoma of tongue	Biopsy. Extraction of tooth opposite lesion.	Ulcer healed in short time. Patient died 7 years later of acute pneumonia.
37. H. N. Fletcher ¹⁵	1949	58	F	Papillary adenocarcinoma ovary	OVARY Excision left ovarian tumor mass and right normal ovary.	Three firm raised nodules 1-1½ inches in diameter present on anterior surface liver noted at time of first operation. 29 months later at subsequent operation liver smooth and only sign of three previous nodules was a puckered scar.
38. J. E. Dunphy ¹¹	1950	54	F	Carcinoma	Biopsy of inoperable mass of pelvis (positive). Removal metastatic lesion right groin 9 years later (positive).	Tumor mass in pelvis absent and uterus freely movable 9 years after biopsy.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
OSTEOGENIC SARCOMA						
39. F. W. Stewart ⁴⁰	1952	—	M	Reticulum cell sarcoma of bone	Amputation of lower extremity through lower femur. Coley's toxin begun after local recurrence and distant metastases developed.	Disease recurred entire length of remaining femur. Metastasis in abdominal wall excised and histological diagnosis confirmed. All disease vanished and patient alive and well after 30 years.
PANCREAS						
40. E. V. Cowdry ⁷	1955	—	F	Carcinoma of pancreas	Exploratory celiotomy and biopsy of tumor mass.	Tumor considered to be inoperable. Patient survived for nine years. Autopsy failed to reveal any trace of cancer of the pancreas and showed death due to pulmonary embolus. M. G. Seelig reviewed and confirmed original diagnosis.
SOFT-TISSUE SARCOMA						
41. A. L. Watson ⁴⁴	1902	36	F	Sarcoma of back	Surgical excision.	27 days after initial removal, biopsy of recurrent tumor was diagnosed histologically as sarcoma by 4 different physicians. Recurrent tumor regressed markedly following post-op. fever.
42. G. L. Rohdenburg ⁴⁵	1918	57	F	Spindle-cell sarcoma of pelvis	Hot air baths (baking) for treatment of sciatic neuritis.	Secondary growth removed from omentum with histological diagnosis spindle cell sarcoma. Patient slowly improved, health restored 2 years later and pelvic mass gone. Patient subsequently died of uremia. Autopsy revealed no neoplasm in pelvis or abdomen.
43. B. R. Shore ⁴⁸	1936	2½ months	F	Fibrosarcoma of back	Surgical excision of primary tumor. Biopsy of recurrent tumor (positive).	Recurrence noted within 2 weeks after excision of primary tumor. 8 months after biopsy of recurrent tumor, mass noted to have decreased in size. 17 months after biopsy no evidence of tumor and 7 years after biopsy child was well.

TABLE I.—Continued

Author	Year of Publication	Age of Patient	Sex of Patient	Histologic Diagnosis of Tumor	Treatment	Comment
44. D. W. Penner ³²	1953	2½	M	Myosarcoma of thigh	Biopsy of tumor	Tumor on thigh began to disappear at age of 5 months and was completely gone by age of 9 months. Examination at age of 5½ years (5 years after biopsy) revealed no evidence of tumor.
STOMACH						
45. C. M. Smyth ³⁰		60	F	Adenocarcinoma of stomach	Celiotomy, biopsy of omentum (positive) and gastroenterostomy to bypass large antral mass.	Large mass in right upper quadrant disappeared and patient alive and well 11 years.
UTERUS						
46. F. W. Stewart ⁴⁰	1952	—	F	Myosarcoma	Radium	No regression noted with radium. Just before completion of treatment patient developed high fever and an allergic response. Tumor completely disappeared. Patient well 10 years later.
47. A. Brunschwig ⁵	1955	—	F	Adenocarcinoma	Radical hysterectomy. Abdominal biopsy 4 months later (positive).	Masses palpable by pelvic examination 4 months after hysterectomy. Abdominal re-pair of incisional hernia 4 months after hysterectomy and biopsy of abdominal tissue histologically diagnosed as adenocarcinoma. 16 months after biopsy no masses palpable in abdomen or pelvis.

excluded in this report would meet the prerequisites of designation as spontaneous regression if we had more data.

TABULATION OF COLLECTED CASES OF
SPONTANEOUS REGRESSION

Table I lists the 47 collected cases of spontaneous regression of cancer with brief comments as to the course of the malignancy. In Table II the cases are tabulated with respect to the incidence of the type or location of tumor involved. Reference to Table II indicates that in this collected series spontaneous regression occurred most frequently in neuroblastoma (ten cases), carcinoma of the bladder (eight cases), malignant melanoma (five cases), carcinoma of the breast (four cases), soft-tissue sarcoma (four cases), and cancer of the uterus (two cases). Spontaneous regression was also found in carcinoma of the colon (two cases), hypernephroma of the kidney (two cases), cancer of the oral cavity (two cases), metastatic carcinoma with primary site unknown (two cases), carcinoma of the ovary (two cases), and one each in osteogenic sarcoma, carcinoma of the lung, pancreas, and stomach.

CLASSIFICATION OF COLLECTED CASES OF
SPONTANEOUS REGRESSION

Classification of the collected cases has been made in Table III. In 22 cases regression of the primary tumor was reported. In 15 of these cases the regression was complete and in seven cases the regression was incomplete. Of the 15 cases in which regression of the primary tumor was reported to be complete, the regression was complete by gross examination only in seven cases, since no microscopic examination of the tissues after regression was done in these seven cases. In eight of the 15 cases of complete primary regression the regression was complete by gross examination and verified by microscopic examination of the tissues after regression. These latter eight cases included four cases of

TABLE II. *Tabulation of Collected Cases of "Spontaneous Regression" of Cancer*

Type or Location of Tumor	Number of Cases
Neuroblastoma	10
Bladder	8
Malignant melanoma	5
Breast	4
Soft-tissue sarcoma	4
Colon and rectum	2
Kidney	2
Metastatic carcinoma—primary unknown	2
Oral cavity	2
Ovary	2
Uterus	2
Lung	1
Osteogenic sarcoma	1
Pancreas	1
Stomach	1
Total number of cases	47

carcinoma of the bladder, a carcinoma of the colon, a neuroblastoma, a carcinoma of the pancreas, and a hypernephroma of the kidney. In seven cases regression of the primary tumor was incomplete. In three of these cases regression was incomplete by gross examination and in four cases regression was complete by gross examination but incomplete by microscopic examination. These latter four cases included three cases of carcinoma of the bladder and one case of hypernephroma of the kidney.

In seven cases regression of both the primary tumor and metastases was reported. Histologic confirmation of the malignancy of the metastases was present in all cases. Regression was complete in all seven cases. The regression was complete by gross examination in five cases and by gross examination verified by microscopic examination of the tissues after regression in the other two cases. These latter two cases include one case of metastatic adenocarcinoma with the primary site unknown and one case of sarcoma of the pelvis.

Regression of local recurrences was reported in four cases. In all cases there was histologic confirmation of the malignancy of the recurrences. Regression was com-

TABLE III. *Classification of Collected Cases of "Spontaneous Regression" of Cancer*

<p>I. Regression of primary tumor—22 cases</p> <p>A. Regression complete—15 cases</p> <p>By gross examination—7 cases</p> <ol style="list-style-type: none"> 1. Papillary carcinoma of bladder (Trabucco) 2. Carcinoma of tongue (Roxburgh) 3. Myosarcoma of thigh (Penner) 4. Myosarcoma of uterus (Stewart) 5. Carcinoma of stomach (Smyth) 6. Carcinoma of ovary (Dunphy) 7. Sympathoblastoma (Van Creveld and Van Dam) <p>By microscopic examination—8 cases</p> <ol style="list-style-type: none"> 1. Transitional cell carcinoma of bladder (Goldberg) 2. Squamous cell carcinoma of bladder (Creevy) 3. Transitional cell carcinoma of bladder (Creevy) 4. Papillary carcinoma of bladder (Fort, Harlin, and Atkinson) 5. Adenocarcinoma of colon (Ferguson and Black) 6. Neuroblastoma (Cushing and Wolback) 7. Carcinoma of pancreas (Cowdry) 8. Hypernephroma of kidney (Hall) <p>B. Regression incomplete—7 cases</p> <p>By gross examination—3 cases</p> <ol style="list-style-type: none"> 1. Bronchiogenic carcinoma (Blades and McCorkle Jr.) 2. Malignant ganglioneuroma (Koop, Kiesewetter, and Horn) 3. Hemangioendothelioblastoma of gum (Graves and Price) <p>By microscopic examination—4 cases</p> <ol style="list-style-type: none"> 1. Adenocarcinoma of bladder (Davis) 2. Papillary carcinoma of bladder (Davis) 3. Papillary carcinoma of bladder (Pearse) 4. Hypernephroma of kidney (Rae) <p>II. Regression of primary tumor and metastases—7 cases</p> <p>(Histologic confirmation of metastases in all cases)</p> <p>A. Regression complete—7 cases</p> <p>By gross examination—5 cases</p> <ol style="list-style-type: none"> 1. Neuroblastoma (Stewart) 2. Neuroblastoma (Goldring) 3. Neuroblastoma (Koop, Kiesewetter, and Horn) 	<ol style="list-style-type: none"> 4. Sympathicoblastoma (Lee) 5. Adenocarcinoma—primary site unknown (Altmeier) <p>By microscopic examination—2 cases</p> <ol style="list-style-type: none"> 1. Adenocarcinoma—primary site unknown (Levine and Weiner) 2. Sarcoma of pelvis (Rohdenburg) <p>III. Regression of local recurrences—4 cases</p> <p>(Histologic confirmation of local recurrence in all cases)</p> <p>A. Regression complete—3 cases</p> <p>By gross examination—3 cases</p> <ol style="list-style-type: none"> 1. Scirrhus carcinoma of breast (Lilienthal) 2. Reticulum cell sarcoma of bone (Stewart) 3. Fibrosarcoma of back (Shore) <p>B. Regression incomplete—1 case</p> <p>By gross examination—1 case</p> <ol style="list-style-type: none"> 1. Sarcoma of back (Watson) <p>IV. Regression of local recurrences and metastases—3 cases</p> <p>(No biopsies of local recurrence)</p> <p>A. Regression complete—2 cases</p> <p>By gross examination—2 cases</p> <ol style="list-style-type: none"> 1. Carcinoma of breast (Mackay) 2. Carcinoma of breast (Scott) <p>B. Regression incomplete—1 case</p> <p>By gross examination—1 case</p> <ol style="list-style-type: none"> 1. Carcinoma of breast (Hodenpyl) <p>V. Regression of metastases—11 cases</p> <p>A. Regression complete—9 cases</p> <p>By gross examination—8 cases</p> <ol style="list-style-type: none"> 1. Adenocarcinoma of rectum (Ellison) 2. Melanosarcoma (Meyer) 3. Malignant melanoma (Pack) 4. Melanoblastoma (Blocker) 5. Papillary adenocarcinoma of ovary (Fletcher) 6. Adenocarcinoma of uterus (Brunschwig) 7. Neuroblastoma (Stewart) 8. Neuroblastoma (Phillips) <p>By microscopic examination—1 case</p> <ol style="list-style-type: none"> 1. Malignant melanoblastoma (Vial and Coller) <p>B. Regression incomplete—2 cases</p> <p>By gross examination—2 cases</p> <ol style="list-style-type: none"> 1. Melanosarcoma (Mathews) 2. Neuroblastoma (Stewart)
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plete in three cases by gross examination. Regression was incomplete by gross examination in one case.

Regression of local recurrences and metastases was reported in three cases. Although histologic confirmation of malignancy was present for the metastatic lesions (areas grossly incompletely removed surgically), the diagnosis of local recur-

rences was clinical without biopsy confirmation. Regression of local recurrences and metastases was complete in two cases by gross examination and incomplete in one case by gross examination.

Regression of metastases was reported in 11 cases. Of the nine cases in which regression of metastases was reported to be complete, the regression was complete by gross

examination in eight. In all 11 cases of this series the malignancy of the primary tumor was verified by microscopic examination of the tissues. In one case regression was complete by gross examination and verified by microscopic examination of the tissues after regression. This latter case was a patient with malignant melanoma. In two cases regression of metastases was incomplete by gross examination.

In 11 cases an area of malignant tissue verified by microscopic examination underwent complete regression, not only by gross examination, but by microscopic examination of the tissues (see Table IV). It is to be noted that the patient reported by Vial and Collier developed an isolated local recurrence (4 cm. in diameter) approximately two years after regression of dozens of pigmented skin metastases. (This local recurrence was excised and microscopic examination confirmed the diagnosis of malignant melanoblastoma. The patient has been alive and well without evidence of neoplastic disease 20 months since excision of the recurrence.)

SOME POSSIBLE FACTORS RESPONSIBLE FOR REGRESSION

There are many factors which might be suggested as being wholly or partly responsible for the spontaneous regression of cancer in these collected cases.

1. *Endocrine influences.* The therapeutic effectiveness of endocrine treatment in the management of advanced cancer of, for example, the breast and prostate is well established. It is possible that hormonal alterations within the body, by menopausal effects or other endocrine factors as yet unknown, may have exerted a beneficial effect in the cases reported.

2. *Complete surgical removal.* Of the 47 collected cases partial removal of the tumor area which subsequently underwent spontaneous regression was performed in a number of cases. It is possible that the

TABLE IV. *Complete Regression Confirmed by
Microscopic Examination*

1. Carcinoma of bladder (Goldberg)
2. Carcinoma of bladder (Creedy)
3. Carcinoma of bladder (Creedy)
4. Carcinoma of bladder (Fort <i>et al.</i>)
5. Carcinoma of colon (Ferguson and Black)
6. Neuroblastoma (Cushing and Wolbach)
7. Carcinoma of pancreas (Cowdry)
8. Hypernephroma of kidney (Hall)
9. Adenocarcinoma—primary unknown (Levine and Weiner)
10. Sarcoma of pelvis (Rohdenburg)
11. Malignant melanoma (Vial and Collier)

remaining tissue was only inflammatory rather than malignant.

3. *Unusual sensitivity to inadequate irradiation or other therapy.* Irradiation therapy was utilized in five cases. However, in all instances the dosage used was small and the response during the period of treatment was such as to suggest that irradiation was not the cause of the regression. However, because irradiation was used in these cases, therapeutic effect due to an unusual sensitivity of the tumor cannot be ruled out.

In one instance, small amounts of nitrogen mustard were used, and in another case small doses of triethylene melamine were used. While these substances are generally completely ineffective in control of the tumors in which they were used, it is a remote possibility that for some unknown reason these tumors were unusually sensitive to these substances. Coley's toxins were also used in several cases.

4. *Fever and/or acute infection.* These factors have frequently been suggested as of importance in cases of spontaneous regression. The complete regression of adenocarcinoma of the colon reported by Ferguson and Black would appear to fit in this category.

5. *Allergic reaction.* Allergic reaction with destruction of the tumor cells might be a factor in some cases. The complete regression of a myosarcoma of the uterus reported by Stewart possibly might be included in this group.

6. *Interference with nutrition of the tumor.* It has been suggested by Rohdenburg that during incomplete removal of malignant tissue the blood supply of the remaining tumor may be so impaired that death of the residual tumor occurs. Likewise, it is conceivable that local or general disturbances of the body metabolism might adversely affect the growth or viability of cancer.

7. *Removal of carcinogenic agent.* The disappearance of eight carcinomas of the bladder (with complete regression confirmed by microscopic examination in four cases) after ureterosigmoidostomy suggests that regression may occur after withdrawal or divergence of a carcinogenic agent.

8. *Incorrect diagnosis of malignancy.* Because of the factor of error in the diagnosis of malignancy, all cases published before 1900 have been arbitrarily excluded from consideration at the suggestion of several pathologists. The accuracy of differentiation between benign and malignant tumor is acknowledged to be a source of error. However, where possible we have requested the slides on which the diagnosis of malignancy was originally made in these collected cases so that we might submit the slides to two other independent pathologists for examination. To date we have obtained this additional confirmation of the diagnosis in only a part of the series, but effort is being made to obtain this confirmation in as many as possible. Because of unavailability of slides this confirmation will not be possible in all.

SUMMARY

A study of the incidence and nature of spontaneous regression of cancer has been initiated. Of over 600 cases published or obtained by personal communication, to date we have considered only 47 cases to have adequate documentation to be accepted as possible examples of spontaneous regression. It is barely possible that if we had more clinical data, a large number of

cases studied but not included would meet our prerequisites. In 11 of the 47 collected cases regression was complete and verified by microscopic examination of the tissues after regression. One of the main purposes of this study is to see if we could identify a significant factor or factors responsible for the regression. Several factors have been mentioned by various authors (particularly Rohdenburg), and noted by us in case histories kindly submitted by our friends. Important among these are endocrine factors, unusual sensitivity to inadequate irradiation or other therapy, fever and/or infection, allergic reactions, interference with nutrition of the tumor, and removal of the carcinogenic agent.

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DR. JOHN ENGLEBERT DUNPHY, Boston, Massachusetts: I think we are all indebted to Dr. Cole and Dr. Everson for this very important and monumental undertaking. My own interest in the subject goes back to 1946, and on several occasions I have started to undertake such a study but have abandoned it, being overwhelmed by the magnitude of the task of confirming the diagnosis.

I would like to give you a brief followup of one of our cases which is included in this series.

(Slide) This patient originally had a carcinoma of the left ovary with generalized abdominal metastases. It was biopsied and no further operation was done, and no x-ray was given.

The patient was lost to followup, although we did see her 18 months later, at which time she had lost considerable weight and had ascites. Arrangements at that time were made for terminal care in a nursing home. She reappeared in the hospital in 1946 and was thought to have an incarcerated right inguinal hernia. Obviously we