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NICOLA PENDE (1880-1970) AND HIS “BIG LAZY CHILDREN”. PARABLE OF A CLINICAL SYNDROME

LIBORIO DIBATTISTA

Department FLESS, University of Bari, I

SUMMARY

*NICOLA PENDE (1880–1970) AND HIS “BIG LAZY CHILDREN”.
PARABLE OF A CLINICAL SYNDROME*

In the first half of the twentieth century, more than a million young Italians were found affected by a new disease: the Pende’s hyperthymic syndrome. Nicola Pende was the renowned clinician who wrote the first great Italian treatise of endocrinology and who later founded the “sciences” of biotypology and orthogenesis. The paper tells the parable of the syndrome, the story of big lazy children and their fate in radiation therapy for the greater glory of Roman Italic race.

Introduction

For many years I have found that in the sphere of infantile growth, many youngsters – who are fat and tall from birth and have very small genitalia – in spite of being teenagers, look like big babies in their appearance, faces and temperament. These children are greedy, heavy water drinkers, lazy, and characterised by a persistent mental infantilism. Their serious anomaly of growth is due to a hyperfunction of the thymus gland¹.

This is what we read in a handwritten interview by Nicola Pende, a renowned clinician from Noicattaro, a town in the province of Bari (Southern Italy). Historians have written exhaustively on Pende’s

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signatures and racism, but they have scarcely dealt at all with his clinical science².

Pende is acknowledged not only as the initiator of “endocrinology”, the science of hormones, but also as the founder of two medical disciplines: biotypology and the science of orthogenesis. In addition, he was a pioneer with regards to the relation between nervous system and endocrine system.

He was very famous during his own lifetime, three times candidate for the Nobel Prize in Medicine³ and acclaimed for his studies on endocrine glands, growth, hypertension in Europe and Latin America. However, he rapidly fell into oblivion and his science took the route of the *histoire périmée*. It was taken up only by connoisseurs of so-called alternative or complementary medicine. To a certain extent, the fate of his science was influenced by his excessive support of the fascist regime. Since Mussolini indicated him as the person in charge of the Università Adriatica of Bari, his willing or unwilling involvements in the racist culture in Italy at the end of the thirties, condemned him to an oblivion that is not always justifiable. In this article, let’s take a quick look at one of the Pende’s clinical trials, through one of his major diagnostic–therapeutic achievements, which is however as transient as the fame of its founder.

In every draft of his *exposés des titres* in which Nicola Pende’s most important original contributions to medicine and human biology were specified⁴, the author regularly indicated *Pende’s hyperthymic syndrome* – to be distinguished from Froehlich’s adiposo–genitalis syndrome (*sic*). In the preface to a treatise edited by two of Pende’s pupils and dedicated to this syndrome, Dante Pacchioni confessed⁵:

I used to think that the subjects indicated as “hyperthymic” by Pende and so exactly described by Gualco and Negro nowadays, were suffering from dystrophia adiposogenitalis or Froehlich’s syndrome ... however, Pende’s publications on the hyperthymic syndrome and this research obliged me to reflect ... After Pende and his pupils’ studies it is necessary

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to admit the existence of an endocrine system of reproduction, whose fundamental parts are the thymus, the (anterior and posterior) hypophysis, the gonads ...⁶.

The Big Lazy Children

Pende had described the subjects affected by this syndrome in a very detailed way from a clinical perspective. At birth they are macrosomatic children, with unilateral or bilateral retained testicles and very small genitals. Their faces are similar to those of Rubens' angels, that is, small mouth, eyes set far apart, short nose. They are voracious during breastfeeding and are heavy water drinkers. However, their syndrome shows its full symptomatology at about age ten, and is characterised by female obesity, adenoidism, epistaxis, asthmatic crises, hyperplastic median upper incisor teeth, *genu valgum*, flat feet. The most remarkable sign is a hypoplasia of the penis or hypoplasia of the labia majora and minora in female subjects (female sex constitutes only 10% of the total). Testicles are abdominal or ascend and descend the inguinal canal up to the scrotum and vice versa. There is frequent amenorrhea in female subjects and a tightened phymosis in male ones, *ergo* hypogenitalism and impotence and/or sterility. The syndrome affects their character too: they are emotionally childish, lazy, apathetic, naughty. "On the whole, a persistent psychic puerilism corresponds to the bodies of big children". (Fig.1)

It is not difficult to notice, as mentioned in the introduction, that one of the main ways to detect the nosological case history of what Pende indicated as "my syndrome"⁷ was to distinguish it from Froehlich's dystrophia adiposogenitalis. In 1900, Joseph Felix Babinsky (1857-1932) – one of the most talented pupils of Jean Martin Charcot (1825-1893) – published the case study of a 17-year-old girl with an underdeveloped genital apparatus related to a hypophysis tumour⁸. Babinsky's article preceded by a few months an analogous report by Alfred Froehlich (1871-1953)⁹.

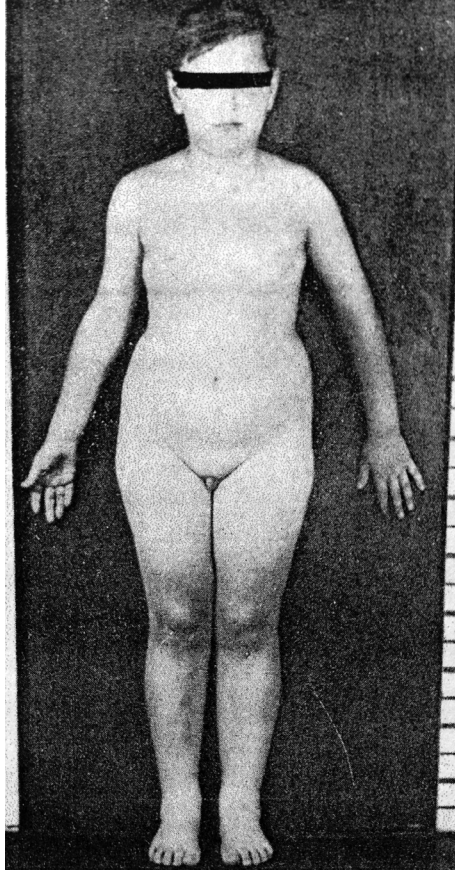


Fig. 1 - Hypersomic patient (sintesi antropometrica secondo Pende) from: GUALCO S., NEGRO A., *La sindrome ipertimica di Pende* (1943), p. 27.

The case described by Froehlich was considered the paradigm of the homonymous syndrome, i.e. dystrophia adiposogenitalis: obesity associated to hypogenitalism due to a lesion – often occupying space – in the hypothalamic-hypophyseal region. In Froehlich's case there was the coexistence of right-temporal-hemianopsia and

left-eye-blindness, owing to a compression of the optic chiasm. In 1909, Harvey Cushing (1869-1939) described another case of this pathology¹⁰, and more importantly, three years later he provided a nosographic frame of the hypopituitarism pathology, also coining the latter term¹¹. In the following years, clinicians didn't always paid attention to link necessarily obesity and hypogenitalism to hypophyseal or encephalic tumours, since they just grouped together these syndromes under the common label of dystrophia adiposogenitalis and generically connected it to a hypophysary hypofunction. Sometimes obesity was interpreted as a consequence of a diencephalic lesion, sometimes it was linked to hypogenitalism, other times it had a psycho-bulimic cause¹².

Pende's syndrome was introduced in 1937, although Pende claimed, in his writings, that since 1935 he had been collecting "in Genoa medical hospital a great many cases that, as still happens in Italy and abroad today, were improperly framed in the diagnostic rubric of the so-called hypophyseal dystrophia adipose-genitalis"¹³.

In the summer of the 15th year of the Fascist era, Pende announced that he had detected this new syndrome during the 1st International Medical Week at Salsomaggiore (*1^a Settimana Medica Internazionale di Salsomaggiore*) and at the same time published its description in two scientific journals¹⁴, resuming the subject again in *Progressi di Terapia* the following year¹⁵.

The main peculiarity of these initial descriptions was that Pende's hyperthymic syndrome seemed to have leapt like Athena from Zeus' head: it was complete, defined in its clinical, semeiotic, biochemical, epidemiological and therapeutic details. During the next thirty years Pende's and his pupils' publications took up the 1937 case history without adding – or deleting – anything significant, except for data acquired in the meanwhile with regards to the thymus physiopathology. It seems necessary to believe that for at least two years the clinician had been collecting case studies and comparing them to "his"

new syndrome. But what is the genesis of this new case history? How could Pende isolate this particular group from the set of sexual *hypoevolutisms*?

According to Paul Thagard, the explanations of a disease, although categorised by differential schemes of pathogenetic mechanisms, tend to make reference to one etiological explicative structure, thus the venerable *scire per causas* remains the fundamental criterion¹⁶. Nevertheless, the history of medicine, and Thagard himself, suggest we recognise that different criteria exist – and have been practiced – if not with regards to their explanation, at least with regards to their “detection” of the diseases. Among the main criteria, which – together with the etiological one – were used by Nicola Pende to define “his” hyperthymic syndrome, I would like to mention at least another two here.

The first is the description of the syndromes: through a collection of signs and symptoms it is possible to recognise specific pathologies. Actually, over the centuries, nosographic categorisation has been primary means of identifying a disease. Indeed, in some cases, a detailed analysis of clinical medicine and pathological anatomy has allowed the differentiation of specific diseases that previously had been collected under a single rubric¹⁷. The second criterion is *ex juvantibus*: if the administration of thyroid extract heals the disease, then the latter consists of a hypofunction of the thyroid.

Let us look briefly at how Pende applied these criteria to detect his syndrome in big lazy children. In the 1937 categorisation of sexual *hypoevolutisms*, it is easy to distinguish syndromes caused by thyroid or genitals hypofunctions by means of semiotics. On the contrary, when this problem has to do with hypophyseal insufficiency, as Pende claimed, it involves the whole gland and causes an easily detectable “universal harmonic infantilism”. Vice versa, in the form of macrosomic adipose infantilism, it displays roughly the same characteristics as Pende’s syndrome.

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According to my recent studies, the latter type of hypophyseal genital hypoevolutism has been included in those forms that I will describe as essentially due to hyperthymism: definitely, hypopituitarism and hypothyroidism are very often associated in children and teenagers¹⁸.

Thus, in terms of syndromes, it is necessary to detect what distinguishes Froehlich's children from Pende's children. The former, unlike the latter, tend to be short of stature and to keep both character and intelligence. Furthermore, their pathology shows up during puberty, whereas Pende's children display their characteristics from birth. Nonetheless, the clear-cut differentiation between the hyperthymic and the adipose-genitalis syndrome is based exactly on an etiological criterion: whereas, in the case of Babinsky-Froehlich's disease, the problem is caused by a pathological process in the hypophyseal-diencephalic area, in Pende's syndrome, the cause is hyperthymism. In the past, this was not verifiable, "because thymus semiology in adolescence and puberty was blocked by the impossibility of highlighting the thymus by means of X-rays"¹⁹. Hence the first move of the clinician:

The transfixing percussion already appeared in the specific literature three years before the syndrome that it helps detect (Fig. 2).

I have found a new percussion method, which I call transfixing percussion ... In this way, it is possible to demonstrate a large thymic obtuseness ... Obviously, it is necessary to compare the findings that concern hyperthymism, with a set of other signs that, according to my clinical studies, are associated with hyperthymism and appear as stereotyped²⁰.

Pende's assistant, Landogna Cassone, emphasises that thymic hyperplasia is not demonstrable through classic percussion, nor through radiography. However, through the method invented by his master, it is easy to highlight gland growth. Thus, Landogna applied such a technique to all the cases of hyperthymism collected at the *Istituto Biotipologico* in Genoa and concluded:

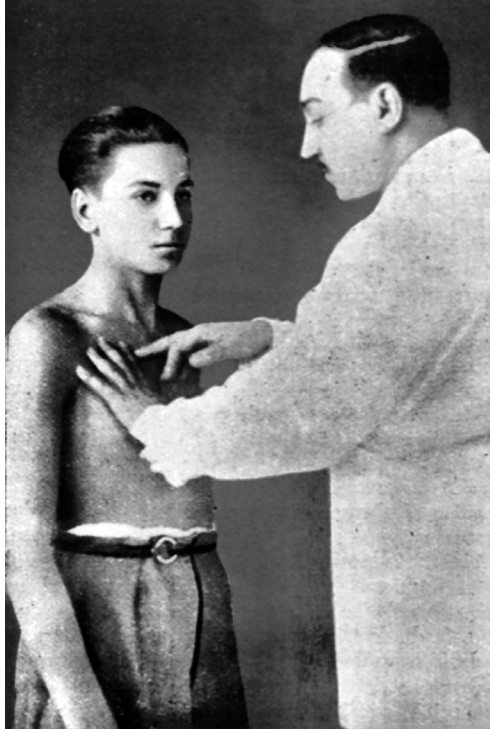


Fig. 2 - The transfixing percussion. In LANDOGNA CASSONE F., *On the Value of a Particular Percussing Method* (1934), p. 5.

I have ascertained that both in children having attributes of angelic beauty, big and pasty bodies, thin and fragile bones, very delicate hair, marked vagotonism, remarkable restlessness, relapsing epistaxes ... and in teenagers having large and effeminate body shapes, sexual immaturity – in short, in subjects having symptoms of hyperthymism – the transfixing percussion allows us to detect the swelling of the gland²¹.

Evidently, in 1934 the hyperthymic syndrome was already part of Pende's agenda, and here again both the clinical and laboratory characteristics of the syndrome are the same as those that will always be described later.

Is it possible to go back even further? According to Landogna Cassone, hyperthymism is described in the third edition of Pende's *Endocrinologia* of 1923-1924. Nonetheless, a check of these texts excludes that the hyperthymic syndrome had already been drafted at that time²². It would suffice to compare the 1923 photograph (showing a subject with a thymic status) to Gualco and Negro's big children to be convinced (Fig.3 e Fig.4). Thus, clinical medicine, etiology and also therapy, i.e. the *ex juvenitibus* criterion. Again excerpted from the first article of 1937:

The new part of the treatment that I would like to describe concerns the great efficacy of Röntgen therapy ... Generally after these cycles of Röntgen therapy, thymic obtuseness disappears and contextually, in 2-3 months, sexual development becomes increasingly normal. Cryptorchid testicles descend, menstruation appears in amenorrheic girls, breast develops in women with hypogenital disorders; also the subjects' character changes²³.

This is the fundamental aspect: the syndrome has been detected, its etiology has been explained, and an effective treatment has been prepared. In the history of medicine, the determining factor is the

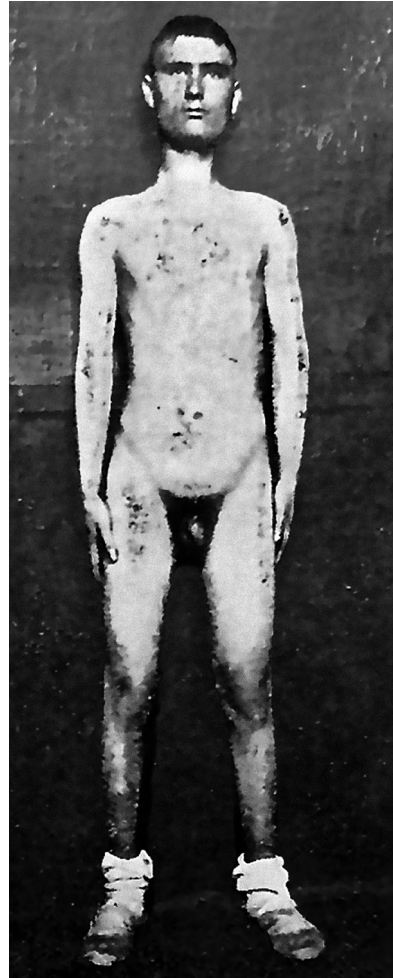


Fig. 3 - Hyperthymic patient from PENDE N., *Endocrinologia* (1923), p. 1025.

moment in which this “art” keeps its promise, i.e. there is recovery. As for the rest, it is science, but does not mean much, compared to the *restitutio ad integrum* from the disease, which is the real prime mover of the *ars longa*.

Pende heals his big lazy children, subjects them to some cycles of Röntgen therapy (actually, by associating hypophysary extracts) and their obesity disappears, their naughty character becomes gentler, and they become fertile. Indeed, probably it is from this point that Pende’s complete intellectual and research work springs. As a matter of fact, the article opens with a peroration of social medicine: “I think that few topics of preventive medicine have such practical importance, in the current evolutionary–historical moment of our country, as the diagnosis and precocious treatment of the infinite reasons that arrest sexuality in men and women”. It is a clinical problem that “cannot but affect family and State in the highest degree”. It is not necessary to emphasise the significance that such statements acquired in Italy in 1937. Indeed, Pende himself and his collaborators stressed such a significance on many occasions.

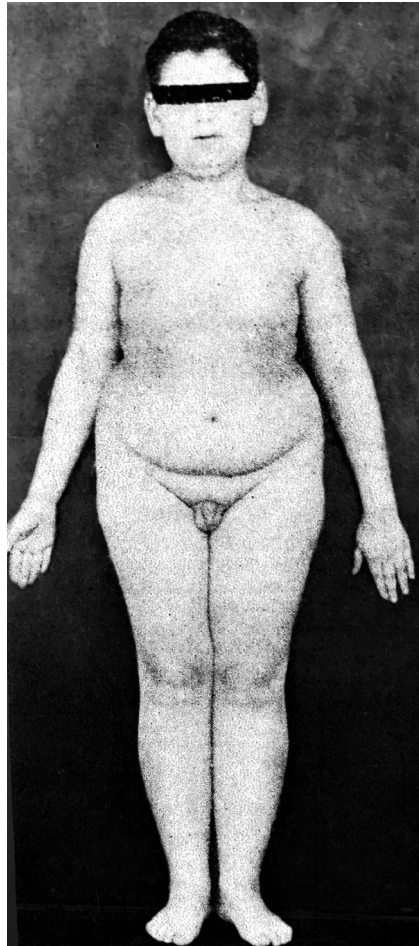


Fig. 4 - Hyperthymic patient from GUALCO S., NEGRO A., *La sindrome ipertimica di Pende* (1943), p. 48.

A Million Italians

For instance, G. Calabrese reported the extraordinary results of Röntgen thymic therapy on cryptorchidisms and *amenorrheas in these angelic anomalies*. Starting from 29 descended testicles out of 36 treated cases, the radiotherapist hazarded the expectation of a million cases yet to be published. As a matter of fact,

It will not be difficult to achieve this number rapidly, because the interest of both His Excellency the Minister Secretary of the Party (Ministro Segretario del Partito) and of the enlightened managers of the Italian Youth of the Lictor (Gioventù Italiana del Littorio, GIL), allows the study of thousands of subjects and their treatment according to this new Italian discovery. The children of the people enrolled in this extraordinary youth Institution will be given the certainty of becoming sound citizens tomorrow, also capable of ensuring the longevity of our race²⁴.

However, these calculations were still approximate by default. A year later, he explained that out of the 5,420 cases which he examined in three years (1939-1941) the percentage of hyperthymic subjects was 43%. This leads us to calculate (we don't know on the basis on what formula since the clinician does not express it) that a percentage estimated between 1.5% and 2% of Italian youngsters aged 0–15 years was made up of big lazy hypogenital children. This is a really huge number,

Which amounts to approximately one million throughout Italy. But, no fear, because I have the pleasure of announcing that, owing to precise orders given by the GIL charitable association, a diagnostic check is already on-going for one million future Italian citizens, who left alone, would almost surely remain permanently hypogenital, sterile and unhappy people²⁵.

This meant saving one million Italians from one of the most serious threats to an individual and his race: impotency and sterility. Nonetheless, Sellina Gualco and Antonio Negro noted that – perhaps because of this high number – “some influential foreign and Italian sources insist on ignoring or diverting from Pende's hyperthymic syndrome”²⁶.

We do not yet have a chapter on Nicola Pende's contribution to social medicine in the first half of the 20th century and this is not the proper place to write one²⁷. What we would like to suggest here is that probably owing to a link between the endocrinologist's clinical and anatomic-pathological work on his biotypological case histories, together with echoes of both 20th century eugenics and the well-known Fascist programmes, Pende's insistence on a clinical syndrome would have deserved less fanfare. Therefore, a typically externalist reasoning – though this historiographical category can be abused or disused – ought to be included in the “explanations” of the disease.

I Insist: “My Syndrome”

Not always and not everybody agreed with Pende in Italy. For instance, Cataldo Cassano (1902–1998), by defining Pende's syndrome “a hyperthymic variant” of Babinsky-Froehlich's syndrome, ended up by denying its nosological individuality²⁸. However, two publications reaffirmed, through clinical and experimental argumentations, the existence and specificity of Pende's syndrome. First of all, there was the above-mentioned volume by Gualco and Negro, pupils to whom evidently Pende entrusted the role of official “tutors” of the hyperthymic syndrome. The monograph published a comprehensive bibliography on the anatomic–physiology of the thymus, and then described Pende's syndrome, which was quoted from the 1942 article by the pupils' master. Finally, the most substantial part was the exposition of 65 case histories of hyperthymism, together with photographic documentation on the efficacy of the radiation therapy prescribed by Pende.

Understanding the function of the thymic gland had always been a challenge in the fields of both human and animal physiology. In 1845, John Simon had collected a detailed history of thymus studies²⁹. Some clinicians, such as William Hewson (1739-1744), had maintained the lymphatic nature of the gland; others, such as Johannes Müller (1801-1858), had considered it as a hematic gland. Francis

Glisson (1597-1677) had been one of the first to indicate the importance of the thymus during the foetal stage, perhaps suggesting a mechanical hypothesis to Govert Bidloo (1649-1713). According to this hypothesis, during the foetal stage, the thymus occupied the thoracic space that at birth had to make room for lung expansion, thus assuring a condition opposite to that of the *vacuum horrendum*³⁰.

The confusion that reigned in this field was not improved by the review dedicated to the experimental physiology of the thymus by Simon, Gualco and Negro 100 years later. Between ablations and ophoterapies, to the thymus were attributed functions affecting the metabolism of calcium, body growth (different from body development)³¹, as well as antigonadic, antitoxic, hypotensive, cardio-accelerator, hydrophilic, anti-hepatic and hyper-pancreatic, anabolic, vagotonic and galactogogue functions. The quotation of René Leriche's work on the efficacy of thymectomy in myasthenia was lost in a sea of contradictory observations³².

Indeed, Gualco and Negro's monograph – except for the 65 case histories – limited itself to transcribing word for word from Pende's article, not only the master's viewpoint on thymus endocrine function, but also the clinical and physio-pathological description of hyperthymism. Pende's conclusions on the thymic function could be summarised as follows: a) Thymus is an anabolic gland; b) as a consequence, it carries out its function during neonatal life and early childhood, being later destined to an involution; c) by stimulating growth and not development, its hyperfunction causes macrosomy and cryptorchidism. Furthermore,

The fact that a constitutional hyperthymism causes in puberty not only macrosomic adipose somatic infantilism, but also a childlike character, demonstrates that an excess of thymus, in the morphogenetic hormonal constellation of the brain, determines an inhibition of the hormones that stimulate the development of character, such as the hormones of the thyroid, of the anterior hypophysis, of the suprarenal, and of the genital glands³³.

The other publication was the one written by Pende in 1945. In this work, he insisted on the nosographic individuality of his syndrome. Before Pende, the first author to describe hyperthymic constitutions and to call them thymocentric personalities had been Louis Berman³⁴, but he was referring to homosexuality and moral obliquity, which on the contrary were missing in big “angelic” Italian children. Berman, moreover, did not detect cryptorchidism, which instead was present in 44% of the cases studied by Pende. This point was fundamental for the specificity of the syndrome: hyperthymism, cryptorchidism, thymus radiation, testicles descending into the scrotum. As to the correlative endocrinology, i.e. the relations between hyperthymism and other endocrine glands – a point on which Pende’s primacy is beyond dispute, at least in Italy – he “declined” the relation between hyperthymic subjects and the endocrine system as follows: hyperinsulinism, exocrine hyperpancreatism, hypoparathyroidisms, surrenal hypercorticalism and hypo–medullary gland, lack of myasthenia reported in “some thymic and thymo lymphatic states”; above all, hypopituitarism is neither constant, nor dominant, nor frequent³⁵. In *La mia sindrome di ipertimismo costituzionale dei fanciulli e degli adolescenti*, the expression “my hyperthymic subjects” recurs nine times. The expressions “my pupils” and “my studies” are also frequent. Thus, in an epoch in which the eponymous designation of a disease was a very frequent fact (nowadays it is becoming obsolete), Nicola Pende claimed resolutely and definitively such a syndrome. In conclusion:

Since I have isolated this pathological state from both the diencephalon–hypophyseal dystrophia adiposogenitalis, (with which it had been so far and is still being confused, even by respected clinicians today), and also from states of hypogenitalism and congenital primary eunuchoidism of teenagers. Since I have brought it back to its real and essential pathogenic factor, which acts starting from intrauterine life, arresting the development of the genital sphere (cryptorchidism) in 44% of the cases, and later the development of the sexual primary, secondary and tertiary characters.

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Since I have introduced, as a pathogenic and specific treatment, the inhibitor Röntgen therapy of the hyperfunctioning thymus gland in the endocrine concert, where – also due to my great personal experience – prolonged treatments based on hypophyseal, genital, thyroid, surrenal (therapy) had failed. Röntgen therapy, as Cassano honestly recognises, against contrary statements by other Italian students, determines in a large percentage of the cases, a sharp evolutive push in the sexual sphere, provocation of puberty, when it was severely delayed, menstruation in amenorrhic women aged over 20, descent of the testicles retained in the canal, disappearance of metabolic changes, correction of character anomalies. All this complex of positive and new facts is more than sufficient to recognise in this syndrome, which I have singled out, the status of an endocrine syndrome to be grouped together, from now on, with other endocrine pathologies that are better known on the nosographic and pathogenic level³⁶.

Greatness and Misery of a Clinical Syndrome

Actually, Pende's great prestige allowed his syndrome to be listed in the treatises of internal medicine and to be mentioned as an "endocrine pathology". Pende also published his syndrome in international journals³⁷, although he took care to limit the emphasis on such a pathology when, for instance in 1955, in a categorisation of male hypogonadisms, he dedicated only a dozen lines "to the form that I singled out as constitutional hyperthymism in adolescents"³⁸.

In the 1950s and 1960s hundreds of big children underwent Röntgen irradiation therapy of the thymus, but slowly the syndrome disappeared both from endocrinology texts and from clinicians' practice. In the meanwhile, thymus physiology emerged from its secular uncertainty to clarify its relation to the maturation of the immune system. All the clinicians who had studied it over the centuries had sensed a relation between thymus and development, but none could have surmised its real function without a theory of immunity. Furthermore, from the beginning, Pende's syndrome had shown its original error: its combination with the hypofunction of the anterior hypophysis.

Notwithstanding his efforts to distinguish it from the latter, as we have seen, Pende could not deny in his subjects the coexistence of a diencephalic hypophyseal deficit. Gualco and Negro had skated over this issue, but had mentioned that “in our hyperthymic subjects, who are not only the 65 that we show today, but also those we have observed over the years, we have always noted signs of evident hypofunction of the anterior hypophysis”³⁹. Dante Pacchioni, whose opinion has been partially reported in the introduction, did not concretely risk passing his judgement – as a paediatrician – on the real existence of the syndrome:

*The endocrine glands being jointly liable as concerns their function ... hypogonitalism with or without cryptorchidism, the alterations of the metabolism ... cannot be unilaterally attributed to an abnormal function of the hypophysis, or of the thymus, or of the gonads, but to an abnormal function of the whole endocrine reproductive system*⁴⁰.

To make matters worse, at the end of his preface, Pacchioni proposed his explanation of hypogonadisms, which contradicted his support of Pende’s hyperthymic syndrome:

In my opinion, the reduced erotic sense of fathers, determined or favoured by an inhibiting force of desiring just one child and by a certain frigidity that city men acquire for economic reasons, and the fact that they get used to their wives’ nakedness and to women showing their bodies – no longer appeals to the other sex with the usual natural energy. The reduced erotic sense of fathers, I say, is passed on to children, who are brought into the world with an endocrine system that is less efficient for reproduction. This means less descended, hard and small testicles, a small penis with a bigger thymus, a hypophysis whose function is abnormal. During their growth, these subjects acquire the somatic and psychic characteristics that Pende has so well indicated in hyperthymism.

Thus, Pacchioni’s coarse Lamarckism criticised Pende’s hyperthymism from the very beginning.

A conclusive remark needs to be reserved for the question of irradiation therapy, so widely spread by Pende's ideas, in order to obtain sexual maturity in teenagers. Cohort studies conducted in the 1980s demonstrated that in subjects who had undergone Röntgen irradiation of the thymus in the 1950s, the risk of thyroid cancer had increased 45 times when compared to the healthy controls, that of thyroid adenoma 15 times, and that these risks persisted for 30 years after the irradiation. Furthermore, also the salivary glands, cutis, bones and other organs close to the irradiated region presented a frequency of benign and malignant tumours equal to twice that in the healthy controls⁴¹. Thus justifying the statement by the "heretic" pediatrician R.S. Mendelshon:

And I confess that I believed in the irradiations of tonsils, lymph nodes and the thymus gland. I believed my professors when they said that, of course, radiation was dangerous, but the doses we are using are absolutely harmless. Years later – around the time we found that the "absolutely harmless" radiation sown a decade or two before was now reaping a harvest of thyroid tumours – I couldn't help wondering when some of my former patients came back with nodules on their thyroids: Why are you coming back to me? To me, who did this to you in the first place?⁴²

BIBLIOGRAPHY AND NOTES

1. This undated manuscript can be probably dated to the last ten years of the clinician's life, owing to a reference to his return from Barcelona, where supreme honours had been rendered him in about 1965. In it, Pende wrote questions and answers, defining himself "the master of endocrinology and orthogenetic world medicine". He also wrote: "Pende has an eternally smiling face, bright and piercing eyes, is endowed with a Latin kindness, and is willing to educate and communicate to others the findings of his research, as a great master". *Nuove conquiste della medicina italiana nel campo della crescita infantile. Intervista col cattedratico di patologia clinica di Roma, il Senat. prof. Nicola Pende.* MS, Bib. Noj. FP, 72-1-2. At the Biblioteca Comunale di Noicattaro there is an archive of Pende's writings. The documents consulted there are

quoted as “Bib. Noj. FP” and are followed by an indication of the folder and paper where they have been archived.

2. With the exception of local hagiographic contributions (AA.VV., *Noicattaro in memoria di Nicola Pende*. Cosenza, Pellegrini, 1983; ALTOBELLI L., *Nicola Pende primo rettore dell'Ateneo barese*. Foggia, Ed. del Rosone, 2006), pamphlet on Pende's racism (MOTTOLA J., *Gente di razza. Così parlò Nicola Pende, tutore della stirpe e pupillo dei Gesuiti*. Foggia, Bastogi, 2010), rare articles on general issues (ARASA F., *Nicola Pende y el neohipocratismo actual*. *Folia Clin Int (barc)*, 1973; 23(4): 245-257; CAMPANACCI D., *Nicola Pende*. *G. Clin. Med.* 1970; 7: 613-615; BUFANO M., *Revisione critica del lavoro clinico e scientifico di Nicola Pende*. *Policlinico Med.*, 1971; 78 (1): 1-18; FEDERSPIL G., *Il ruolo del costituzionalismo nell'evoluzione del pensiero medico*. In FERRO F.M., *Passioni della mente e della storia. Protagonisti, teorie e vicende della psichiatria italiana tra '800 e '900*. Milano, Vita e Pensiero, 1989; DI GIANDOMENICO M., *La firma della contesa*. In de CEGLIA F.P. (ed.), *Scienziati di Puglia*. Bari, Adda, 2007, pp. 407-411). The only known example dedicated to Pende's clinical medicine is: MAURA E. & PELOSO P.F., *Allevatori di uomini. Il caso dell'Istituto biotipologico di Genova*. *Rivista sperimentale di freniatria* 2009; CXXXIII(1): 19-35. With regard to essays dealing with eugenics in general and Pende, see note 26.
3. Cfr. “Nomination Database – Physiology or Medicine”. www.nobelprize.org.
4. For instance: *Contributi originali del prof. Nicola Pende all'Endocrinologia*. Dattiloscritto, Bib. Noj. FP, 72-1-6.
5. GUALCO S., NEGRO A., *La sindrome ipertimica di Pende. Studio clinico e terapeutico su 65 casi*. Bologna, Cappelli, 1943.
6. *Ibid.*, p. V.
7. PENDE N., *La mia sindrome di ipertimismo costituzionale dei fanciulli e degli adolescenti*. *Radiologia*, 1945; II: 359-371.
8. BABINSKY J.F., *Tumeur du corps pituitaire sans acromégalie et avec arrêt de développement des organes génitaux*. *Rev. neurol.*, Paris 1900; 8: 531-535.
9. FRÖHLICH A., *Ein Fall von Tumor der Hypophysis cerebri ohne Akromegalie*. *Wiener klinische Rundschau* 1901; 15: 833-836; 906-908.
10. CUSHING W. A., *Sexual Infantilism With Optic Atrophy in Cases of Tumor Affecting the Hypophysis Cerebri*. *J. Nerv. Ment. Dis.* 1906; 33-11; 704-716.
11. MEDVEI V.C., *The History of Clinical Endocrinology. A Comprehensive Account of Endocrinology from Earliest Times to Present Day*. New York, The Parthenon Publishing Group, 1992, p.175.

12. Cfr. NETTER F.H., *Atlante di anatomia, fisiopatologia e clinica. Vol 5: Apparato Endocrino e malattie metaboliche*. Milano, Masson, 2002, p. 16; *The Trattato Italiano di Medicina Interna diretto da Paolo Introzzi* in 1980 classified Babinsky-Froehlich's syndrome among the secondary hypogonadotropic hypogonadisms. Furthermore, in 1980, the same lengthy treatise only dedicated three pages to the hyperthymic syndrome according to Pende – *Sindrome ipertimica secondo Pende* – (only half a page was devoted to dystrophia adiposogenitalis) in the chapter on thymus diseases.
13. PENDE N., see ref. 7, p. 359.
14. PENDE N., *L'ipertimismo e la roentgenerapia del timo nelle deficienze sessuali degli adolescenti*. Rassegna Clinico-Scientifica. Periodico di Dottrina e Pratica Medica a cura dell'Istituto Biochimico Italiano, 1937; XV, 7: 267–269; a synthesis appears as: *L'hyperthimismo e la roentgenerapia del timo nelle insufficienze di sviluppo sessuale degli adolescenti*. Bulletin et mémoires de la Section d'Endocrinologie 1937; III: 8.
15. PENDE N., *Le anomalie di sviluppo sessuali degli adolescenti e loro cura mediante la roentgenerapia del timo*. Progressi di Terapia 1938; 27, 9: 131-135.
16. THAGARD P., *La spiegazione scientifica della malattia*. Milano, McGraw-Hill, 2001. In particular see pp. 21-39.
17. An example is in this sense the titanic work carried out by J. M. Charcot for a nosographic categorisation of myopathies, which before him had been generically classified as muscles diseases, or worse, paralyses. It was obtained through a careful examination of anaemnesitic, clinical and anatomo-pathological findings. Only a century later has this categorisation begun to be supported by the etiologic classification. See DELAPORTE F., *Histoire des myopathies*. Paris, Payot, 1998.
18. PENDE N., see ref. 14, p. 268. It signals – as I will show later – the weak point of Pende's nosologic interpretation.
19. Ibid.
20. LANDOGNA CASSONE F., *On the Value of a Particular Percussing Method (the so-called "Transfixing Percussion" according to Pende) for the Detection of Thymic Hyperplasia*. Excerpted from *Riforma Med.* 1934; 7: 1-9. Bib Noj FP.
21. Ibid., p. 6.
22. "As regards the syndrome of hyperthymism, we only know pathological states in which the dominant anatomo-clinical factor is a *hypertrophy of the thymus*; however, on the one hand, we are not sure that it corresponds to a real

hyperfunction of the organ; on the other hand, other functional anomalies of other endocrine glands coexist ... according to the notions that we possess on the thymus, hyperthymism should manifest itself with signs of exaggerated development of the body mass (macrosomic children) and a remarkable psychic liveliness". PENDE N., *Endocrinologia. Patologia e clinica degli organi a secrezione interna*. Milano, Vallardi, 1923, vol. 2, pp. 1022-1023. Thus, big, but not lazy, children. More importantly, Pende had not linked hyperthymism to hyposexuality as yet: "Regarding its influence on genitals development, thymic insufficiency, according to still unspecified circumstances, can produce acceleration or inhibition of sexual development". *Ibid.*, vol. 1, p. 673.

23. PENDE N., see ref. 14, p.269.
24. CALABRESE G. A., *Tecnica e risultati della irradiazione roentgen del timo nella sindrome ipertimica di Pende*. Policlinico 1941; XLVIII: p. 6-7.
25. PENDE N., *La sindrome ipertimica costituzionale*. Gazzetta Internazionale di Medicina e Chirurgia 1942; LI: 11-12.
26. GUALCO S., NEGRO A., ref.5, p.17.
27. On this subject see MANTOVANI C., *Rigenerare la società. L'eugenetica in Italia dalle origini ottocentesche agli anni Trenta*. Soveria Mannelli, Rubettino, 2004; BURGIO A. (ed.), *Nel nome della razza*, Bologna, il Mulino, 1999; CASSATA F., *Molti, sani e forti. L'eugenetica in Italia*, Torino, Bollati Boringhieri, 2006; CASSATA F., *La difesa della razza*. Torino, Einaudi, 2008; POGLIANO C., *Scienza e stirpe: Eugenetica in Italia (1912-1939)*. Passato e presente 1984; 5: 537-557; IPSEN C., *Demografia totalitaria, Il problema della popolazione dell'Italia fascista*. Bologna, Il Mulino, 1997; ISRAEL G., NASTASI P., *Scienza e razza nell'Italia fascista*. Bologna, Il Mulino, 1998; MAIOCCHI R., *Scienza italiana e razzismo fascista*. Firenze, La Nuova Italia, 1999.
28. CASSANO C., *Rilievi intorno alla fisiologia ed alla clinica delle sindromi ipertimiche*. La settimana medica 1943; XXXI.
29. SIMON J., *A Physiological Essay on the Thymus Gland*. London, Renshaw, 1845.
30. MEDVEI V.C., ref. 11, pp. 97-99.
31. This supported Pende's hyperthymism: the hyperthymic function stimulates the growth of *big children*, but prevents their development in the sense of their differentiation and sexual maturity.
32. LERICHE R., JUNG A., *Thymectomy dans un cas de myasthénie*. Mém. Acad. Chir. 1939; 65: 334-340.

33. GUALCO S., NEGRO A., ref.5, p. 23. Of course, also on this question of psychic infantilism in hyperthymic subjects, Pende stimulated the scientific production of his pupils and collaborators. We quote, for instance, NARDI A., *Ipertimismo e psiche*. Rivista di Psicologia; 1942; XXXVIII: 1-12. The conclusions of this research demonstrate that “these subjects are in general minus-values in school and in life because in most cases they show mediocre and limited intelligence, good memory, scarce attention, good affectivity, excessive emotiveness, a remarkably scarce determination, and insufficient progress at school”.
34. Louis Berman (1893-1946) was a controversial figure in the field of U.S. endocrinology during the first half of the 20th century. His works on parathyroids were accepted as classics (See MUNSON L.P., *Parathyroid hormone and calcitonin*. In: McCANN (ed.), *Endocrinology: People and Ideas*. Baltimore, Waverly Press, pp. 239-284). His fame rests on ideas concerning the possibility to modify the physical and moral nature of human beings thanks to hormonal cures. From this perspective, it would be interesting to investigate whether and how Berman influenced Pende or vice versa. In his controversial volume of 1921 *The Glands Regulating Personality: A Study of the Glands of Internal Secretion in Relation to the Types of Human Nature* (London, Macmillan), he maintained the existence of human “types”, according to the prevalence of one or another among the main endocrine glands and that there was the possibility to intervene on these “types” through opotherapy or glands removal. In this essay, Berman described his *thymo-centric personalities*. If it is true – as Pende claimed – that these personalities are characterised by sexual deviations not verifiable in Italian hyperthymic subjects and who are not suffering from cryptorchidism, for the rest, in 1921 they seem to presage Pende’s big children: “The “angelic child” is the type: regularly proportioned and perfectly made, like a fine piece of sculpture, with delicately chiselled features, transparent skin changing colour easily, long silky hair, with an exceptional grace of movement and an alertness of mind. They seem the embodiment of beauty” (p. 217). Furthermore, girls are amenorrhic, have small breasts, etc. Also in Berman, the etiopathogen explication requires the antagonistic function of the thymus on genital development. On the other hand, in this text, Berman quoted Pende as “the great Italian student of endocrines” (p. 189). On Berman, see NORD-LUND C., *Endocrinology and Expectations in 1930s America: Louis Berman’s Ideas on New Creations in Human Beings*. Br. J. Hist. Sci.; 2007, 40: 83-104.
35. Cfr. ref. 17. Eight years after the announcement of the syndrome, on this point Pende was more careful: if in 1937 he had declared that *very often*

hyperthymism and hypopituitarism were simultaneously present, in 1945 he corrected himself, indicating this association as neither constant, frequent nor dominant. As a matter of fact, as will be shown, it entailed the nosographic individuality of "his" syndrome.

36. PENDE N., ref. 7, pp. 369-370.
37. PENDE N., *The Syndrome of Constitutional Hyperthymism in Children and Adolescents, and its Differential Diagnosis from Froehlich's Disease*. Harefuah, 1950; 38 (2): 17-19.
38. PENDE N., *Sistemazione nosografica nosogenetica degli ipogonadismi maschili*. Folia Endocrinologica, 1955; VIII, 5: 673-682, in particular, p. 678.
39. GUALCO S., NEGRO A., ref.5, p.11.
40. Ibid., p. VI.
41. SHORE R.E., WOODARD E., HILDRETH N., DVORETSKY P., EMPERMANN L.H., PASTERNAK B., *Thyroid Tumors Following Thymus Irradiation*. J. Natl. Cancer Inst. 1985; 74(6): 1177-1184; HILDRETH N.G., SHORE R.E., HEMPELMANN L.H., ROSENSTEIN M., *Risk of Extrathyroid Tumors Following Radiation Treatment in Infancy for Thymic Enlargement*. Radiat. Res 1985; 102 (3): 378-391.
42. MENDELSON R.S., *Confessions of a Medical Heretic*. New York, McGraw-Hill, 1979, p. X.

Correspondence should be addressed to:

liborio.dibattista@uniba.it