haloperidol and [^{3}H]-dopamine binding associated with dopamine receptors in calf brain membranes. *Mol Pharmacol* 12:800-812, 1976
6. SEEMAN P: Brain dopamine receptors. *Pharmacol Rev* 32:229-313, 1980
7. LEFUR G, GUILLOX F, UZAN A: *In vivo* blockade of dopaminergic receptors from different rat brain regions by classical and atypical neuroleptics. *Biochem Pharmacol* 29:267-270, 1980
8. TEWSON TJ, RAICHLE ME, WELCH MJ: Preliminary studies with [^{18}F]-haloperidol: A radioligand for *in vivo* studies of dopamine receptors. *Brain Res* 192:291-295, 1980
9. BITTIGER H, BICHOFF S: *In vivo* [^{3}H]-spiroperidol binding: Characterization of dopamine and serotonin receptors in different areas of the rat central nervous system. In *Neurotransmitters and Their Receptors.* Littauer UZ, Dudai Y, Silman I, Teichberg VI, Vogel, Z, eds. New York, John Wiley & Sons, 1980, pp 67-71
10. ZANZONICO PB, BIGLER RE, SCHMALL B: Neuroleptic binding sites: Specific labeling in mice with [^{18}F]haloperidol, a potential tracer for positron emission tomography. *J Nucl Med* 24:408-416, 1983
11. ARNETT CD, FOWLER JS, WOLF AP, et al: Specific binding of [^{11}C]-spiroperidol in rat brain *in vivo. J Neurochem* 40: 455-459, 1983
12. LADURON PN, JANSSEN PFM, LEYSEN JE: Characterization of specific *in vivo* binding of neuroleptic drugs in rat brain. *Life Sci* 23:581-586, 1978
13. WAGNER HN, JR., BURNS HD, DANNALS RF, et al: Imaging dopamine receptors in human brain by positron tomography. *Science* 221:1264-1266, 1983
14. CREESE I, BURT DR, SNYDER SH: Dopamine receptor binding predicts clinical and pharmacological potencies of antischizophrenic drugs. *Science* 192:481-483, 1976
15. SEEMAN P, LEE T: Neuroleptic drugs: Direct correlation between clinical potency and presynaptic action on dopamine neurons. In *Antipsychotic Drugs: Pharmacodynamics and Pharmacokinetics.* Sedvall G, Uvnas B, Zotterman Y, eds. New York, Pergamon Press, 1976, pp 183-191
16. SEEMAN P: Anti-schizophrenic drugs—membrane receptor sites of action. *Biochem Pharmacol* 26:1741-1748, 1977
17. KUHAR MJ, MURRIN LC, MALOUF AT, et al: Dopamine receptor binding *in vivo:* The feasibility of autoradiographic studies. *Life Sci* 22:203-210, 1977
18. WOODARD HQ, BIGLER RE, FREED B, et al: Expression of tissue isotope distribution. *J Nucl Med* 16:958-959, 1975
19. GLOWINSKI J, IVERSEN LL: Regional studies of catecholamines in the rat brain-I. The disposition of [^{3}H] norepinephrine, [^{3}H] dopamine and [^{3}H] DOPA in various regions of the brain. *J Neurochem* 13:655-669, 1966

Re: Thyroid Iodine Content Measured by X-Ray Fluorescence in Amiodarone-Induced Thyrotoxicosis

I feel compelled to comment on the article of Leger et al. (*1*) concerning the x-ray fluorescent (XRF) measurement of thyroid iodine stores (ITI) in hyperthyroidism, because they referred to our own work (*2*), in my opinion out of context. They quoted us to support their findings that most of their patients with Graves' disease (GD) presented with a normal ITI, whereas we specifically stressed the fact that in our experience about two thirds of these patients presented with an ITI lower than normal. Furthermore, in one of their own publications (*3*), the same group shows that 20% of their hyperthyroid patients had a subnormal ITI. A wide range of ITI values has been reported in the literature in normal glands as well as in thyroid disease, the trend being that higher values are found in areas where iodine is supplemented in the diet. It has therefore been suggested that XRF measurements might be less useful from a clinical and individual point of view in these areas (e.g., the U.S.), than in other parts of the world (*4*).

As far as the main subject of the article is concerned—namely ITI in amiodarone-treated patients—our own experience is also at variance with the author's data. We have examined many patients taking amiodarone and, although only one short series has been formally published (*5*), we consistently find that the patients under amiodarone therapy that remain euthyroid generally accumulate a significant amount of iodine in their glands. The nature of the mechanism for this remains unclear (*6*); there is a wide range (20 to 100 mg) and a mean of about four times normal (35 mg as opposed to 9 mg). Most of the patients becoming hyperthyroid while on amiodarone therapy, but not all, fall in this range, so that an ITI determination is not diagnostic in this situation. On the other hand, we agree that the ITI evolves in close parallel with the thyroid state in treated patients or in patients recovering or recurring spontaneously (*5*), making the XRF measurement a very useful tool for follow-up. We feel that it is at this place that the authors should have referred to our article (*2*) because hyperthyroid patients taking amiodarone behave like the hyperthyroid patients with iodine overload that we described, as far as the relationship between ITI and circulating hormones is concerned. It is also our experience that when the amiodarone-treated patients have antibodies against the thyroid, they have a subnormal ITI and are either hyperthyroid (GD) or hypothyroid. We therefore use the information yielded by means of XRF in a way different from that proposed by the authors: if a patient taking amiodarone presents with an ITI lower than 20 mg, and has been on the drug for a period longer than 3 mo (it takes about 6 wk to obtain a plateau of the ITI), he is strongly suspected of developing either hypo- or hyperthyroidism and is very closely examined and followed up.

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REFERENCES

1. LEGER AF, FRAGU P, ROUGIER P, et al: Thyroid iodine content measured by x-ray fluorescence in amiodarone-induced thyrotoxicosis: Concise communication. *J Nucl Med* 24: 582-585, 1983
2. JONCKHEER MH, DECONINCK F, SWAENEPOEL L: Upon the importance of differentiating between two forms of hyperthyroidism by means of x-ray fluorescence scanning. In *Thyroid Research VII.* Stockigt JR, Nagataki S, eds. Australian Academy of Sciences, Canberra, Austr. 1980, pp 637-640
3. FRAGU P, SCHLUMBERGER M, AUBERT B, et al: Thyroid iodine content measurement helps for the diagnosis of hyperthyroidism with undetectable radionuclide uptake. In *X-ray Fluorescent Scanning of the Thyroid.* Jonckheer MH, Deconinck F, eds. Boston, Martinus Nijhoff Publishers, 1983, pp 145-162
4. JONCKHEER MH, WAHNER HW: Clinical usefulness of X-ray fluorescence thyroid iodine quantitation and scanning. In *X- ray Fluorescent Scanning of the Thyroid.* Jonckheer MH, Deconinck F, eds. Martinus Nijhoff Publishers, Boston, 1983, pp 163-180
5. JONCKHEER MH, HUYGHENS L: Effects of amiodarone on the thyroid gland. In *New Aspects of the Medical Treatment Of Tachyarrhythmias.* Breithardt G, Loogen F, eds. Munchen

and Baltimore, Urban and Schwartzenberg, 1983, pp 239-244
6. JONCKHEER MH: Stable iodine and thyroid function. In *X-ray Fluorescent Scanning of the Thyroid Gland.* Jonckheer MH, Deconinck F, eds. Martinus Nijhoff Publishers, Boston, 1983, pp 100-116

Reply

We must agree that our results differ slightly from those of Prof. Jonckheer. It is our experience (*1*,*2*) that if patients show no antithyroid antibodies, and remain euthyroid under amidarone, only half of them will show thyroid iodine contents that are above normal. On the other hand, 80% of the patients who become hyperthyroid under amiodarone therapy have higher than normal thyroid iodine, the mean content being 2.8 times normal (*2*). We look forward to reviewing Prof. Jonckheer's data upon publication and comparing it with ours.

In Graves' disease, the thyroid iodine content was normal in 58% of our cases, high in 20%, and low in only 22%, which is at variance with Jonckheer's data (*3*). However, we agree that our statement should have been more precise. Furthermore the total iodine content in most iodine-induced thyrotoxicosis is high, whereas most patients with Graves' disease have a normal *or low* thyroid iodine content (*1*). In fact, what we wished to emphasize is the lack of elevation of the thyroid iodine content among patients with Graves' disease. This stresses the role of x-ray fluorescence in discussions of the hypothesized mechanism of iodine-induced hyperthyroidism.

We agree that patients with antithyroid antibodies, when treated with amiodarone, should be followed up very closely. We have shown recently (*4*) that in one third of these patients with thyroid antibodies, iodine supplementation (500 μg/day) progressively increased the thyroid iodine content, up to very high levels in some cases; nevertheless, none of these patients became hyperthyroid. In patients with high cardiovascular risk, measurements of the thyroid iodine content during amiodarone therapy could prove to be useful in the prediction of amiodarone-induced hyperthyroidism.

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REFERENCES

1. LEGER AF, FRAGU P, ROUGIER P, et al: Thyroid iodine content measured by x-ray fluorescence in amiodarone-induced thyrotoxicosis: Concise communication. *J Nucl Med* 24: 582-585, 1983
2. FRAGU P, SCHLUMBERGER M, AUBERT B, TUBIANA M: Thyroid iodine content measurement helps for the diagnosis of hyperthyroidism with undetectable radionuclide uptake. In *X-ray Fluorescent Scanning of the Thyroid.* Jonckheer MH, Deconinck F, eds. Boston, M. Nijhoff, 1983, pp 145-162
3. JONCKHEER MM, DECONINCK F, SWAENEPOEL L: Upon the importance of differentiation between the two forms of hyperthyroidism by means of x-ray fluorescence scanning. In *Thyroid Research VIII.* Stockigt JR, Nagataki S, eds. Australian Academy of Sciences, Australia, Camberra, 1980, pp 637-640
4. FRAGU P, SCHLUMBERGER M, TUBIANA M: Effets de l'iode 127 sur le contenu thyroidien en iode (CTI) et l'hormonosynthèse thyroidienne dans les thyroidites autoimmunes asymptomatiques. *Ann Endocrinol* (Paris), 44:189, 1983 (abst)

Re: Thyroid Iodine Content Measured by X-Ray Fluorescence in Amiodarone-Induced Thyrotoxicosis: Concise Communication

The report of Léger et al. (*1*) in the July issue of the *Journal* is interesting in that the syndrome described differs markedly from iodine-induced thyrotoxicosis occurring in other parts of the world. I would make the following points:

1. The incidence in this series appears to be much greater than the 80 per 100,000 population that is usual in the Iodbasedow syndrome (*2*).
2. Decreased radioiodine uptake was certainly not a feature in our series.
3. In the great majority of cases from other centers, once thyrotoxicosis has developed it continues despite iodine withdrawal.
4. Response to antithyroid drugs was a feature in our patients.

It is noteworthy that the amount of iodine consumed by the French patients was much higher than that required in others, and that the "hardness" of their glands was so obvious. When describing the Iodbasedow phenomenon in Tasmania, we found that clinical assessment was a mandatory part of our investigation, and this is curiously lacking in the article under discussion. Johns et al. (*3*) describe several patients who were clinically and biochemically euthyroid before amiodarone, but who developed biochemical but no clinical evidence of hyperthyroidism when taking this drug. Clinical thyrotoxicosis did not develop in these patients when the drug was continued.

I suspect that Léger et al. are describing the effect of excess iodine plus the peripheral and central effects of amiodarone, namely the combined effect of reduced T_4 to T_3 production with increased T_3 and increased TSH response to TRH, producing increased T_3 and T_4 output (*4*).

This is not Iodbasedow or iodine-induced thyrotoxicosis as described by Kocher (*5*), others, and ourselves.

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REFERENCES

1. LEGER AF, FRAGU P, ROUGIER P, et al: Thyroid iodine content measured by x-ray fluorescence in amiodarone-induced thyrotoxicosis: Concise communication. *J Nucl Med* 24: 582-585, 1983
2. CONNOLLY RJ, VIDOR GI, STEWART JC: Increase in thyrotoxicosis in endemic goitre area after iodination of bread. *Lancet* 1:500-502, 1970
3. JOHNS JA, FEDERMAN J, HARPER RW, et al: Amiodarone therapy for life threatening or refractory cardiac arrhythmias. *Aust NZ J Med* 13:248-256, 1983
4. BURGER A, DINICHERT D, NICOD P, et al: Effect of amiodarone on serum triiodothyronine, reverse triiodothyronine, thyroxin and thyrotropin. *J. Clin Invest* 58:255-259, 1976
5. KOCHER T: Ueber Iodbasedow. *Arch Klin Chir* 92:1166-1193, 1910

Reply

We were surprised at Dr. Connolly's suspicion that we have confused amiodarone-induced thyrotoxicosis with the known other