Anxiety states,—which, in different degrees, vary from intermittent or continual restlessness to real anxiety, and, from thence pass to the large clinical picture classified as anxiety neurosis,—are gradually becoming habitual in the greater part of humanity.

And, really, if one takes into account that the deep rootedness of the anxiety state constitutes, in a more or less marked manner, a real or possible danger, we must agree that no age in the history of man has been rich, as is our own, in similar stimuli capable of generating, and maintaining in life, the anxiety state itself.

It has rightly been observed that the anxiety state is analogous to the state of fear, except that whereas, in the latter, there appears to us to be a more or less clear vision of more or less immediate danger, in the anxiety state there exists a general state of sedimentary fear; sedimentation composed of real geological emotive strata, which, in the Unconscious, are in a continual state of fermentation, even though the Conscious is detached from same.

The great progress made in modern studies of anatomo-functional links between the cerebro-cortical and thalamo-hypothalamic centres has succeeded in satisfying the desire for pathogenetic clearness inherent in modern Neurology; and thus today it may be established that "the emotive component of conscious states may be explained on the basis of anatomical and physiological correlation" (Belloni).

Emotive activity unconnected with intellectual activity seems possible, according to the fundamental experiences of Benussi confirmed by Belloni. In such a case, from a bio-pathological point of view, thought must turn to anatomo-functional alterations in the thalamo-hypothalamic structures, whereas, in the psychological field, appears what I have called emotive sedimentation, in the sense that distant emotional stimuli (perhaps foetal, often infantile, or

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contingent, at times even ancestral), leaving a mark of their passage in the likeness of common mnemonic impressions, may fully preserve their dynamic potential, even if the intellective sphere, that is, cortical, has forgotten, or seems to have forgotten, the distant emotive stimulus.

On the whole—in repeating the words of Belloni—a large part of the Freudian unconscious could be included in this particular field of emotive recollections released from their respective original conscious states and which brim over into morbid manifestations, in an attempt to reach the sphere of the conscious Ego, that is, to rejoin the field of corticality.

And we both feel, and find, in the affirmations of modern medicine, the intuitions of the great genius Proust. And thus, paraphrasing a famous aphorism of Wilde, we can say that, in this case, Nature has copied Art, that is, Science.

With this in mind, independently of the fact that the anxiety state corresponds to an emotive state sustained by a contingent fact, or else by a buried emotion emerging from the unconscious, we reach the threshold of those thalamohypothalamic nerve centres which are the most "important station of the neuro-vegetative and neuro-endocrine systems."

Broadly speaking, those neuro-endocrine, neuro-vegetative, tissutal and humoral phenomena are derived from the above centres, and which, later transformed into signs and symptoms, create the somatic façade of emotions, such as we see variously depicted in the different forms of psychoneurosis.

As far as we internal clinicians are concerned, the presence of tachycardia, extrasystolic arrhythmia, polyuria, sweating, sudden changes in blood pressure and other phenomena of a vasomotor nature, may at times lead us to estimate purely in an objective manner the phenomena themselves, without carefully examining their causes, which is, therefore, none other than a way of underestimating their effects.

Among the various apparatuses that are involved in this suffocated tempest, as anxiety neurosis can well be defined, that which, in our opinion, functions as "loud-speaker", almost in contrary measure to the well-known distress it entails, is the respiratory apparatus.

In fact, the mechanisms which regulate breathing with their nerve impulses, whether their origins be of a sensitive peripheral pulmonary or extrapulmonary nature, and, above all, if they arise in the sensitive centres of the neuraxis, have never been greatly taken into consideration, as far as their clinical echo-warning system is concerned. The same may be said of the variations in the chemical and electrolytical composition of the blood, with the indirect, or direct, influence which the former exercise on the respiratory centre.

And the above also holds for several alterations in costo-phrenic dynamics.
which, on account of having become habitual, appear to us devoid of pathological meaning, in such a way as to escape just clinical estimation and direct pathogenetic interpretation.

In the autumn of 1950, during a series of lectures I held at the invitation of the Universities of Argentina, Brazil and Uruguay, I spoke at length on this matter, attracting the attention of the physiologist Houssay, and of the Argentinian clinician Mariano Castex, as well as that of cardiologists such as Pedro Cossio and F. Herrera Ramos.

From then onwards, I have continually pointed out how easy it is to observe both in ourselves and particularly in those subjects forced to lead a tense, sedentary life, a varied gamut of momentary, and often prolonged, respiratory standstills of stoppages, caused either by emotive or occasional tensive factors, or, more often, by habitual and, therefore, pluri-quotidian factors. With this in view, we reported several easily checked examples, such as the standstill manifest during the tensest moments of car-driving (steep gradients, corners, overtaking, etc.), and during particular telephone conversations, or else when listening to certain unpleasant facts whilst in a highly charged emotional state, or while reading a long-awaited letter, or else during moments of internal tension arising while following the train of particularly important, tense thoughts. But the foregoing are merely partial, incomplete examples of the thousand occasions to which we respond in this unnatural way.

Ever since then, it was, nevertheless, right to take into consideration the quantitative and qualitative accentuation of these stoppages whilst sitting in a humped-up position in one’s office chair, as is also the case on the front driving-seat of one’s car. Following this, one realizes to what extent sedentariness, which characterizes the so-called dynamic modern life, diminishes the functionality of diaphragmatic play itself.

In the age-group 30–35 we meet patients, mainly men, complaining that for some time, immediately after meals, that is, during the digestive activity, when the circulatory demands in the gastro-mesenteric vascular region is greatest, they experienced a marked sense of abdominal tension. This led to the need to open the top trouser buttons, was relieved by eructation which brought up, at least, the scents of the ingested food. A simultaneous symptom that could not be overlooked was a state of general psycho-physical torpor which often ended in a weighing-down desire to take a nap, from which the patient did not wake rested. In addition, there is a condition of marked and unexpected asthenia; a most valuable element in the clinical picture.

This train of symptoms, less marked after the evening meal, might nevertheless appear during the night, between midnight and three in the morning, more particularly between two and three a.m., not rarely forcing the patient
to sit up in bed in the hope of one or more relieving eructations.

Although these discomforts are more marked after qualitatively or quantitatively heavy meals, these cases are prone to talk about "indigestion" even after medium or normal meals. Because of the time sequence of symptoms, it is easy to confuse these cases with cases of hepatic disease, gall-stones, etc.

It is to be noted especially that, though a series of more or less prolonged eructations will relieve the gastric discomfort, the very valuable and even pathognomonic symptom of asthenia remains.

The important findings of Cassano and his School have thrown much light on the problem. The symptom complex we have just described agrees, that is, with those "haemodynamic modifications secondary to a massive retention of blood in the abdomen, hastened by the gastric dilation". To this we add gastrocolic dilation.

There thus follows a marked retention of blood in the splanchnic area, that is, splanchnic engorgement. This effect is certainly the explanation of the sleepiness which we found so often in plethoric patients with squat chests, and irregular Kussmaul or Cheyne-Stokes breathing.

We had already in 1951 drawn attention at the Medico-Physical Academy of Florence to the low blood pressure, and this was confirmed by Cassano and his pupils in May 1953.

Basing ourselves on Constitution, as understood by Greppi, not only biometric, but also attitude and specific pathological tendencies, we hold still to our early classification into 3 groups:

1) Dyspeptics of atonic type, normal or hyper-chlorhydric, often thin, ptotic, asthenic, longilinear. In this group of patients splanchnic engorgement will entail the whole chain of reflexes incident to pulling on the mesentery. These are the people who feel an impelling need to lie down after meals, scarcely finished.

2) Dyspeptics of hypertonic type, normal or hyper-chlorhydric, clear signs of Greppi's "florid plethora", sometimes with bouts of ulcer, diabetes or gout; they are often fat, stocky types, with psycho-physical hyperactivity and a kind of erethism (generalized irritability). In this group we find the poor masticators, and the hurried eaters, the so-called "air-eaters".

These people are also victims of post-prandial sleepiness: they prefer to have a nap in an arm-chair rather than lie-down, so that there is less diaphragmatic play. These patients, more than other groups, have a disturbed respiratory rhythm during their nap: apnoea, stertor, deep groaning inspirations. The signs impress the relatives, so that they point them out spontaneously to the physician. In these patients more than in others there is evidence of bulbar anoxaemia during digestion. They are people in whom can be found
those changes of thoracic respiratory rhythm or absolute disorganization of rhythm brought about by digestive loading such as is found in Rosenbach's syndrome, according to Cassano et al.

3) Hepatic cases in broad sense, from slight choleemia of the French authors to manifest gradations of xanthomatosis.

In this group we find the variegated family of allergies, visceral and cutaneous. These have been cleverly identified by Huchard and have found a clear nosological classification in the modern presentations of Frugoni, of Melli and of Bascourret.

Neuro-depressives of melancholic or cyclothymic type abound in this group; they may be regarded as cases of Stress; the term psycho-somatic as applied to them may be of value both in diagnosis and therapy. These cases show irascibility at fixed times, for example, at meal-times. There may be a hypoglycaemic component; we have found this many times but more investigations are required.

Not a single case in these 3 groups, broadly defined as they are, draws our attention to his cardio-vascular system. They come because they feel and wish to be treated for gastric troubles. But it is in these 3 groups that, after 8, 10 years, we find the most rich crop of coronary cases, varying from coronary insufficiency to classical angina pectoris and to myocardial infarction.

There remains, then, at the centre of our description of symptoms, "aerophagy", with the already described diffuse gastro-colic meteorism. From what we have said, it is not a question of meteorism which precedes, accompanies and ends a real coronary attack, almost always with eructations, as in the classical account given by Heberden two centuries ago. What we are dealing with, in the classical case, is an epicritical phenomenon; what we wish to emphasize in our discussion is the phase of gastro-intestinal meteorism which precedes by many years the coronary symptoms, and which, as we have often written, almost seems to announce it from after.

In fact, whilst the critical meteorism of Hebedern points to the disappearance of the arterial spasm in the gastric bed with relative re-establishment of gastric motility, which, in the typical case, occurs with eructations, early gastro-intestinal meteorism (the premonitory significance of which we have long recognized) is the result, in the gastro-mesenteric field, of what will later happen in the coronary, peripheral arterial or cerebral arterial field.

The resulting regional anoxaemia in the coronary, results in anginal pain, in the cerebral in transitory psycho-motor defect, in the peripheral in typical nocturnal muscular spasm (cramps) and during the day disturbance of acid-base balance. In the gastro-intestinal field there will be found, as a result of local anoxaemia, a passive dilation at first (the patients speak of feeling
“blocked by gas” and, indeed, the abdomen is tense and tympanitic) and later, on return of regional oxygen supply, a re-establishment of active, isolated or grouped, waves of contraction.

In close and unquestionable analogy with what occurs in the other regions, we see in the gastro-mesenteric the appearance of the appropriate abnormal phenomenon corresponding to the specific physiological stress of the digestive tract, namely, meteorism after the absorption and digestion of food. Here, then, in another guise, we meet the conception of Rokitansky: regional over-work of organs.

We have, on other occasions, maintained that, from the fact that functional wear and tear of the digestive apparatus finds its raison d’être in this obviously chronological and increasing biological necessity, it is not surprising that such wear and tear should be both early and of supreme importance.

It is well-known, in fact, that from birth to the end of the second year of life human pathology is predominate digestive. Thus, with the growth and gradual development of psycho-sensory life, by means of nervous links so finely analysed in his fundamental work by Spadolini, the digestive apparatus becomes to a greater and greater extent the most powerful “loud-speaker” of our emotive life.

Apart then from the anatomo-pathological basis of our assertion, it does not seem possible to shake the conception that if the début of pathology in man appears in the digestive tract, it must be there also that the first signs of stress and of functional fatigue will appear, and there can arise only on a circulatory background.

Having reached this view, we can speak of post-prandial meteorism as a result of a failure of a sufficient blood supply to meet a needed functional efficiency, discrepancy according to the expression of Condorelli. We would then rightly be able to name this meteorism stress meteorism or meteorism from digestive stress. This is the typical and dominant sign, not only as the most striking clinical manifestation, but also as, for analogical, anatomico-functional and, as we shall see, anatomo-pathological reasons, it has seemed to us legitimate to define it as Mesenteric Insufficiency.

This can be defined as the expression of a diminished regional circulatory efficiency, transitory but periodic since it appears during typical functional stress in those organs which are supplied by the gastro-mesenteric tree.

Turning back now to the gastro-mesenteric circulation if an inadequate collateral circulation, with more or less marked sclerosis of the vascular lumen or a total vascular occlusion, explains to us the establishment of the typical picture of the mesenteric infarct, we can readily imagine the effects of a relatively minor, but constantly inadequate irrigation (with critical accentuation in the hours of maximum digestive activity), which may explain the state of
certain abdomens which at certain times seem fat, whilst, in fact, they are only tense because of ischaemic atonic meteorism.

It is easy to see that a diminished nutrition of the intestinal wall must lead to disturbances of the secretory activities of the digestive glands with the consequent disarray of the normal chemistry in the intestinal tract leading to those abnormal reactions and fermentative changes which have always attracted the attention of physician, distracting them from the true causal, which is basically and pre-eminently circulatory.

The most sensitive index of the inadequate circulation is the nervous regulation of tone and motility of the gut which, of course, depends upon the biphase action of the vagus and the sympathetic, linked with the name of Spadolini. The chemical mediators of this oscillatory, biphase function are acetyl-choline and adrenaline.

The principle of reciprocal innervation by means of which the motor sympathetic control of the sphincters of the gastro-intestinal tract occurs, probably extends also to the stomach, the small intestine and the colon by means of those "preganglionic fibres which run in the lesser and greater splanchnic, are interrupted in large measure in the Solar Plexus (coeliac and superior mesenteric ganglion) from which the post-ganglionic fibres emerge which run with the vagus into the gastric and mesenteric plexuses" (Spadolini).

We have thus before us a subject with prior vascular changes leading to anoxia and with consequent effects on organs supplied by the vascular net involved: we know the resulting nervous system repercussions, the altered chemistry in the gastro-intestinal tract, the abnormal selective permeability of the intestinal barrier: these are the stages that, on the one hand, lead to the discomft of meteorism, which is its most apparent sign, and, on the other, develop into the so-called intestinal toxaemia with its somewhat empirical flavour, but that still remains, as we have stated on other occasions, one of those obligate cross-roads at which, from time to time, Science and Empiricism, Medical and Laymen, meet. The Mayo Clinic studies by Alvarez have largely confirmed this point of view.

Still keeping to the abdominal sphere, we recall another element which seems to us of growing importance, the more one thinks about it. This element is the altered diaphragmatic dynamics arising from altered rhythm and from reduced respiratory expansion. As we have been repeating for several years, modern man is forgetting how to breathe properly, forced thereto not only by the many anxieties acting as "mutilators of breathing", which at the end of a day are very numerous, but also by the increasing speedy transport vehicles. Two things result—one a psycho-tensive state in the drivers and, as a result of the restricted position in which the patient sits in any motor vehicle, he
is subjected also to obstacle the free play of abdominal breathing.

There follows, from these facts, the situation we have called *Slight Chronic Anoxia*, an element which, added to other inevitable hypoxic bulbar disturbances, may be at the root of many serious road accidents, and which is, as regards our present thesis, the background of a *generalized chronic hypoxia*, with marked special repercussion on the splanchnic area.

On this background of generalized anoxia, enriched by multiple interferences, already considered, such as allergy, dysvitaminosis, endocrine dysfunction, and reinforced at periodic intervals (e.g. meals) by the different reciprocal reflex effects, the sensitive *anoxic mechanism of arteriosclerosis* finds an easy port of entry.

It is on this background, also, that we see appearing one day the regional asphyxial distress of the myocardium. But this, as we have repeatedly insisted, is a late phenomenon. In fact, the clinical coronary episode is but the 3rd act of a drama, the first 2 acts of which are concerned with troubles in the digestive tract of an eminently functional kind and with the meteorism as one of its main manifestations.

Having in mind the anatomo-pathological data, the original syndrome of Roehmheld-Ceconi, the arrhythmia of Rosenbach, the so-called "aerophagic circulatory collapse" would all seem to belong to the 2nd act of our imaginary drama.

The remarkable condition of *haemodynamic turbulence*, well documented by Cassano's school, cannot, we think, be imagined as a purely functional condition: we feel impelled to regard it as a condition favouring the initial change in the gastro-mesenteric vessels studied by Weber and myself.

And if the *typical disturbances*, attributed to the various symptoms, become established, it is because the adaptation of individual regions no longer operates perfectly. The nearby organs function, but the cardio-vascular response is already evidently inadequate. The threshold of silence of the troubled organs has been exceeded. For many years we have had this view, faced by the finding of the low blood pressure and of the slight transitory flattening of the ST wave.

It did not, therefore, seem unreasonable to regard these subjects with mesenteric insufficiency, these pseudo-gastro-enteropathies among our ambulant patients, as *potential coronary cases*. And this will be the more so as more systematic take up research of what Greppi has called *humoral spies*.

And so, when in addition to the post-prandial asthenic periods, and the nocturnal awaking in anguish at fixed hours, attributed to dietary errors or a heavy digestion, with reduced post-prandial psycho-physical efficiency, we will find marked hypercholesterolaemia, already reported by Coppo (especially
in the region of Emilia), hyper- or hypoglycaemic levels, and we will have sufficient ground not to discard such patients into the diagnostic wastebin with so-called Neuro-depression with dyspepsia.

On the contrary, seen in the light of our secret suspicion of coronary potentiality, we will note them down and ask them to return to us periodically, submitting them to biochemical tests. It is superfluous and psychologically, harmful at this stage to start tests of a cardio-vascular character: *there is no need to put these patients into a panic. The alarm should be and remain in us.*

It must be stated at once that we must avoid excessive therapeutic measures and aim at moderate ends. It is not by lowering the level of blood cholesterol (easy though it may be), nor by lowering the level of carbohydrate intake, in a patient with a high blood sugar, nor by reducing a moderate hypertension with hypotensive drugs, that we will attain our true task.

It must not be forgotten that there are biochemical and haemodynamic situations held in balance which must be respected; that there are climacteric hypothyroidic states, in men and women, stabilized in order to protect the circulation, which it would be hazardous to disturb, especially with too vigorous a treatment.

It is our view that it is above all by means of a sensible dietetic regime that these patients will attain those brilliant results that are implicit in our premises.

One should be able to put order into a tenor of life which has become psychoemotively profoundly altered. Apart from the psychosomatic component which is never missing, it is the tension in these patients, often culminating in anxiety neurosis, that must be kept in mind. The equilibrating influence of the physician would be easy and profitable, were it not that these patients flit from one doctor to another (*medical nomadism*). In fact, they go from one physician to another seeking relief from the nuisance of meteorism, and being, not rarely, judged to be neurotic, they are removed from our qualitative and quantitative dietary limitations and put on the antithetic diets, which they wish to find justified. That is why we wish to disseminate among practitioners the guiding concept which derives from what we have already explained and which we will summarize in the following practical advice:

1) *Prevent, by all available means, the onset of obesity which begins after the 30th year of life.* At this period, after the years of feeding for growth requirements, the body enters into the phase of maintenance, but having regard to the different types of activity, we cannot prescribe for a manual labourer what we would prescribe, for example, for a sedentary worker, such as a lawyer.

Unfortunately the relatives of these patients are not our collaborators, especially because they have seen the patient’s nervousness before meals, bad-temper at any delay in being served, haste in the ingesting of food, which comes
to be regarded as a clamant need, so that the slightest restriction is resisted.

We have already stated that these patients often have a pre-prandial low blood sugar, so that it is advisable to take a small meal or snack at 11 a.m.: fruit juice, a dry biscuit with a small piece of low-fat cheese. This prevents the patient coming to table hungry and overcomes the real or presumed hypoglycaemia.

2) *Enrich the diet*, principally composed of *protein* and *carbohydrate*, and on the whole sub-caloric, with only smallest additions of fats (animal or vegetable); Vegetables (raw, fresh, cooked) and preparations of poly-Vitamins enriched with iron salts should be given. Powdered skimmed milk appropriately prepared with materials above-mentioned is useful and pleasant.

3) *Train the patient to a very light evening meal*, advising him that after this as well as after the midday meal, he should take a walk in the open air. If, however, he cannot forego a nap after meals, he should *lie down in a horizontal position, not in an arm-chair*, loosening neckties, collars, trousers or anything that might impede easy respiratory movement.

4) In the event of high-grade hypertension or of any tendency to tissue hydropenia, revealed by variable weight from day to day, or especially by varying abdominal girth, a sodium-poor diet must be imposed.

5) Administration of the so-called lipotropic factors or labile methyl carriers is useful, particularly *Choline* and *Inositol*, which, by promoting a better lipoid metabolism, aids hepatic function. But there are limits of usefulness as has been suggested by Campanacci (Cardiol. Pract. 6: 85, 1955).

6) The use of Heparin which, apart from its anti-coagulant effect, has a demonstrable capacity of modifying the lipo-protein picture in serum to one opposite to that arising in arteriosclerosis is today being applied with excellent results (see Hahn, 1943, and Greppi, 1953).

7) Traditionally *lodine* has been used, though its efficacy is at best dubious. If, however, it is given, it should be used in *organic preparations* associated with the B-complex.

8) We have often recommended the use of purines (aminophylline, simple or sedative) from the earliest phase of the Meteorism of mesenteric insufficiency. Given rectally, in combination with sedatives, in the evening one can assure a good night’s rest, as well as more satisfactory breathing.

9) Only if, to a strong tendency to put on weight, there are indications of a climacteric character (reduced libido, reduced memory etc.), should hormones and small doses of corticosteroids be given and only for short periods. We, not infrequently, give small doses of thyroid preparations; sometimes a decided fall in blood Cholesterol follows.

10) *Respiratory exercises* and *general graded exercise* such as cycling or a daily
long walk, should also be recommended.

*Sports are contraindicated.* With their intensive and, indeed, damaging effects in these cases, they make no contribution to the end in view.

These then are the elementary headings of a prophylactic and therapeutic approach to the problem of coronary and myocardial sclerotic disease which accompany one another, as well as to that of senescence, to which not only the Gerontologist but also the general practitioner must turn his mind.