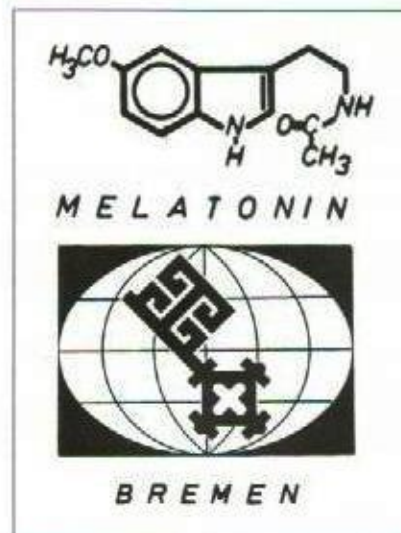


Institute for Preventive Endocrinology Bremen
and
Centre of Human Genetics and Genetic Counselling
of the University of Bremen



ABSTRACTS AND PROGRAM

INTERNATIONAL SYMPOSIUM ON MELATONIN

September 28-30, 1980

EDITORS: N. BIRAU AND W. SCHLOOT

BREMEN
Federal Republic of Germany

Melatonin: an essential factor for the treatment and recovery from leukemia and cancer.

In addition to its endocrine effects, other non-endocrine functions have been attributed to the pineal gland, such as those displayed on the CNS (1). And yet habenular nuclei stimulation causes an increase in blood platelet count (2), in the same manner as injected Melatonin, particularly in the case of splenectomized and/or epinephrectomized ratas. According to our belief, the platelets, and Melatonin too, play an essential role in leukemia etiopathogenesis; we have therefore assayed the effects of Melatonin treatment on leukemia and cancer patients for seven years, with the following results:

- 1) It is practically impossible to eradicate leukemia or cancer without Melatonin treatment.
- 2) Melatonin is a necessary, though by itself alone, not sufficient, remedy for leukemia and cancer cure.
- 3) A supporting action is often simultaneously required, that rests upon a parallel use of ACTH, of anti-free-radical drugs, ADH, SRIF, PIF, mineralcorticoids.
- 4) Melatonin may be administered by mouth, as well as parenteral route, without any dangerous instant or late effect, even though the administering is protracted for months or years.
- 5) Some leukemia patients have arbitrarily discontinued the Melatonin therapy, without any trouble or relapse. That supports the conviction that leukemia can be truly definitively healed.
- 6) The treatment does not generally entail, or only rarely, any hospitalization, apart from a periodic blood analysis.
- 7) Myeloid, acute or chronic, leukemia has to be cured with significantly lower dosages of Melatonin.
- 8) Good or excellent results have been reached in epithelial or connective tissue tumors, where a steady yearslong equilibrium may be reached, which allows a normal, or almost usual existence.

The mechanism Melatonin works with, is a manifold one. The main topics are perhaps the inhibition of GH and prolactin secretion (3), and the impairment of mitosis (4).

REFERENCES

- 1) ANTON-TAY E., J.L. DIAZ & A. FERNANDES-GUARDIOLA: *Life Sci.*, 1971, **10**, 841-850;
- 2) DI BELLA L., M.T. ROSSI & G. SCALERA: *Progr. Brain Res.*, 1979, **52**, 475-478;
- 3) KOSTYO J.L. & O. JSAKSSON: *Int. Rev. Physiol.*, 1977, **13**, 255-274;
- 4) BANERJEE S. & L. MARCULIS: *Exp. Cell. Res.*, 1973, **78**, 314-318.

Platelet turnover as influenced by melatonin.

After finding that stimulation of habenular nuclei is followed by a transitory blood platelet count increase (1), many speculative inductions have been put forward and many practical applications have been carried out, among which the most important are now the profit that several primitive platelet diseases have turned out from Melatonin administration, as well as the very useful supporting role that Melatonin takes upon when antineoplastic chemicals or radiation cures are undertaken, which frequently cause a dangerous and rapid decline in blood platelet count. Melatonin increases the circulating blood platelet count through several mechanisms:

- a) inflow into the streaming blood of bordered platelets;
- b) antiadhesive and antiaggregating action on blood platelets (2);
- c) promotion of bone marrow platelet production by megacariocytes (3).

The success of Melatonin cure is depending upon the nature of the etiology, the most hardly manageable disorders being those related to hypersplenism and to increased platelet destruction by platelet autoantibodies. Willebrand's disease, Glanzmann thrombasthenia, Bernard-Soulier's syndrome are not at all, or only moderately improved by the administration of Melatonin. Idiopathic Thrombocytopenic Purpura (ITP) is best cured by oral or parenteral Melatonin, by dosages of 1-2 mg/day. Purpuric signs fade away quickly enough, even though the blood platelet count subsists at relatively low levels. The ITP can be definitively healed by Melatonin particularly in young male and female subjects. Neither physical, nor psychic, nor growth troubles have been ever detected following Melatonin treatment, even when the treatment is protracted for 2-3 years, or longer. In some cases platelet blood count raises within a few days from the beginning of Melatonin administration; in most cases, however, hemorrhagic disorders disappear promptly, while blood platelet count reaches its normal levels within several months or some years of cure with Melatonin. Melatonin accelerates and promotes platelet production even *in vitro* (3); Melatonin seems indeed to be rapidly metabolized by megacariocytes, unless sphingosin, or sphingosin derivatives are added to the suspension medium. Several of the foregoing events can be best interpreted, when the action of Melatonin, even on blood vessel endothelia, is more clearly known.

- 1) DI BELLA L., M.T. ROSSI and G. SCALERA, *Progr. Brain Res.*, 1979, **52**, 475-478
- 2) SCALERA G., L. DI BELLA, M.T. ROSSI and G. SCALERA, *Boll. Soc. It. Biol. Sper.*, 1979, **55**, Abstr. 114.
- 3) DI BELLA L., L. GUALANO, M.T. ROSSI and G. SCALERA, *Boll. Soc. It. Biol. Sper.*, 1979, **55**, 389-393.

Red blood cells generation and melatonin.

Melatonin has revealed itself as a most effective and vigorous, available erythropoietic hormone, both in normal and in functionally defective bone marrow, unless the bone Reticulo Endothelial System conditions are seriously impaired.

The exciting erythropoietic action has been successfully tested in aplastic and uremic anemia, in hemoglobinopathies, in several hemolytic anemias and in acute blood loss anemia.

In aplastic anemia the results are depending on the seriousness, the duration and the etiology of the syndrome, as well as on the patient's age. The transfusions are more or less thinned put, or quite dismissed after Melatonin administration, and the subjective conditions are considerably improved.

The dosages are reasonably low: 1-2 mg/pro die/per os; they are sufficient in mild cases. In seriously ill patients, intramuscular or i.v. injected 2-5 mg give more complete and more quickly efficient results. The action mechanism resides in a more intense and quick reproduction of erythroid series bone marrow cells, as well as in a quicker transit into the bone marrow sinusoids of erythroblasts and reticulocytes, as is shown by the appearance of reticulocytes and erythroblasts in the circulating blood in high percentage. In anemias as well as in other hemopathies, the treatment can be protracted for several years without any appreciable noxious effect. A secondary effect, observed in both male and female patients, in both young or adults patients, is a certain, more or less deep drowsiness, particularly when Melatonin is injected i.m. or i.v., rather than administered by mouth. The favourable effects can be strengthened by α -tocopherol, which raises the osmotic and mechanical resistance of erythrocytes by ACTH, when the systemic arterial pressure is lower than normal; by testosterone, especially in old age, on chronically anemic patients. In hemoglobinopathic patients the transfusion may be diminished by 25% or more; in some adult splenectomized patients, blood Hb levels of g 9% can be maintained, without transfusion, for months and years. In some, but not in all patients, there seems that A-V O₂ difference is increased by Melatonin, so that low hematocritic values, and low blood Hb levels down to g 6% are well born. DPG erythrocyte amounts are not significantly changed by Melatonin injected into rats (1,2).

REFERENCES

- 1) DI BELLA L., M.T. ROSSI, G. SCALERA and G. TAROZZI: *Boll. Soc. It. Biol. Sper.*, 1976, **52**, Abstract n. 221
- 2) SCALERA G., L. DI BELLA, M.T. ROSSI and L. GUALANO: *Boll. Soc. It. Biol. Sper.*, 1976, **52**, Abstract n. 24.