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Original Articles

THE CONCENTRATED COFFEE ENEMA IN THE THERAPEUTICS OF SHOCK

(Its study from 1916 to 1941)

Carlos STAJANO

SUMMARY - Chance permits a fact to be proven (1916). A second stage of the application permits the result to be ratified again (1918-22). Coffee's empirical application stage. Interpretive test (1922). Period of discussion and controversy. The claimed action of caffeine. The clinic recognizes the suspected existence of other very active alkaloids in coffee independent of caffeine (1924 and following). In Surgical, Traumatological, Obstetric practice. The physiopathological concept of "shock" constitutes a true synthesis of the mechanisms which characterize it, while permitting interpretation of the diverse etiology (traumatic-toxic-psychic) acting on the same yet complex effector system. (1922 and following).

Therapeutic simplism in the pathology of shock victims. Notions of experimental physiology on the medicinal action in shock victims. Coffee enema and its results in a fixed period of time truly evident. New coffee alkaloids. The stage which corresponds to the

chemical laboratory and experimental physiology.

The fruitfulness of a well-documented event and its results in one course of investigation.

It is in the year 1916 that a fortuitous circumstance gives us the opportunity to witness a phenomenon, without a doubt extra-ordinary, and which, with the passage of time, was full of consequences, not only on the practical side, but also in the field of the physiopathology which arose from it. In fact we had a patient in a deep coma; a young woman 24 years of age, healthy until then, an artist, who was suspected of having ingested some toxin. Hypothermy of $35\frac{1}{2}$, imperceptible pulse, waxen pallor, superficial respiration; pupils widely dilated. Auscultation revealed very attenuated cardiac sound and irregular tachycardia. Patient in such critical condition, that an entire arsenal of cardiotonics is administered (sparteine, digalen, strophanthus, camphorated oil, intramuscular ether, caffeine). It is a veritable orgy of cardionics, but even if they were not correctly indicated, they were at least justified, given the gravity of the case. By the third hour of the fruitless struggle, in the face of imminent death we had proven that we were dealing with a massive intoxication of cocaine. The case was reported to the coroner (Dr. J. May), who justified the indicated therapy, recognized the seriousness of the case and predicted death within a couple of hours at the most. In an hour, a second coroner, Dr. Lorient, corroborated the opinion of Dr. May and advised the police. We do not know why the exotic way in which we proceeded in this case occurred to us, (but) we preferred fighting to passively awaiting death. At the 5th hour of the struggle we proceeded to introduce,

by enema, a 400 gr. coffee infusion obtained from one kilogram of powdered coffee in a sufficient quantity of water, filtered twice. We were aware that we could not increase the seriousness of the case, and that if the worst occurred, our intentions would be justified. In fact: in front of the entourage, (the police inspector and representatives of the patient), an unforgettable situation developed. Twenty minutes after the patient received the enema, we began to notice a change in the color of the ears and nose. The cyanotic pallor became pink; the livid lips became tinged a soft pink. The imperceptible pulse began to show progressive and rapid, the dull and remote heartbeats became sharp and violent. And this entire reactional situation developed within 20 to 40 minutes, leaving no room for doubt as to the change which had taken place in such a radical way. After 40 minutes, not only had the autonomic sphere transformed totally, but an intense psycho-motive stimulation was added; four people were nearly unable to restrain this patient, who 45 minutes before was dying.

243 This toxic rage left no significant trace, other than some ecchymosis from the intramuscular ether injections and a small, empty cocaine bottle (10 grams), under the rug in the apartment. Drs. May and Lorienté were advised of this exceptional verification. No greater importance is given now, or was given at the time to this happy event than the fact that a life was saved by chance.

Second Verification - In the year 1918-19 we were working in the Management of the Clinic of Prof. Pouey. We were actively involved in surgery of the pelvic sympathetic (hypogastric sympathectomies). Our post-operatives were perfect, to the point where we had no critical case for which progress

was worth recording. (We reproduced the extract of this observation published on page 72 of our book Trophism and Cancer).

Trophic illness of the genital apparatus. Pre-Kraurosis. Genital prolapsus. Cure of the prolapsus. Bilateral hypogastric sympathectomy. Post operative reaction very critical. Acute cardiac insufficiency. 48 hours. Dramatic result of concentrated coffee enema within 40 minutes.

Details: in the second stage of a medium laparotomy we obtained good arterial retraction after freeing the hypgastric adventitia.

After the denudation, it was still the size of a thick pen-holder or a radial artery. We did not have to work in this case, as in others, on the sigmoidean mesocolon.

Post-operative. In spite of a very fast, very clean and only slightly traumatizing operation, this patient was taken from the table in critical condition. At one hour: pulse of 120 to 130; weak, irregular, intermittent. Painful abdominal distension. The cardiac sound was indifferent and inactive. A discrete cyanosis appeared. At 24 hours: condition alarming. Intense cardiac weakening. Peripheral cyanosis. Emotive indifference and nearly complete obnubilation. Superficial respiration. Loss of temperature. At 48 hours, Dr. Artuccio studies her and affirms: acute miocardia insufficiency. Embryocardia beat at a rate of 160-170 with frequent intermittencies. Paralytic distension of the abdomen with diffused pain. Vagino-rectal tactum, nothing worthy of note. The patient has only autonomic life. She does not react to the cardiovascular drug, or to the smooth fiber stimulant (Pituitrin, from Parke-Davis). It is as if we injected distilled water.

While involved in this struggle we remembered the results of the coffee enema in 1916 and we prepared it personally with good quality coffee, especially purchased. (Hospital coffee is only part coffee: as we had suspected). At 56 hours we gave the dying patient the strong coffee enema. A new unprecedented and extraordinary result. In 20 to 40 minutes, rapid and radical transformation. Large belches testify to the recuperation of visceral motility.

The face regained color. The psyche abandoned drowsiness and expresses euphoria and well-being. The circulatory impasse changed from one moment to the next. The cardionic which we injected sterily that afternoon now produced its usual result. From this point on we give no general medication and the post-operative continued normal until the patient's release 18 days later. It was at this period that we advised different surgeons, gynecologists and obstetricians of the use of coffee in similar cases, and that we can provide case histories of patients in different hospitals where the correct indication gave its result. It is lamentable that Prof. García de San Martín had not published some of the cases of obstetric shock in his clinic. From our experience in Prof. Pouey's Clinic we became personally convinced of the extraordinary therapeutic success obtained in different circumstances with the concentrated coffee enema, and we have used this treatment on patients in Italian, Spanish, Pereira Russell, Pasteur and Maciel Hospitals, as well as others.

We also recorded the unanimous resistance of the surgeons of the area to accepting the extraordinary action of coffee in the required cases. Some never tried the treatment. Others wasted therapeutic routine and did not

245 dare (even) in the face of imminent death to use this treatment that could have saved lives. Others injected high doses of caffeine into the muscles and veins, but they did not achieve the same results as with whole coffee. During several years in the Service I had under my control 0.20 gr., 0.30 gr. and 0.40 gr. ampoules of caffeine which we used to analyze and compare their characteristics. The clinical conclusion based on numerous cases was: the beneficial reaction of the coffee enema in shock syndrome cases is not attributable to the caffeine. There are without a doubt other substances, more than likely alkaloids, as yet unknown, the dynamic medicinal action of which on the autonomic system should be studied.

This seems to revive traumatism or accidental intoxication from the traumatic or toxic lethargy caused by an operation. Doubtless there are in coffee specific substances which work against that functional autonomic inhibition which is characterized by the stroke shock syndrome.

Incursion into Physiopathology - Observed facts, when accumulated, permit an opinion to be formed in practice and its application is done empirically, unless a physiological or general pathological fact can interpret and explain it. At that point it ceases to be an empirical fact and it becomes a scientific fact. In fact: How did coffee produce that resurgence in the case of cocaine intoxication? How did that same coffee enema act similarly in the same time span of 20 to 30 minutes, solving an unsolvable impasse in the post-operation sympathectomy?

Alkaloid intoxication in one case; traumatic and surgical aggression in the other. A syndrome, if not equal in intensity, similar in quality of the profuse symptomatology in both cases. We find the connection between both syndromes in the central autonomic nervous system.

Since then we have incessantly accumulated clinical facts which are incomparably more exact than the experimental physiological laboratory, which has enriched us with concrete conquests and has founded concepts which time has only been able to strengthen. For example: the physiopathology of visceral pain, its specific reagents, the role of acute distension, the differential character with pain in the motor sensitive sphere; the excentric repercussion and general phenomena which result from traumatic aggressions; the laws which explain splanchnic pain, its localization, its irradiation and its projection, etc., etc. and it is in this rhythm of constructive thought that we could see clearly into the cloudy chapter of shock. It is since then, 1922 and 1923, that with clinical and physiological material, we have conceived the turbulent symptomatic storm which characterizes shock in a synthesized way.

SYNTHETIC CONCEPT OF SHOCK

Acute, intense and unusual aggression of the great system of the organo-autonomic state results in:

- a) Sudden death; or
- b) The overall picture of shock, compatible with the state; or
- c) Partial syndromes of dysfunction or hypofunction; which we have called segmentary shock.

Different intensity of the aggression does not justify a fundamental difference within a same elemental process, which gives mortal aggressions in one case; critical in others, and passing and very light in so many others.

Different quality of aggression, on the other hand, can give clinical and etiological varieties of shock. Thus we will have: purely traumatic shock, when the aggression is exercised mechanically on the nerves of the state in relation to or on the autonomic plexa, either directly or through more

or less long peripheral neurons. We will not insist on the influence and centripetal repercussion of peripheral traumatisms; e.g., the shock of disarticulation of the hip or that of the visceral crises at the beginning of certain processes (twistings, strangulations) as well as operatory violences, or the shock in the course of a simple pleural puncture, etc.

The toxic etiology in the proteiform intoxications of duodenal occlusions, or in advanced appendicitis, gives us a toxic shock, where the symptomatology arises from the large system of the organo-autonomic activity, which feels the toxic aggression in all sectors. As in the previous case it perceives the disturbing action of trauma.

Was not the alkaloid intoxication (cocaine) we observed, as in the first case, the purest exponent of autonomic sideration by toxin?

In other cases, the circumstantial etiology is multiple.

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In extensive superficial burns, for example, in the large area of uncovered skin, traumatic aggression is combined in an autonomic innervation zone, with the toxic aggression of the resultant proteiform disintegration.

Here are two etiologies which occur in sequence, which reinforce their effects, which make things worse and which give special clinical circumstances and demand adequate therapeutics, but, as we will see, show a series of coincidental symptoms, at least pathogenically, since they come from the same effector apparatus.

Our synthetic conception of shock accepts the generalization of all aggressions to the organo-autonomic activity system and it is through this activity

coordinating physiological system that we are permitted to develop this unique and physiological concept of interpretation.

Pure traumatic shock, toxic shock, medical shock, regional trophic shock, psychic shock or moral shock are included in this generalization, as well as the association of all of them and the analyzing of all these disconnected pathological circumstances, that with more evidence, something may manifest that general surgeons or premature specialists overlook: I refer to the physiological functional unity, viewed through disorders.

Functional unity in normal activity, as well as in the current pathology, takes us to what we think physiologically. Thus, in the clinic we observe panoramically and collectively and not merely by an organ or a sick part, or in functional change. The psychic sphere, the domain of autonomic innervation and the related activity of the sensory-motor territory, intermingle their stimuli and influence one another in such a way that the separation of their reactions, which we have studied separately in chapters about the corresponding pathology, is unreal and has been created exclusively by man, who in his desire for specialization, has built a segmentary and artificial pathology.

Consequently, the clinic suffers from this precept, a fatal simplism, a consequence of that separatist concept, in accordance with the molds of morphological pathology and exclusively anatomical pathology which should be relegated to the history of knowledge.

Upon studying emotive shock and analyzing its organic manifestations, we will see how the entire organo-autonomic activity system is affected by the action

of psychic trauma and at certain moments there is no differentiation from the organic manifestations of traumatic or surgical shock. At the same time we see in this that the psychic sector participates in the scheme within the context of the other symptoms common to all shock.

This synthetic concept of shock permits us to unite, through very diversified clinical circumstances, the notion of individual organic reactivity. On the other hand, the study of post-operative shock not only lets us study the consequences of surgery itself and all related aggressions, but it also lets us zero in on the temperamental category of each subject, their predisposition to shock, causes which favor it, individual susceptibilities, prognosis and even simplification of treatment.

Symptomatic Sources of Shock⁽¹⁾ In this analytical review (see outline) we will attempt to summarize briefly post-operative complications. Its multiple reactions, variable in intensity and extension, will give us the post-operative syndromes which are manifested, either in an overall and universal way, or in a partial and segmentary way on one or more sectors of organo-autonomic activity, giving us the segmentary picture of post-operative shock. These isolated manifestations are not generally called by their true name in the clinic; but as we proceed we will see the error that everyone commits, not only in the concept that we form of the process on occasion, but also of that which emanates in practice, from it, which is the therapeutic action.

(1) We begin with the study of post-operative shock, on that for which we have clinical and experimental documentation.

POST-OPERATIVE

THE MULTIPLE CLINICAL MANIFESTATIONS OF SHOCK

AUTONOMIC NERVOUS SYSTEM SECTORS

CLINICAL MANIFESTATIONS

Innervation of the gastro-intestinal
smooth fibers

Regional, upper regional visceral,
perivisceral autonomic plexi

- a) Paresis or paralysis of the gastro-intestinal tract syndromes. Total or segmentary atony.
- b) Acute dilatation of the stomach.
- c) Ileocolic paralysis (neuromotive lethargy of the post-operative.
- d) Gaseous colics.
- e) Bladder paralysis of the post-operative.

Innervation of the bronchotracheal
pulmonary smooth fiber

Visceral, perivisceral, regional
and upper central autonomic plexi.

- a) Tracheal paresis (very frequent)
- b) Partial or total passing or fleeting bronchoplexias.
- c) Pseudobronchitis of the post-operative.
- d) Tracheal obstructions of phlegm attributed to ether (within 24 hours).
- e) Atelectasis.

Vasomotive innervation

Perivascular sympathetic and
mesocephalic areas.

- a) Arterial hypotension
- b) Venous capillary repletion.
- c) Arterial vasoconstriction.
- d) Venous vasoparalysis.
- e) Pallor.
- f) Peripheral cyanotic pallor.
- g) Splachnic autohemorrhage.

Cardiac innervation

Vagal and sympathetic autonomic system, peripheral ganglion and upper areas.

- h) Repletion of the portal system.
- i) Autotransfusion.
- j) The spleen and the liver, as sponge organs.
- a) Passing and ephimeral tachycardia (sine materia) of 24 to 48 hours.
- b) Bradycardia (rare).
- c) Arrhythmia of the post-operative. Extrasystoles and intermittencies.
- d) Acute miocardial insufficiencies, and episodic (24 to 48 hour) post-operative or post-traumatic asystoles.
- e) Embryocardia (fetal beat).

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Tissular innervation

Organic metabolism.

Upper mesoencephalic areas.

HUMOR MODIFICATIONS IN GENERAL

- a) Salt and water metabolism disorders: anhydremia - hypochloremia - hypochloruria - achloruria.
- b) Proteiform metabolism. Constant post-operative hyperazotemia (Del Campo).
- c) Fatty metabolism: acidosis of the post-operative, alkalosis.
- d) Hydrocarbonated metabolism, hyperglycemias, acidosis.
- e) Oxygen and CO₂ metabolism.
- f) Absorption retardation.
- g) Insensitivity to medicines or toxins.

Tissular innervation

Regional trophic activity

Tissular innervation

Interstitial cellular indicated
activity

LOCAL TROPHIC SHOCK

- a) Pallor.
 - b) Cyanotic pallor.
 - c) Nearly mortal atony of the wounds.
 - d) Local stupor, during the first hours after the contusion or the wounds in intoxicated subjects.
 - e) Lack of defense against infection.
 - f) Detention or diminution of organic tissular changes.
-
- a) Interstitial edema.
 - b) Active condition of the capillary laxis.
 - c) Temporary disturbance of the capillary endothelium physiology.
 - d) Permeation of red globules with intact vessels. Erythrodiapedesis is an evident phenomenon.
 - e) Permeability of serum, with its salts and proteiform material, into the capillary network.
 - f) Loss of biochemical balance of tissular albumin. Cellular, interstitial and sanguineous.
 - a) Temporary disturbance of cellular physiology. Episodic permeability.

Permeability of glandular secretions to anatomically intact excretor canals. (Pancreatic juice - bile - in the visceral crisis of those organs. Intolerance shock (Couvelaire) in the pathology of the visceral apoplexies.

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Innervation of the parenchymas and the noble glands

Involuntary innervation typical of the viscera, the extravisceral, large splanchnic plexi and centers.

- a) Hyposecretory syndromes of the stomach and intestine in the post-operative.
- b) Oliguria - anuria - selective elimination disorders in the renal function.
- c) Salivary hyposecretion.
- d) Sudoral secretory disorders. Cold sweat. Hypersudation.
- e) Episodic hepatic dysfunction (little studied in particular in this transitory (condition) of the post-operative).
- f) Tracheobronchic paralytic hypersecretion.
- h) Dislocation or momentary suspension of the specific cell function.

Innervation of internal secretion glands

Autonomic system and endocrine system.

EMOTIVE AND MORAL SHOCK

- a) Transitory and massive post-traumatic hyperthyroidism.
- b) Massive post-emotive hyperthyroidism, true discharge of the "Leyden bottle".

- c) The Basedow experiment in acute emotion.
- d) Suprarenal discharge in severe traumas.
- e) Suprarenal discharge in strong emotions.
- f) The glandular syndrome in surgical shock.
- g) The glandular syndrome in emotive or moral shock.
- i) Post-emotion amenorrhea.
- j) Lactation and emotive shock.

Intracerebral involuntary life

Upper centers of psyche

Little known.

Psychic and somatic activity

- a) Emotive indifference of shock in any of the known etiologies. (Purely nervous, toxic, combined, emotive or moral).
- b) The critical shock coma. (Emotive ictus).
- c) Is the erethic form a kind of cerebral automatism which corresponds to pure shock or to other injuries?

Involuntary calorification centers

- a) Primitive post-traumatic hypothermy.
- b) Primitive post-emotive hypothermy.
- c) Extreme hypothermies in slower toxemias, destructions of the peritoneals, obstructions, gaseous gangrenes, etc.

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Respiratory center

- a) Scarcely perceptible superficial respiration in inhibitory traumas.
- b) Toxic siderant action in serious toxemias. (Peritoneals, obstructed, infected).

Let us remember the specific action of certain toxins arising from anaerobia which excite that center specifically, originating "lack of air", an anguishing symptom of suffering in the respiratory center, noted in certain gangrenes. Shock of the center happens to this phase of excitation, leading to coma and death, a true expression of the toxic sideration.

In order to express in didactic form which are the clinical and the symptomatic manifestations of shock we have made this artificial outline of anatomical sectors and sources of symptoms, with the sole purpose of organizing the explanation. Let us not forget that the separation into items is a purely pedagogic exercise, and done, therefore, with this utilitarian purpose in mind. We wish to demonstrate how the functional unit, not only in the physiology, but also in the domain of pathology, is a reality. There is a pathogenic unity in all shock syndromes; this is imposed upon us by the common effector system by all its symptomatology. This privilege of unification and correlation corresponds to the autonomic nervous system, the coordination system of all vital functions, from the simple cell activity in the cell cavity to the complex vital function of the whole, including that of cerebral activity with all its subtleties and very complex attributes.

It is to the intimacy of cell activity that we must go to be able to understand the transcendancy of the imbalance which is in motion in shock. To the

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ostensible and most clinical phenomenon, hypotension - a symptom around which all hypotheses of shock were woven - was added, as what was thought through. most deeply and reasoned more physiologically, all the resultant manifestations are developed and condition one another, to the point that that process becomes the most general, universal and most intimate disorder of the overall pathology, distorting vital function from its very base. From the physiology of the membranes and protoplasm of our cellular frame with its transcendent physiological destiny to its most elevated function.

Since 1922 our orientation in teaching has been to try to inculcate this physiological thinking, rounding out exclusively anatomical thinking, so ingrained in the spirit of many contemporary teachers.

We do not understand how pathology can be taught and clinical training in it founded, without stretching the horizon outside the limits of the diseased organ or the circumspect anatomical lesion. General pathology and all its areas of specialization should dedicate their first chapters to the study of the physiology of the involuntary nervous system. The condition of the conjunctive tissue, for example, studied by the anatomist, leaves the physiologist an immense field of exploration, full of secrets, unsuspected by the former, which managed to designate that tissue, the most noble of all, filler tissue or support tissue. That concept, which we have accepted for so long, only shows one of the very limited aspects of our shortsightedness in the true notions which should govern pathology and guide modern clinical practice.

Summing up: There is no apparent opposition among the various shock syndromes. All etiologies are possible. All roads serve to reach the centers: the

centripetal nervous tract, the humoral tract, the psychic tract.

An injury shakes up the involuntary system and this, with eloquent clinical proof, demonstrates: functional unity (Pi y Suñer), giving manifestations in all sectors, either in discrete dysfunction or in total afunción.

Serious injuries give: a) the overall framework of shock, with the shut-down of all organo-autonomic functions. It is acute and complete neurovegetative dystonia.

Not so violent or less aggressive injuries show: b) Partial shock syndromes, or segmentary clinical manifestations, frequently observed in post-operative incidents, from which category we can give as examples:

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- a) Certain post-operative "sine materia" tachycardia, with hypotension; in other cases, only bradycardia.
 - b) The improperly named acute post-operative and post-traumatic asystoles.
 - c) Gastro-intestinal paresis or paralysis.
 - d) Acute stomach dilations.
 - e) Reflexive bladder paralysis.
 - f) Post-operative or post-traumatic bronchopulmonary syndromes. Tracheo-bronchial paresis. Bronchoplexies. Post-operative pseudo bronchitis. Atelectasis, begun within hours of the operation.
 - g) Nutrition syndromes: Alkalosis, azotemia, hypochloremia, acidosis, etc.

In the course of these clinical syndromes, one does not talk of the shock of this or that etiology; rather they are called by the dominant symptom. One concept of physiology and its emanation, that of pathological physiology,

lets us not only recognize them, but also interpret them, and more interestingly, to assign them a therapeutic in accordance with their true mechanism. To summarize, we will also say that shock syndrome, and all its manifestations, has the tendency to dissipate spontaneously, as long as the determining cause is suppressed. In the case of pure traumatic aggression, the manifestations disappear totally between 40 and 48 hours.

In some circumstances, and especially in post-operative, where the primary situation is complicated by numerous incidental factors, there can be a chain reaction and toxic aggressions can follow an initial purely traumatic shock complicating the resultant shock and prolonging or retarding it (tardio-prolonged shock). This is exactly what happens in shock from extensive burns. The initial shock of the burn (extensive autonomic dermal aggression) continues within a few hours with the characteristic humorotissular toxic syndrome.

"Constant dystonia which we would call normal after any surgery, is variable in duration, generally no greater than 48 hours, in which there are functional disorders, apparent clinically (isolated manifestations) or a state which we would call disturbance potential. It is what Leriche gave by naming it: 'the post-operative sickness'".

That is the time frame, which clinical experience has taught, that is needed by the nervous system for its functional reintegration.

EMPIRICAL THERAPEUTICS AND SCIENTIFIC AND LOGICAL THERAPEUTICS

Therapeutic empiricism and routine in practical indications

Many times we have asked why clinics do not publish case histories and analyses of the therapeutic results they observe - but choose not to publicize,

because: they either are not interesting enough or because other matters demand more attention. Accumulated casuistry and the confirmation of certain observations from twenty years before permit us to synthesize that experience which could be of use to others.

Cardiovascular therapeutics in shock. Hypotension is the impressive clinical phenomenon and it is attacked, in our judgment, mistakenly. The entire peripheral dynamics disturbed by the shock (capillary permeability) is that which makes the plasma escape from the veins (exhemia); the arterial torrent is precipitated in the dead sea of the portal system and the hepatic and splenic sponge harbor enormous quantities of blood.

It is not simply a mechanical phenomenon: it is a profound and complex imbalance in the cardiovascular innervation. From another direction a cardiac disturbance intervenes, through dysneurotonia, where the vagus predominates, in that resultant vagosympathic hypotonia residual (Brusch).

The miocardium sometimes reaches the maximum grade of insufficiency.

Peripheral tensional insufficiency, capillary insufficiency, cardiac insufficiency, these are the objectives on which uncontrolled practitioners focus in the handling of their therapy.

Strychnine, caffeine, especially in salicylate form, adrenalin, sparteine, hypophysis, camphor, hexeton, digitalis, strophantus, etc. are injected de riguer, and, in summary, the immediate result is nothing; the usual medicinal response is not observed; nonetheless: who can abstain from injecting so many noble drugs, which, in these cases, act as if distilled water had been injected?

What fundamental modifications exist, then, in the organism of the shock victim?

Here is a clinical fact that experimental therapeutics lets us understand.

As a matter of fact:

The organism in the state of shock fundamentally modifies its reactional ability to medicine. There is a period of total insensitivity to a specific medicine. In teaching we have called it: Period of reactional lethargy, and it lasts exactly as long as the phenomena of shock, that is to say 40 to 48 hours in the post-operative, and, similarly, that period is similar in post-traumatic shocks in general.

In the slower or retarded shocks of toxic origin, this same "Medicinal reactional lethargy" occurs and this proof, on which we have already insisted in 1922 at the Surgical Society⁽¹⁾, has not warranted any great attention from practitioners. Without thinking about how useless this medication is, more complex cardiovascular therapy is continued to be used on shock victims. It was thought once to explain this phenomenon as a defect in absorption, given the slowness of the interchange of plasmas, but soon it was seen that it was not that, since intravenous administration did not modify the result. Evidently, there exists a more complex general nutrition disorder, more intimate, that experimentation brings out, confirming that which has been perfectly observed in the treatment of humans.

Lethargy to medicinal action in shock. Experimentally, during the period of shock, the absorption and reactive physiological functions are either diminished or suppressed, to such a point that, during this period, intoxications are

⁽¹⁾ Discussion in the Surgical Society. "Annals of the Montevideo Medical School" Volume VII, 1922, page 506

retarded. Nutrition and metabolic changes are either suspended or detoured, and the reactivity to medicinal or specific toxic stimuli is either delayed or does not appear.

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The experiences of Roger with veratrine and strychnine, those of Galeazzi and Busquet, with the "curare" are instructive and show the practical physiological effect of toxins in the normal state and in the state of shock in animals, using drugs with well defined action.

They provoke shock with stupor in toads or larger animals:

- a) with electrical discharges in the dorsolumbar region;
- b) with diverse traumatisms, cephalic contusions (Roger);
- c) with abdominal traumatisms on the plexi; coolness; contusion, tearing, caustics. (several experimenters).

It is a physiological fact that shock retards intoxications, nutrition is slower or it detours from its normal type. In a word, absorption and trophic sensitivity ability functions diminish or disappear in such a way that they make it insensitive to the effects of toxic substances, which, in the normal state, would provoke serious disorders. (Drugs of known action and in current use in physiology).

Roger studies the action of strychnine in healthy animals (toads). The injection of 0.02 gr. of sulphate of strychnine provokes an exaggeration of spasmodic reflexes at 5 minutes. Strychnine tetanus is evident at 15 minutes.

In animals in a state of shock:

Same injection: 0.02 gr. of strychnine sulphate. No exaggeration of reflexive action until 30 to 40 minutes have passed. The strychnic tetanus appears after one hour.

Roger uses and studies the action of veratrine.

In healthy animals (toads): toxic dose of veratrine provokes a toxic reaction in 5 minutes, registerable in the muscular contraction curve; specific and known action on the last phase of muscular contraction, revealing considerable retardation.

In animals in a state of shock: toxic dose of veratrine does not provoke the slightest explorable symptom in the muscular contraction curve, except after 40 minutes.

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I will not insist on all similar investigations that have been made by modern physiologists which confirm the experiences of Roger. I will recall the Italian School, with the works of Galaezzi and the works of Busquet done with the "curaré" before Roger; but which coincide completely (as to results).

In reality, these experiences permit us to interpret the insensitivity of certain surgical patients to all of the most active drugs which the surgeon injects at the moment of shock, manifesting either in an overall way or in any of the organo-autonomic system activity sectors. There is a total lethargy to medicinal action, an absolute insensitivity of that system dominates, dulled by inhibition, and so it is, that to avoid causes of error, the experimenters have utilized the intravenous method to administer the toxins and the effect has been exactly the same. The toxic effect appears when the inhibitory phenomenon ceases. Physiological function and the ability to react either to medicine or toxin return.

WHAT CONCLUSIONS OF PRACTICAL THERAPEUTICS CAN WE EXTRACT FROM THIS BODY
OF FACTS OF EXPERIMENTAL PHYSIOLOGY?

1st) Recognize as imaginary in effectiveness, and consequently useless, that rash of therapeutics which routinely and indiscriminately is used in the multiple visceral and general manifestations of shock.

The situations we have enumerated by synthesizing their manifestations (see previous pages) tend to evolve towards integral, spontaneous cure on the average in 24 to 48 hours after the suppression of the determining cause. (Pure traumatism or intoxication). This circumstance has permitted attribution of the complex medication used as beneficial, when in reality it is a natural evolution of the process. The patient was cured in spite of everything. We have not seen modification of tension, cardiac rhythm, capillary permeation with any of the cardiogenic medicines used (digitalis, strophanthus, caffeine, camphor, etc.)

We find the title acute and irreducible insufficiencies of the myocardium in our notes and we saw, surprisingly and unexpectedly, its brusque evolution without transition in a period of a few hours (48 hours).

As for the parectic manifestations or paralysis of the smooth fiber, not only tracheobronchial but also gastrointestinal, vesical, etc., etc., we will say the same thing, as we will about its specific medication: posterior hypophysis. (1)

(1) and (2) Stajano and Crocogini. The constant ileoparalytic of the post-operative. "Archives of the Uruguayan Med., Surg. & Spec. Soc.", Volume V, 1934, page 559.

Stajano: The dynamic syndrome of the tracheobronchialpulmonary smooth fiber. From the book, Shock, page 100.

2) Notwithstanding that period of profound disorder, we must respect and be discerning: to do little and to not do it badly.

For our part, we dealt in general terms with:

a) chloruration by 20% hypertonic injections each 3 to 4 hours, intravenously (10 to 15 cm³) and we resorted to the salinoglucoside injection with insulin when the humoral state demanded it.

b) We radically suppressed in the surgical patient (who we knew to have been organically well in the pre-operative) cardiac and tonivascular medication, since it is inoperative and has no reason to be.

c) For the same reason we suppressed hypophysiary medication, inoperative in cases of shock (numerous casuistry and personal experiences in this respect).

We considered it useful only when the intestine and the rest of the smooth fiber reacquires its physiological ability. (See previous pages).

d) The only medication which we recognized as active, and which impressed us for its dramatic effectiveness and rapid action, and the evident relationship of cause to effect, is the large dose of coffee, administered by enema. Concentrated infusion of 500 gr. of coffee.

Enemas no greater than 300 gr. to be retained.

e) We consider the action of coffee, as a specific against "medicinal lethargy" common to shock, and that powerful action we attributed, for such a long time, to certain supposed alkaloids, with the exclusion of caffeine, which undoubtedly work on the autonomic centers.

260 New coffee alkaloids. In 1936, during a visit to the Butantan Institute (São Paulo), we had occasion to interest doctors H. Slotta and Cl. Neisser in the problem which interested us so much as clinical practitioners, with respect to possible new alkaloids in coffee besides caffeine, and which we

have defended with so much vehemence with practitioners in our country, without being heard.

In 1938 those same investigators communicated to us that they had isolated several new alkaloids, thus confirming a purely clinical prediction, made with determination since 1922. It was then that we thought it useful to recognize the outstanding physiologist, Prof. Thales Martines, to whom we communicated the possible actions of these new alkaloids (action on the smooth fiber, several kinds of actions on the autonomic in its diverse centers). Here is the entire investigative program planted earlier in clinical experience, and which has doubtless now borne some fruit. Many conquests have been made within the physiological sciences in their clinical applications: from there our body of notions related to general processes which characterize shock interpreted from its physiological aspect, analysed from its productor mechanism and treated later in a continually improved manner, shifting the therapeutic objectives of the disturbed organs or systems to the central autonomic system, the site of the disorder.

Here is the evolution from the empiric to the scientific and with this example, we add one more [item] to the history of the evolution of knowledge.

The last stage of this profitable investigative trail belongs to the experimental physiological laboratory, and to the clinical practitioner, especially the surgeon. From his point of view, the post-operative, he can continue to enrich science with positive data, at the same time informing about the definite and concrete action of the new coffee alkaloids, indicating the dosage, emphasizing the instructions and replacing the heroic and primitive coffee enema with injections of specific active substances on determined centers.

Here is the evolution and consequences of a casual fact, born of chance in a happy moment. (1916-1941).