

## Illustrations of Some Therapeutic Results

According to our paradigm, all diseases showing a Th1 autoimmune profile (excessive cellular immune activity) present a neurochemical profile similar to endogenous depression: high NA + normal Ad = raised NA/Ad ratio values (greater than 5) + low TRP plasma levels. On the contrary, all diseases showing a Th2 autoimmune profile (excessive humoral immunity) present a neurochemical profile similar to that registered in chronic uncoping stress patients: low NA + high Ad + low NA/Ad ratio values (less than 2) + raised or normal TRP + raised f5HT plasma levels.

The Th1 (endogenous or major depression) profile would express the following CNS neurochemical profile: hyperactivity of the LC NA neuronal group + hypoactivity of the pontine serotonergic nuclei DR and MR + hypoactivity of the C1-adrenergic medullary nuclei.

The Th2 (chronic uncoping stress) profile would express the following CNS neurochemical profile: hypoactivity of the LC-NA + DR-5HT + MR-5HT nuclei + hyperactivity of the C1-Ad medullary nuclei. Both those 5HT nuclei send excitatory axons to the two vagal motor nuclei, nucleus tractus solitarius and nucleus ambiguus. Vagal nerves are the excitatory drive responsible for the release of 5HT by enterochromaffin cells. Intestinal 5HT constitutes the only source of blood serotonin. Ninety percent of blood 5HT is stored in the platelets (p-5HT). For this reason, p-5HT shows significant rise during postprandial periods and during sleep, at which time hyperparasympathetic activity is registered. According to all the above, adrenomedullary-sympathetic and parasympathetic activities are liberalized from the pontine NA-5HT control and would display alternating predominances. Two factors cooperate to maintain the increased free serotonin (f-5HT) in the plasma of uncoping stressed mammals: (a) adrenaline-triggered platelet aggregation during hypersympathetic predominance, and (b) acetylcholine-induced inhibition of platelet uptake during parasympa-

thetic activation. The raised Ad + raised f-5HT converge to suppress Th1 immune activity and favor Th2 predominance.

Neuropharmacological therapy of Th2 immune disorders is the treatment we prescribe for all uncoping-stress associated diseases. Malignant diseases are included among this group. However, Hodgkin's lymphoma and pancreatic adenocarcinoma are not included in this group. Neuropharmacological manipulations are addressed to increasing central noradrenergic (neural sympathetic) activity. The following drugs are routinely administered:

- (1) NA precursors (*L*-tyrosine, *L*-phenylalanine).
- (2) NA-releasing agents ( $\alpha_2$ -antagonists) such as yohimbine.
- (3) Small doses of  $\beta$ -blocking agents (propranolol).
- (4) NA uptake inhibitors (desipramine, maprotyline, doxepin, etc.).
- (5) NA + dopamine enhancer drug (buspirone). These NA-potentiating drugs should be administered early in the morning.
- (6) Small doses of 5HT precursor (5-OH-tryptophan = 25 mg) + a 5HT-releasing agent like trazodone 25–50 mg before bed.
- (7) GH-releasing agents such as GH-RH hormone and arginine should also be administered before bed. GH is the most powerful Th-1-activating agent. However, GH itself should not be administered in cancer patients. This factor provokes macrophage accumulation around tumoral cells and granulomas are induced. These granulomas simulate tumor growth in which biopsies, however, detect nontumor cells. In some cases, tumoral cells are found in the deepest zones of such GH-induced granulomas.
- (8) Dopaminergic agonists like amantidine in small doses (100 mg two times weekly). This drug should be used in good sleepers only.
- (9) Levamisole (50 mg), twice weekly.



**Fig. 14.1.** Ulcerated mammary adenocarcinoma, before and after 4 months of neuropharmacological therapy. The great improvement registered in this patient permitted surgical resection (she died 7 years later).

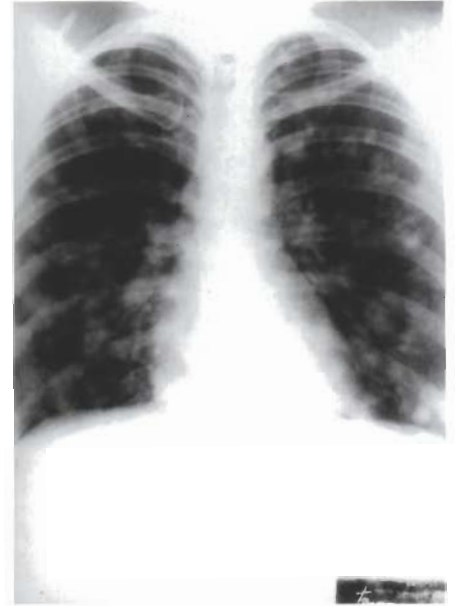
Up to the present we have treated some 3,000 advanced cancer patients. Most came to our institute when all conventional therapies had failed. We have presented our results in the most important cancer hospitals of the US (see references).

We present here a small sample of various cured or greatly improved malignant tumors. It is not our intention to announce a cure for malignant diseases, but to demonstrate the close association existing between uncoping stress situation, Th-2 immune profile, and malignant dis-



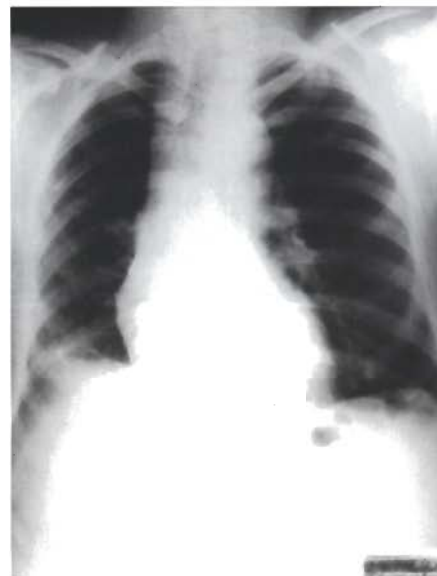
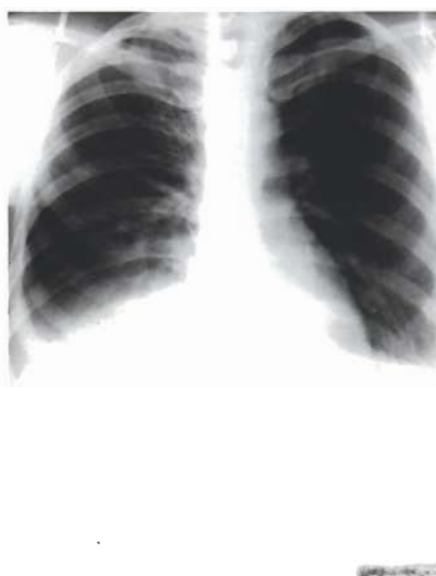
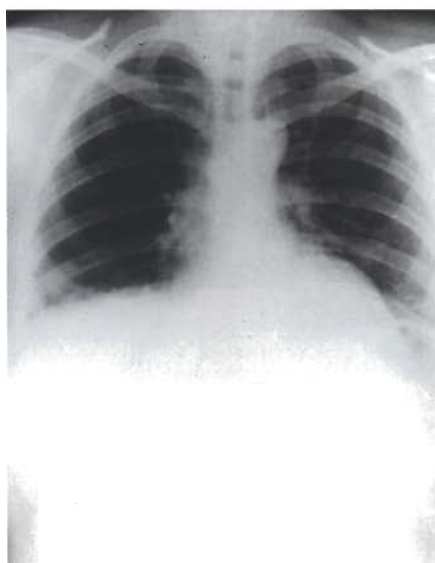
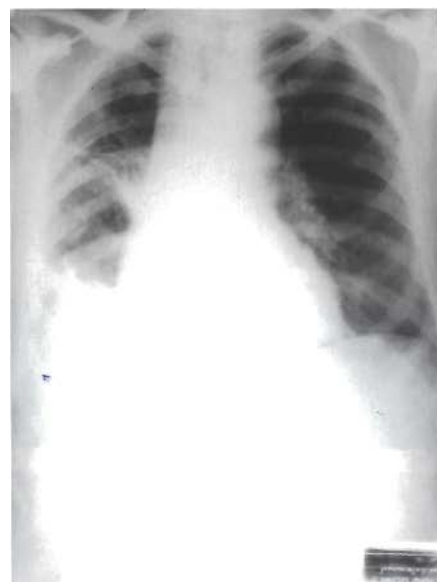
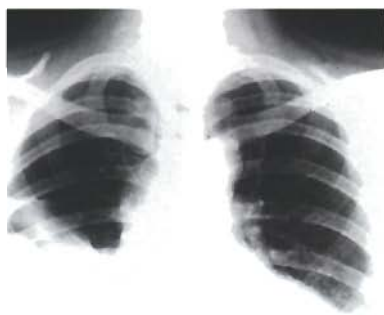
**Fig. 14.2. a** Ulcerated mammary adenocarcinoma, before and after 5 months of neuropharmacological therapy.

ease. When we lectured, by invitation at conferences in several US oncology hospitals and universities, oncologists were greatly impressed. However, they asked us for a package treatment like chemotherapy and radiotherapy. They could not accept treatments based on neuropharmacological, neuroendocrinological or neuroimmunological



**Fig. 14.2. b** The same case: multiple, bilateral pulmonary metastasis almost disappeared also.

manipulations. Their hospitals are not provided with neurochemical laboratories. These specialists felt unable to design appropriate neuropharmacological therapy according to neurochemical + immunological findings. Unfortunately, this obstacle is still present. For our part, we continued applying our therapeutic approach on cancer



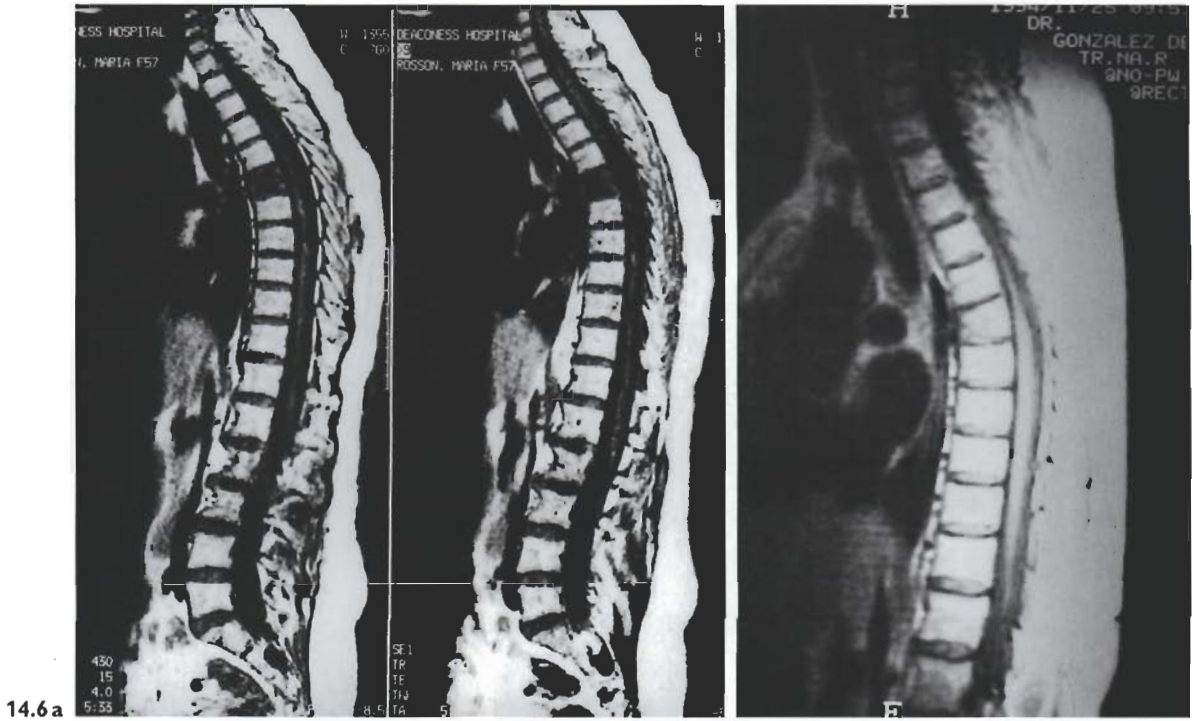
**Fig. 14.3.** Pulmonary metastasis in the right lung, secondary to previously resected mammary gland. Total disappearance was observed within 4 months of neuropharmacological therapy. No relapses occurred.

**Fig. 14.4.** Right pleuropulmonary metastasis, secondary to previously resected mammary gland. Total disappearance was observed after 3 months of neuropharmacological therapy.

**Fig. 14.5.** Breast metastatic lung cancer before and after 5 months of neuropharmacological therapy (mammary adenocarcinoma).

patients attending our institute and gave up reporting our experience to medical journals because they lacked adequate reviewers and asked for double-blind studies. Sadly, the great majority of our patients are short-term survivors of chemo- and radiotherapy who have been informed that their days are numbered. They visit our institute to alle-

viate pain and perhaps prolong their lifespan. After they leave the institute they are in God's hands. In our long experience, the low percentage of patients having previously received neither chemotherapy nor radiotherapy, show the best response to neuropharmacological treatment.



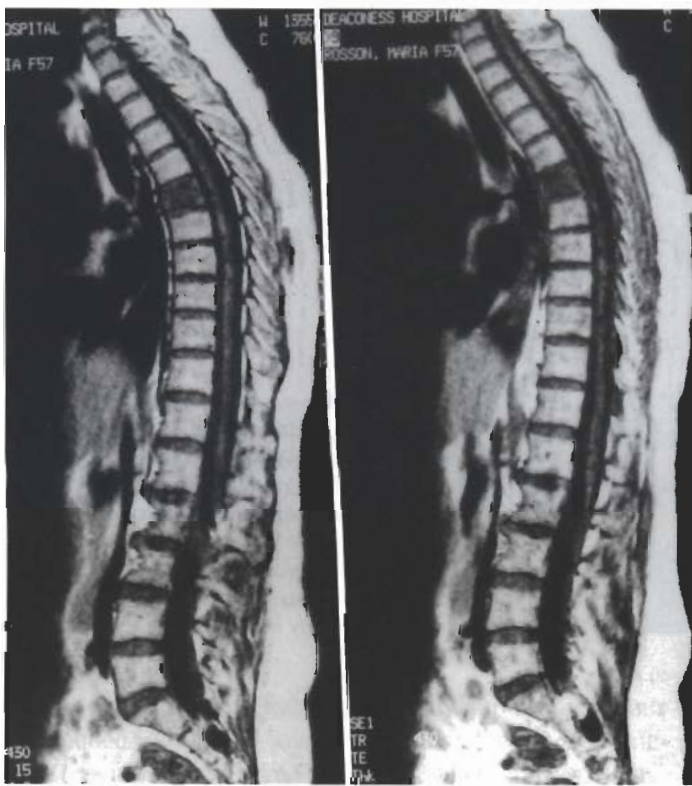
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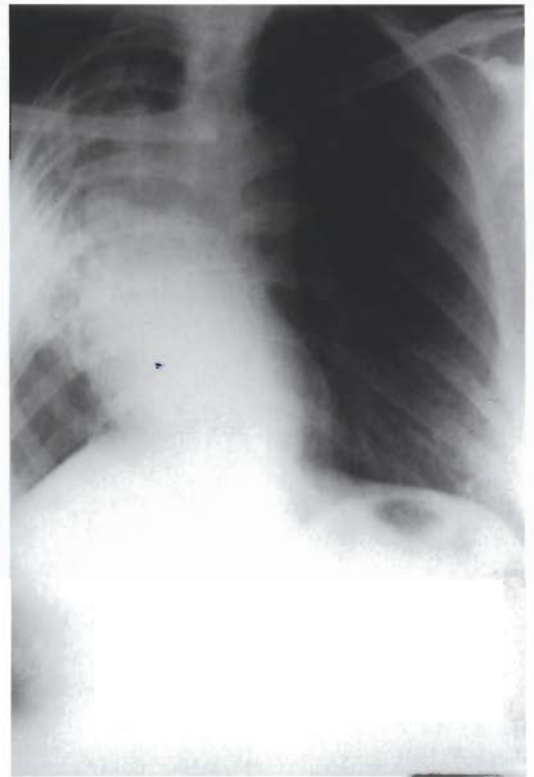
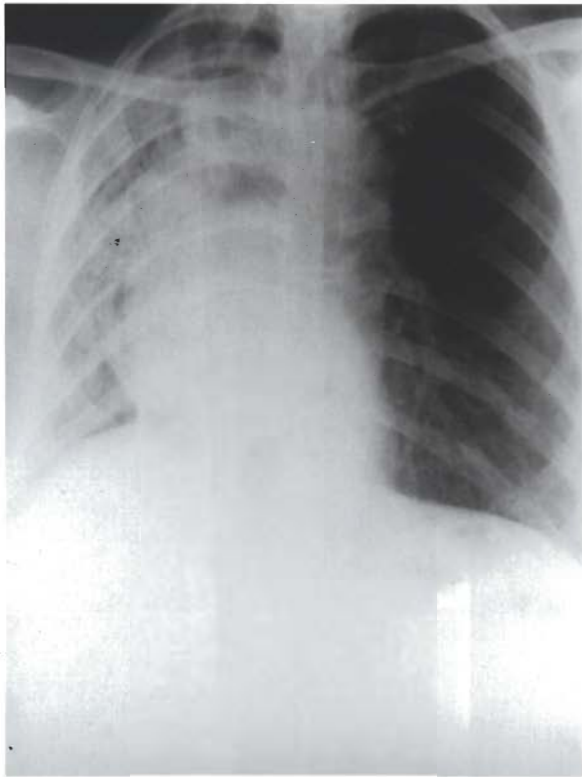
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(Fig. 14.6c, see next page.)

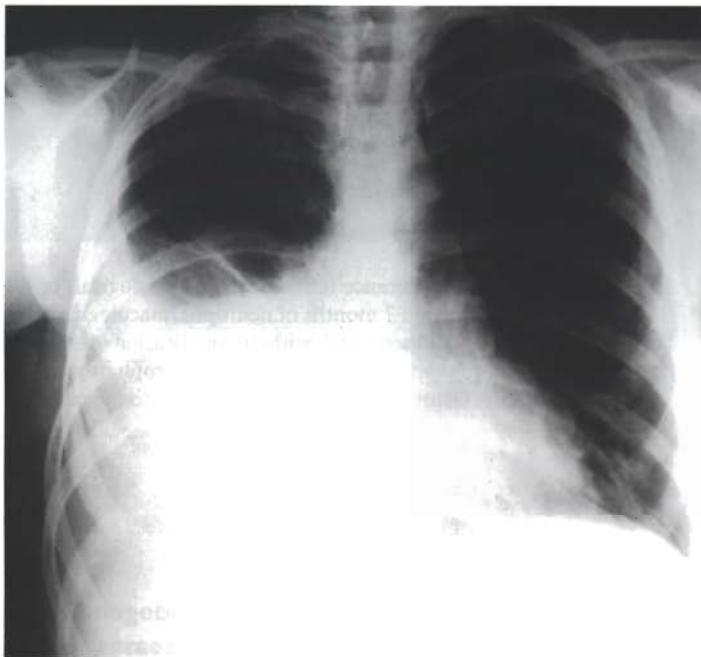
**Fig. 14.6 a-c.** Bone metastasis at the 6th thoracic vertebra. After 5 months of neuropharmacological therapy the bone was healed. The primary tumor, a pulmonary adenocarcinoma, was resected 1 month before at the Deaconess Hospital in Boston (USA), where post-surgical radiotherapy was suggested to alleviate pain. No radiotherapy was applied.



14.6c



14.7



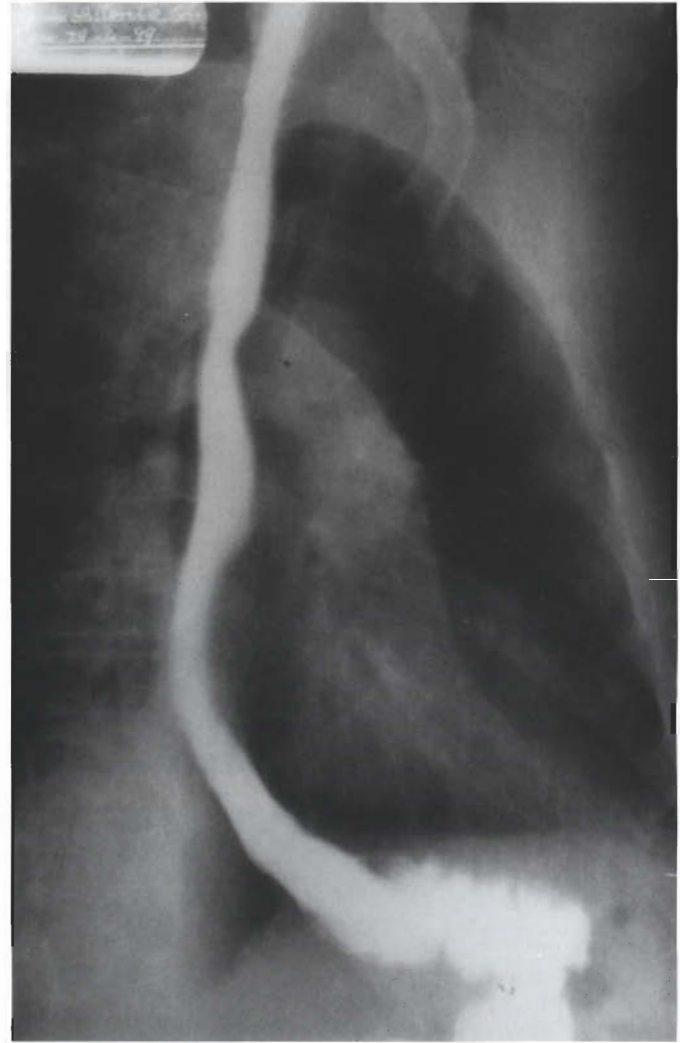
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**Fig. 14.7.** Lung cancer (adenocarcinoma) + supraclavicular metastasis. Eight months after chemotherapy + radiotherapy courses, cancer symptoms reappeared and the patient entered neuropharmacological therapy. Within 2 years, significant reduction of tumoral images was obtained and the patient was discharged symptomless. She then traveled to San Francisco (USA) where she attended her severely diseased mother, night and day, for several months. She died 2 months after her mother's funeral.

**Fig. 14.8.** Right pleuropulmonary metastases from a previously resected mammary adenocarcinoma. Normalization was obtained after 4 months of neuropharmacological therapy.



**Fig. 14.9. a** Carcinoma epidermoid of the esophagus (radiological plus endoscopic diagnosis).



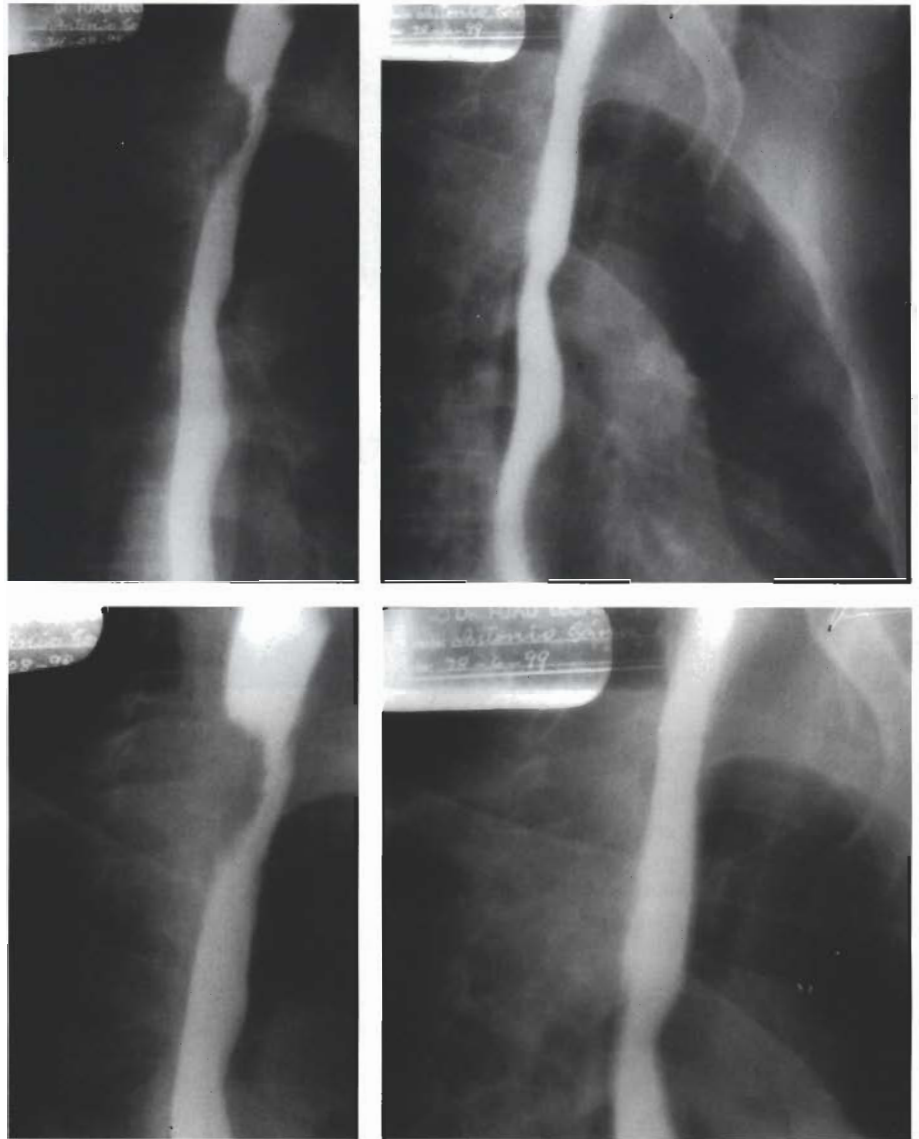
**Fig. 14.9. b** Total disappearance (endoscopic + radiological) of the tumor was obtained within 7 months of neuropharmacological therapy. The patient was absent and without medication during 13 months. The tumor reappeared and he entered neuropharmacological therapy again in October 2000 continuing this up to the present.

### **Other Diseases Associated with Uncoping Stress Profile (Th2 Autoimmune Diseases)**

We have treated many other patients showing a neurochemical profile of uncoping stress and a Th-2 immune profile. These patients received neuropharmacological therapy addressed to increasing central noradrenergic activity and to bridling peripheral adrenomedullary activity. To date we have successfully treated patients suffering from myasthenia gravis (over 800 cases), thrombocytopenic purpura, Guillain-Barré, atopic dermatitis, stress-associated female infertility, gastric malthoma, and non-Hodgkin lymphoma.

### **Neuropharmacological Therapy of Endogenous Depression Neurochemical Profile Diseases (Th1 Autoimmune Diseases)**

These diseases frequently present a Th-1 immune profile. Rheumatoid arthritis, Sjögren disease, psoriasis, scleroderma, Raynaud disease, multiple sclerosis, Crohn's enteritis, dermatomyositis and pemphigus are included among the Th-1 profile diseases. In the following section,



**Fig. 14.9. c** The same case (No. 9) after and before neuropharmacological therapy.

we give some examples of the effects of neuropharmacological therapy on the progress of this type of diseases.

Neuropharmacological therapy is addressed to reducing central noradrenergic activity and to increasing DR-5HT + MR-5HT activity. To this end, we use the following neuropharmacological manipulations:

(1) Cursors of 5HT, for example 5-OH-TRP (50–100 mg).

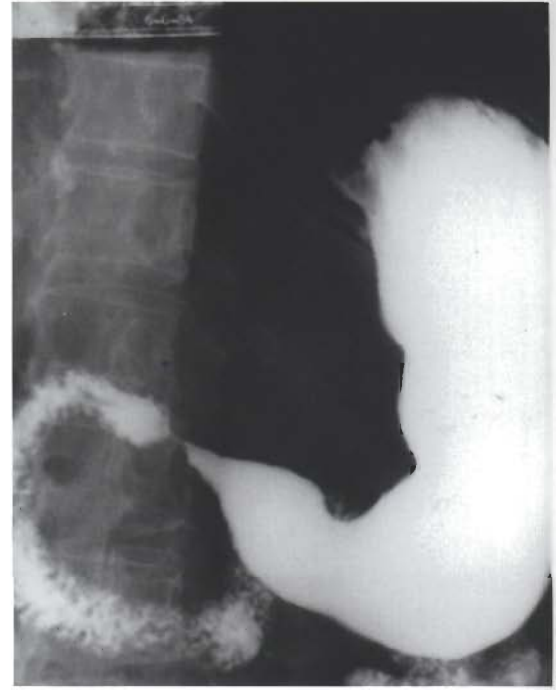
(2) 5HT-releasing agents like the 5HT<sub>2</sub>-receptor antagonist trazodone (25–50 mg).

(3) 5HT<sub>1A</sub>-antagonist such as pindolol (2.5 mg); inhibitors of 5HT uptake including sertraline (25–50 mg) and paroxetine (20–40 mg).

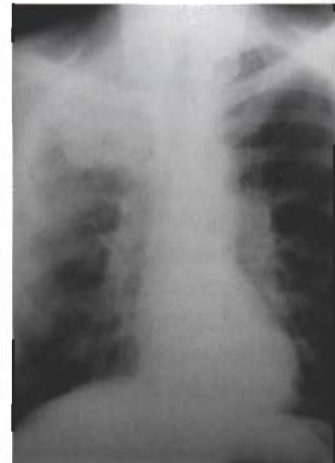
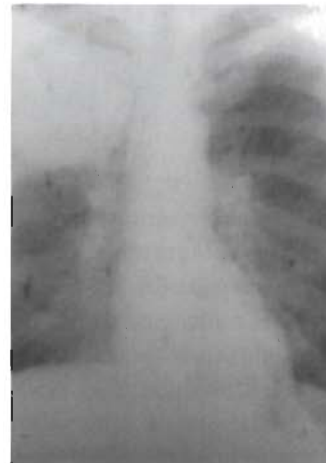
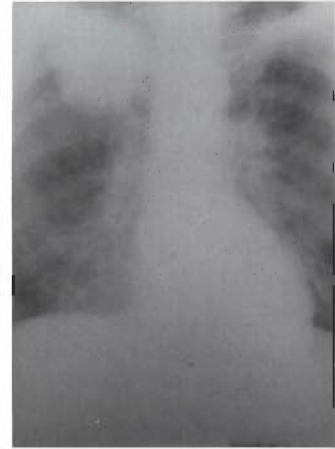
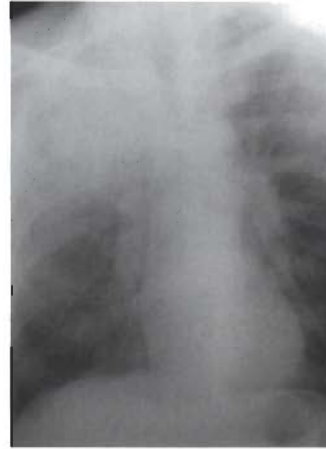
(4)  $\alpha_2$ -Agonists like clonidine (0.15 mg).

(5) Tizanidine (4 mg).

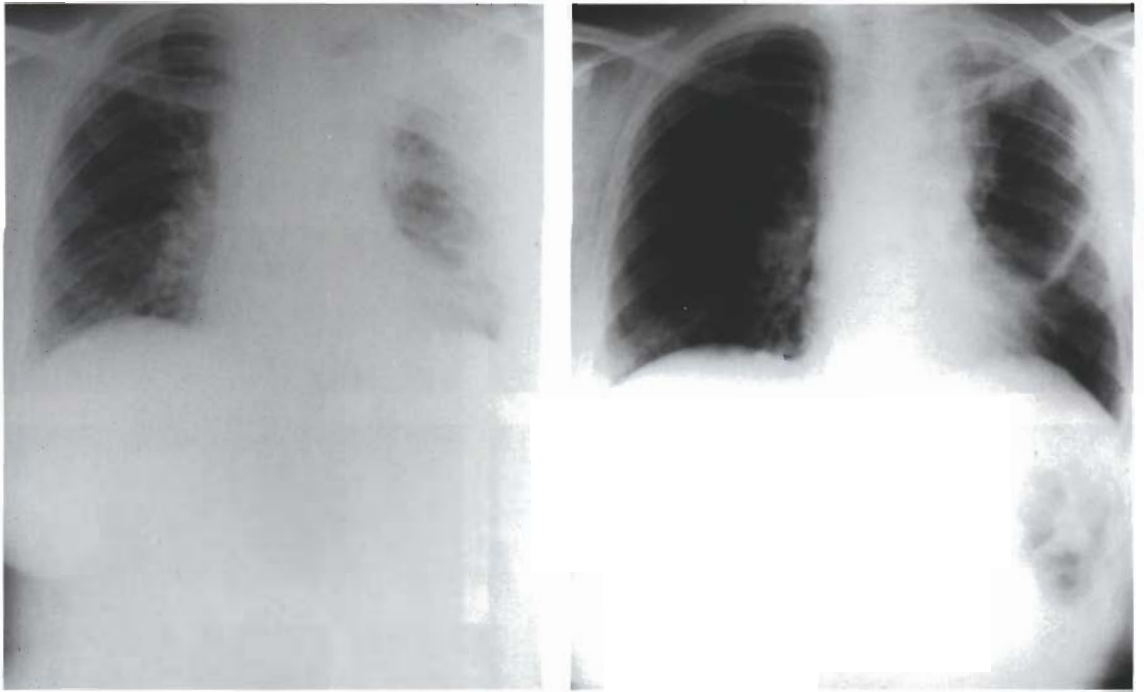
(6) Trifluoperazine (2–5 mg).



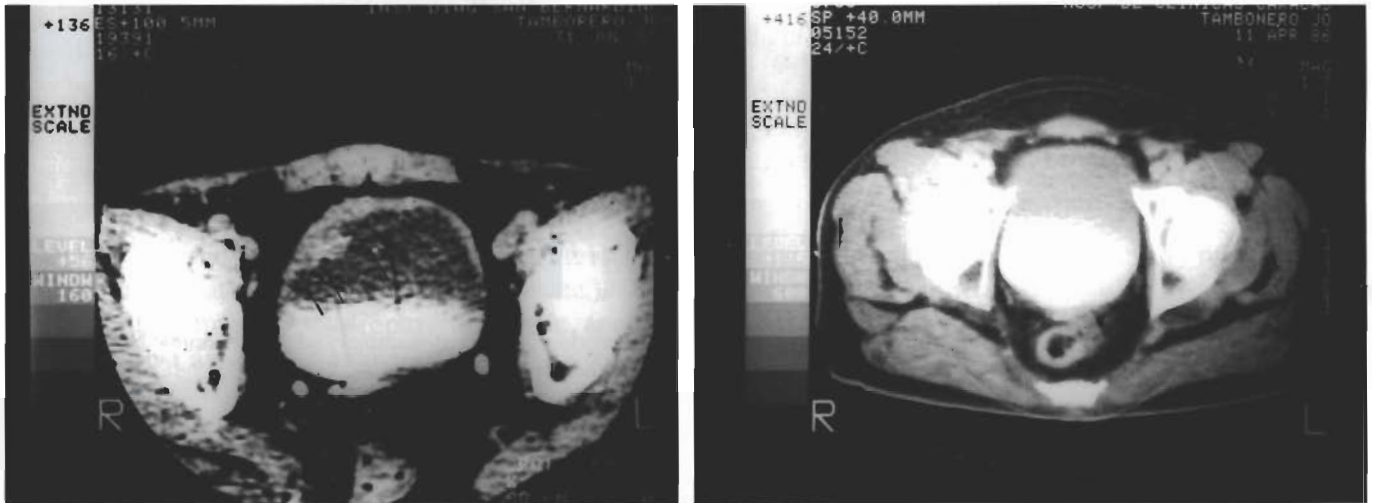
**Fig. 14.10.** Age 71, female. At first visit in January 1984 gastric adenocarcinoma was diagnosed in this patient who refused surgery in favor of neuropharmacological therapy. In 6 months, she showed radiological normalization of her tumor. Rejecting new endoscopic investigation, she remained free of symptoms until 1991 when she died of a cerebrovascular accident.



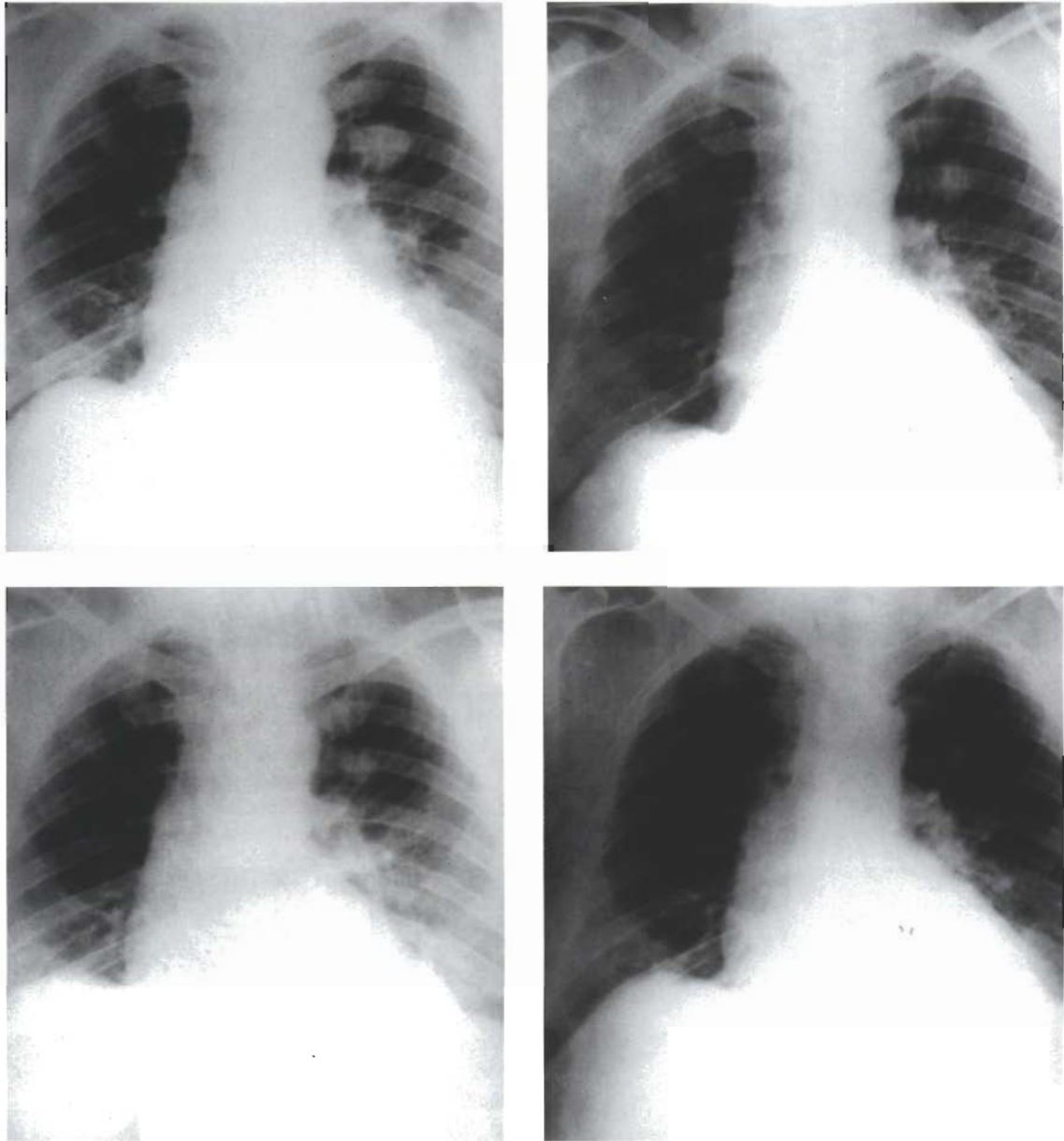
**Fig. 14.11.** Age 56, male. Pulmonary adenocarcinoma. Great parenchymal infiltration of the upper right lung lobe. He received neuropharmacological therapy during 3.6 years. He remained symptomless. He died following an accidental fall.



**Fig. 14.12.** Pleuropulmonary metastases from a previously resected mammary adenocarcinoma. Significant improvement was obtained after 3 months of neuropharmacological therapy.



**Fig. 14.13.** Age 59, male. In July 1985, the patient underwent endoscopic resection of urinary bladder adenocarcinoma, followed by chemotherapy in August 1985. Bladder tumor reappeared in March 1986. Endoscopic biopsy revealed transitional cells adenocarcinoma, degree IV (Ash classification). Total disappearance was obtained after 3 months of neuropharmacological therapy. Last control in July 2000.



**Fig. 14.14.** Left pleuropulmonary metastases from a previously resected mammary adenocarcinoma. Normalization was obtained after 3 months of neuropharmacological therapy.

(7) DA antagonist that reduces NA and facilitates 5HT activity.

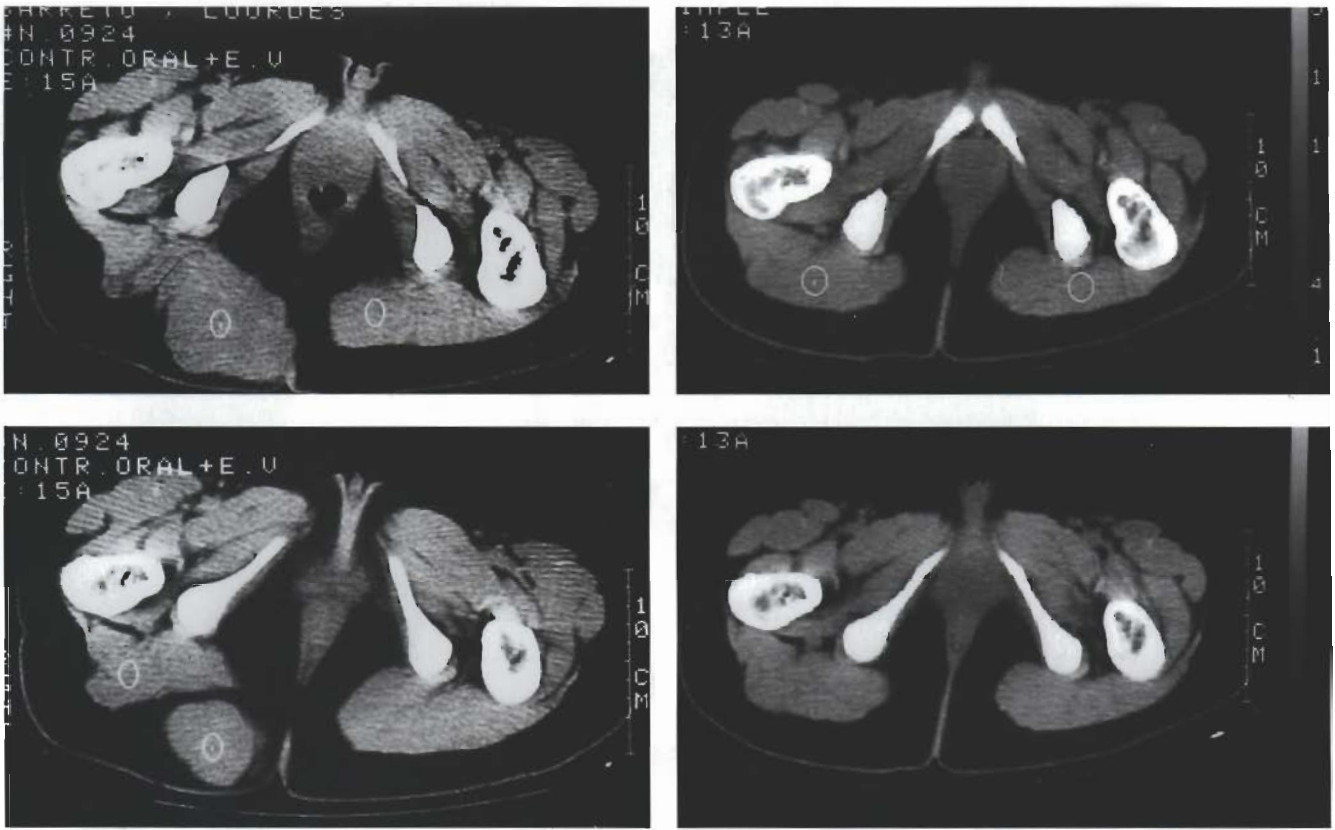
(8) Methotrexate (2.5–5 mg weekly).

(9) In some severe cases lithium salts are added (200 mg twice weekly).

(10) *L*-Tryptophan does not cross the BBB easily. We use this 5HT precursor in some cases of rheumatoid ar-

thritis looking for beneficial peripheral effects. It has been demonstrated that plasma 5HT is able to reduce macrophage activity.

We have treated many cases of multiple sclerosis with the above neuropharmacological therapy. One of these cases was an MD (ophthalmologist) who had lost his vision. He recovered his sight completely (he is now per-



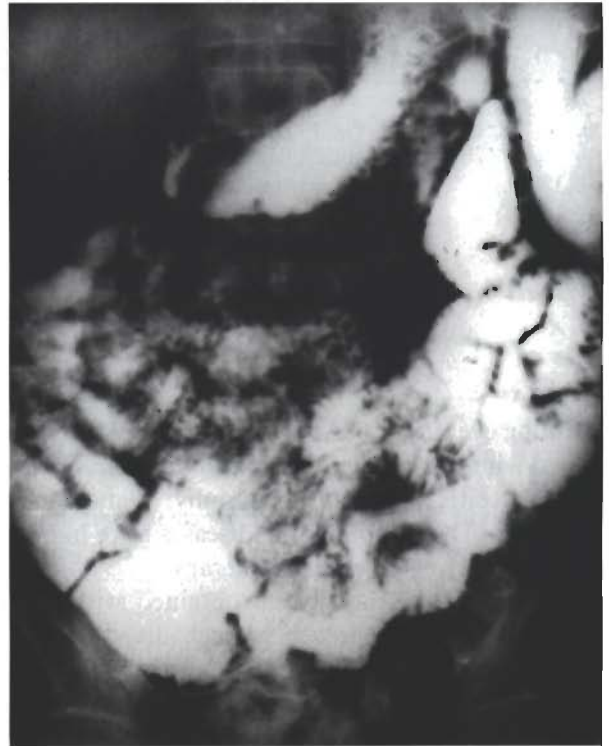
**Fig. 14.15.** Female, age 15. First visit in February, 1991. Surgical resection of Antoni type B schwannoma in the right gluteal region was performed in March 1989. Recidivant tumor was diagnosed in December 1990. The patient and her parents refused further surgery and visited our Institute. Neuropharmacological therapy began in March 1991. CAT scan showed complete remission after 3 months of treatment. The patient has remained symptomless. Last control in January 1995.

forming eye surgery). All types of therapy had previously failed with this patient (steroids,  $\beta$ -interferon, etc.). Dermatomyositis, muscular dystrophy, hemolytic anemia and other Th-1 autoimmune diseases have likewise been successfully treated with this therapy.

Summarizing, the success obtained with the neuropharmacological approach to such diverse organic (somatic), nonpsychiatric diseases is consistent with the hypothesis that the CNS circuitry, the immune system, the endocrine and the autonomic nervous system are closely interlinked, and thus all pharmacological manipulations addressed to normalizing the CNS circuitry lead to normalization of both central and peripheral physiologic disorders. In our opinion, treatment of patients should return to the hands of scientific doctors. With this aim, practitioners should receive scientific, interdisciplinary

training. Medical technology is necessary but should not be the only pillar of therapy.

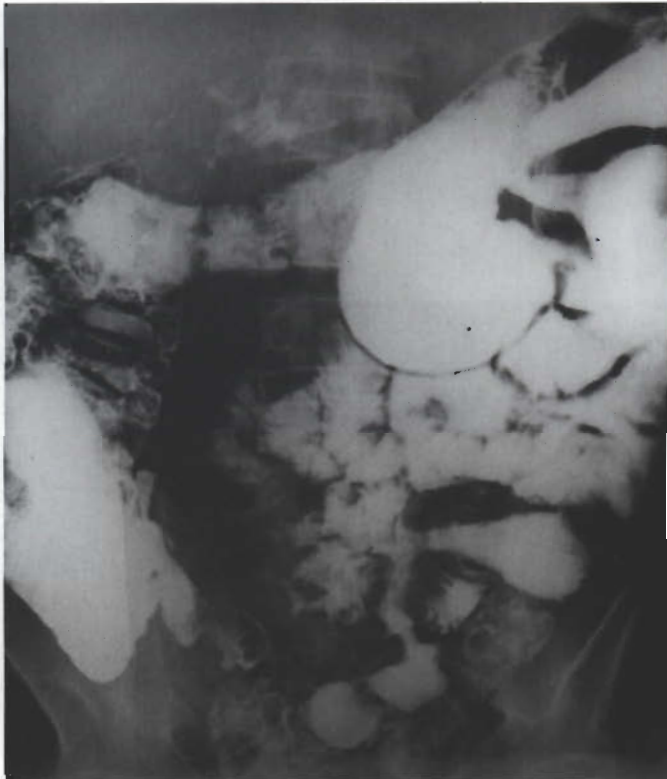
In the following pages, we illustrate results obtained with the above neuropharmacological approaches with some cases.



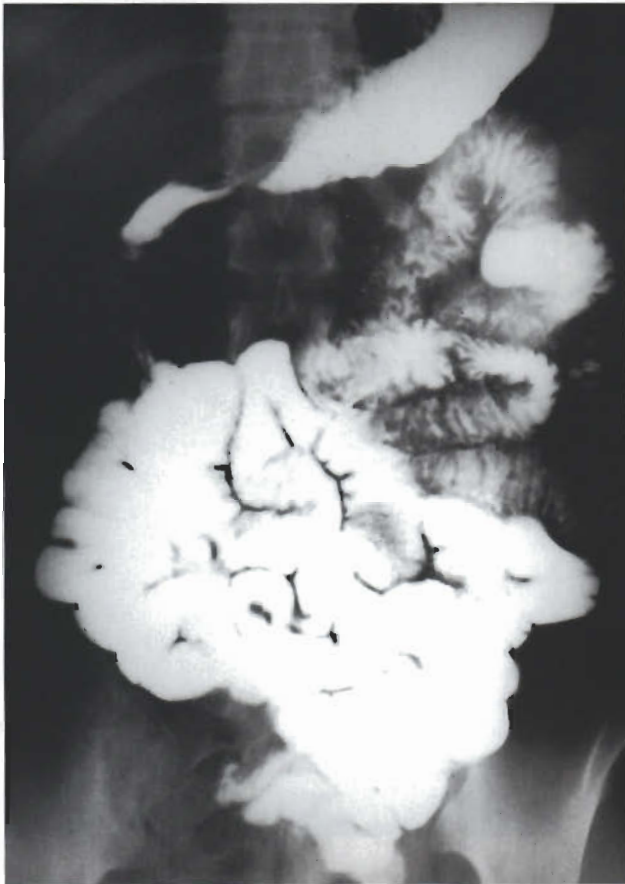
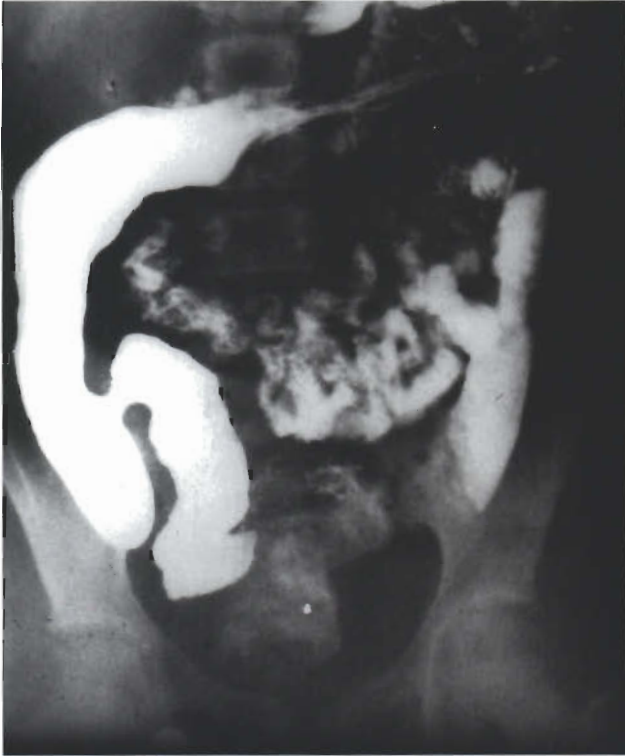
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**Fig. 14.16.** Small bowel X-ray of a severely ill Crohn's patient. Radiological and clinical normalization occurred within 1 year of neuropharmacological treatment.

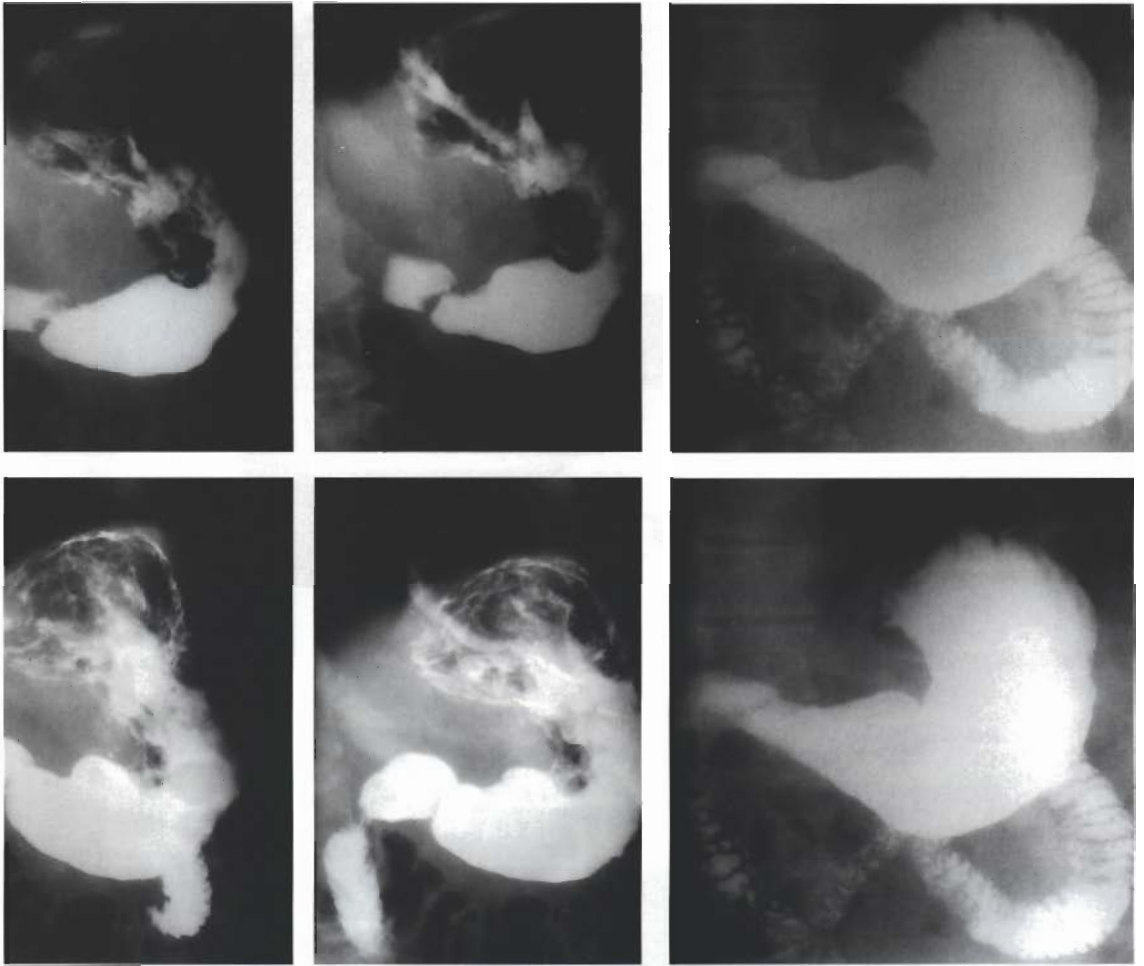
**Fig. 14.17.** Small bowel X-ray of a severely ill Crohn's patient. Radiological and clinical normalization occurred within 7-8 months after receiving neuropharmacological treatment.



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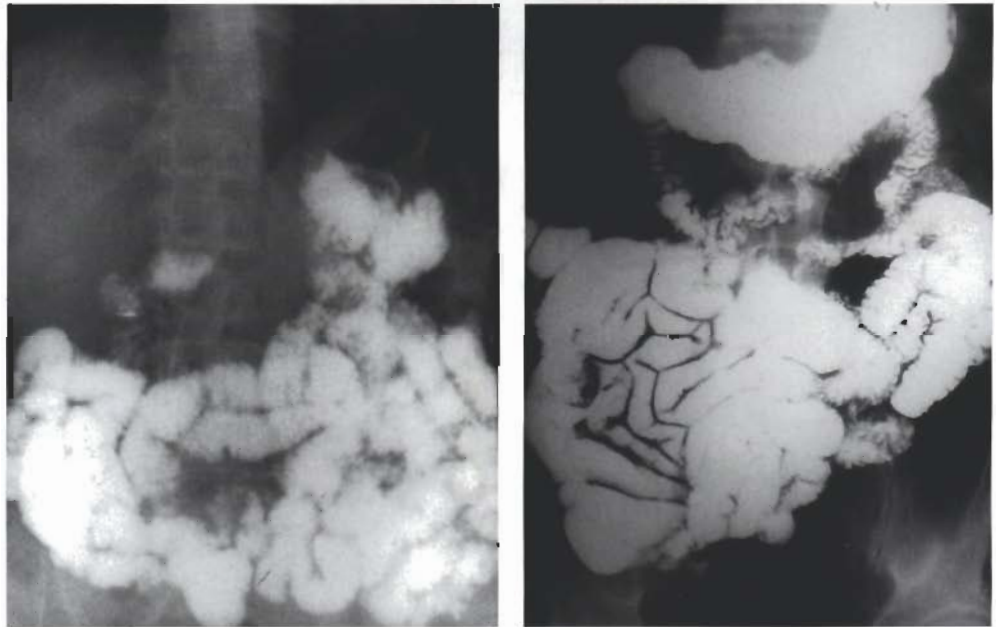


14.18



**Fig. 14.18.** Small bowel X-ray of a severely ill Crohn's patient. Radiological and clinical normalization occurred within 5–6 months after receiving neuropharmacological treatment.

**Fig. 14.19.** A severe case of Crohn's disease affecting the stomach and small bowel. The patient showed clinical + radiological + endoscopic normalization in 7–9 months after neuropharmacological therapy.



14.19



**Fig. 14.20. a** A severe case (No. 20) of pemphigus. Normalization of all lesions was observed after 6 weeks of neuropharmacological treatment.



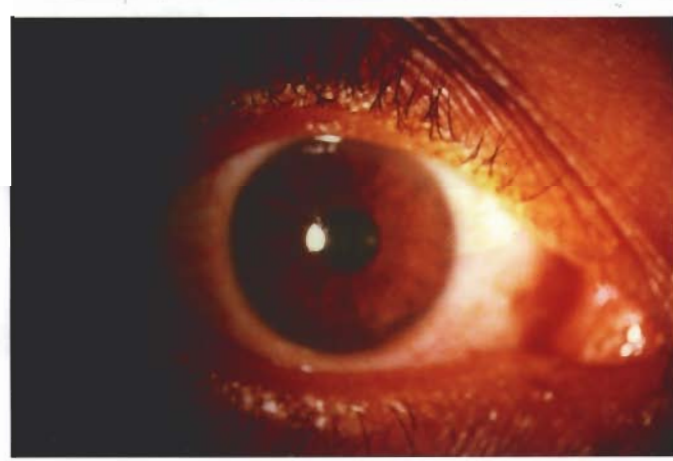
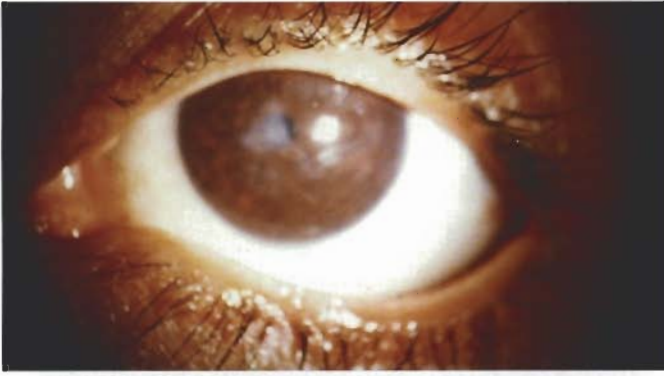
**Fig. 14.20. b** The same case with severe pemphigus. After and before 6 weeks of neuropharmacological treatment.



**Fig. 14.20. c** The same case with severe pemphigus. After and before 6 weeks of neuropharmacological treatment.



**Fig. 14.21.** A severe case of psoriasis was normalized after 6 months of neuropharmacological therapy.



**Fig. 14.22.** A severe case of Sjögren was normalized after 3 months of neuropharmacological therapy. Steroid therapy had failed. The patient also presented severe rheumatoid arthritis which showed great improvement under the neuropharmacological therapy. She did not use a wheelchair anymore, after treatment.

**Fig. 14.23.** A severe case of Sjögren was normalized after 5 months of neuropharmacological therapy. Steroid therapy had failed. This patient had been referred to surgery for extirpation of the eye because of corneal ulceration. The patient also presented severe rheumatoid arthritis which showed great improvement under the neuropharmacological therapy. She did not use a wheelchair anymore after treatment.



**Fig. 14.24.** A severe case of atopic dermatitis before and after 5 months of neuropharmacological therapy.