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ALUMINUM—POTASSIUM NITRATE IN
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OSTEOMYELITIS

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ALUMINUM-POTASSIUM NITRATE IN THE TREATMENT OF SUPPURATIVE CONDITIONS, PARTICULARLY OSTEOMYELITIS

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THE World War brought forward many advances in the treatment of infectious processes, both from the viewpoint of improved surgical technic, and also the pre- and post-operative treatment by means of improved anti-sepsis, greatly facilitating the surgeon's work, and in many cases rendering surgical intervention unnecessary.

All of the accepted methods, however, included the use of an antiseptic or germicidal agent, chief of which were the iodine and chlorine derivatives, the earlier simpler mercurials and phenols having been practically discarded. Many highly organized organic compounds, such as diaminomethyl acridinium and its chlorides (acriflavine) have been investigated and proposed in the effort to reach the desideratum—that of low toxicity and high germicidal index free from effects tending to delay or inhibit the natural regenerative processes.

The writer's experience in the management of infected cases closely parallels that of most surgeons with the comparatively small proportion of satisfactory results compared to those obtained in other fields of practice, and a considerable portion of time has been diverted to the observation and investigation of the cultural, non-antiseptic, aluminum-potassium nitrate method. A preliminary report upon which is herewith presented.

In the selection of a definite line of investigation, we are at once confronted by two diverging paths—one leading along the well-beaten track of antiseptics including the employment of a germicide specific to the organism known to be present—the other pointing to the "antibody" method by which natural processes within the body tend to eliminate the invading or infecting organism. This latter path was followed, paralleling in many ways that of vaccine and serum therapy, *with the one striking difference that the "antibody" is developed in the original host instead of being transplanted and evolved in an animal.*

The aluminum-potassium nitrate compound method of treatment is the direct development of observation of the meat preserving industry where the so-called "brine" containing potassium nitrate is employed as the oxidizing agent. A number of cases were treated with successful end results, using potassium nitrate alone, but it was found to produce great irritation and sloughing of tissues, together with maceration of surrounding normal tissues, all of which rendered its use alone almost prohibitive. The potassium nitrate action seemed to be cumulative, reaching the maximum in about ten to fourteen days, with its attendant irritation. Reduction of the dosage, while

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decreasing the irritation, also reduced the reaction to such a degree as to be of little value. It became evident at this point that some modifying agent must be added which would admit of maximum reaction with a minimum of irritation. Many combinations, covering a great variety of salts, were tested out, and it was found that aluminum nitrate, astringent and non-irritant itself, seemed to have the property of inhibiting the pain, yet not interfering with the oxidizing properties of the potassium salt when combined in a dressing of low aqueous content, but had the drawback of falling apart in aqueous solution, again permitting the potassium element to exercise its irritant and macerative properties. Research was continued in the direction of finding a non-aqueous solvent to obviate this condition, and at the same time other experiments were carried on with a view of introducing a third element to stabilize the combination of the other two. Finally a compound was prepared by crystallizing aluminum nitrate and potassium nitrate from concentrated nitric acid which does not cause hydrolysis of the aluminum nitrate. The quantity of aluminum nitrate and potassium nitrate used should be in the proportion of the molecular weight of one molecule of aluminum nitrate to three times the molecular weight of one molecule of potassium nitrate. For example, 375 grains of aluminum nitrate and 303 grains of potassium nitrate in sufficient hot concentrated nitric acid to dissolve the substance will produce a solution from which the double salt $\text{Al}(\text{NO}_3)_3 \cdot 3\text{KNO}_3 \cdot 10\text{H}_2\text{O}$ will crystallize out on cooling and after drying the product it contains approximately 31 per cent. aluminum nitrate, 44 per cent. potassium nitrate and 25 per cent. water of crystallization. About 500 c.c. of concentrated nitric acid, kept hot by means of the water bath, is a suitable quantity of acid in which to dissolve one kilo of aluminum nitrate and potassium nitrate mixed in the proportions previously indicated. The described salt crystallizes from the concentrated nitric acid solution in the form of colorless rhombic and monoclinic crystals. They are readily soluble in cold or warm water in substantially all proportions. They possess an astringent slightly metallic taste. This product is further diluted with nine parts of potassium nitrate and the resultant mixture is incorporated in the dressing used in the treatment.

BACTERIOLOGICAL EXPERIMENTS

The nature of the infection in individual cases was determined by culture and subsequent plating and the relative number of organisms determined by direct smear from the exudate of the lesion. In the greater number of cases a mixed infection was found, staphylococcus aureus predominating. In many of the foregoing a Gram positive organism was present of saprophytic type. A small percentage of cases showed a pure culture of short chain streptococcus. It is of interest to note that in none of the cases diagnosed clinically and radiographically as tuberculous osteomyelitis were tubercle bacilli found on examination of the excretion. Staphylococcus aureus or a sterile fluid was invariably present. Examination of the smears before and during treatment show a marked increase in the number of colonies progressing with the course of

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treatment and only decreasing in number and finally totally disappearing in the terminal cycle of treatment.

In an endeavor to determine the germicidal index of the aluminum-potassium nitrate compound, many experiments were carried out with the final conclusion that instead of possessing antiseptic and germicidal powers, *it actually assists and intensifies the growth of bacteria when added to the culture media.*

A uniform suspension of bacteria well distributed through diluted bouillon when introduced into media containing various percentages of the aluminum-potassium nitrate compound solution, showed growths varying from two to five times those found in the untreated media. These results were found constant in a large number of laboratory experiments.

ANIMAL EXPERIMENTS

The toxicity or rather non-toxicity of the aluminum-potassium nitrate compound was tested first on guinea pigs, then on rabbits and finally on monkeys (*Macacus Leoninus*) by the intravenous, subcutaneous and oral routes. The results in all instances show that the aluminum-potassium nitrate compound is entirely non-toxic, irrespective of its method of administration. Two large monkeys weighing 42 and 45 pounds, respectively, were given single intravenous injections of 80 grains each, and later the same amounts introduced intra-abdominally and intra-muscularly without the least untoward effect. The same animals were at the same time fed two ounces each of the salt each feeding. No loss of weight or decrease in activity or function could be noted. The intravenous and subcutaneous doses in these experiments were over double the average amount used *externally* in the treatment of human patients.

CLINICAL MANIFESTATIONS UNDER TREATMENT

In chronic cases of osteomyelitis of many years' standing, with sinus formation, where there has been only a thin serous discharge, which under the microscope shows a few epithelial cells and an occasional leukocyte, there appears within twelve to twenty-four hours after application of the dressing, a marked purulent discharge containing innumerable polymorphonuclear leukocytes and tissue shreds, although no reaction is apparent on the skin. This indicates that in these twelve to twenty-four hours, some element from the dressing must have passed into the deeper tissues to produce this acute reaction calling forth an increased leukocytosis expressed in terms of the pus discharge.

Dialyzation through the skin may be further observed by inserting a tube into the sinus, sealing same to the surrounding skin and observing the volume and character of the discharge. After this observation, a dressing of aluminum-potassium nitrate compound is applied, and a comparative observation made, when it will be noted that there has been a tremendous increase

in the volume, and a great change in the character of the discharge, which now consists almost entirely of leukocytes and débris.

If the dressing is discontinued, the discharge will immediately subside, and within a few days will resume its original amount and character. This conversion of a thin serous fluid into a purulent discharge can be due only to an acute reaction within the tissues, producing a rapid autolysis and liquefaction of the diseased area. This liquefaction and autolysis is produced first by the influx of leukocytes and phagocytes, and second by the nascent oxygen acting on the diseased tissues without affecting the normal. The nascent oxygen is probably derived by the splitting of the nitrate ion in its passage through the skin into the deeper tissues. Nascent oxygen does not alter normal healthy tissue, but the infiltrated tissues which are contaminated with organisms are affected by the aluminum-potassium nitrate compound, accounting for the selective action of this compound in attacking only the diseased structures.

The vesicle and pustule formation is probably the result of stimulation of the latent bacteria into marked activity by the aluminum-potassium nitrate compound which has been proven experimentally to be an excellent culture medium. Some of these pustules seem to connect with the deeper tissues. Fine probes have been passed through the skin pustule into the bone cavity.

Clinically, we are not able to produce a reaction beyond the area of disease or the point of infiltration of the soft tissue. In the case of a small area of osteomyelitis in the middle third of the femur, with an infiltration of the adjacent soft tissues, a dressing applied over the entire length of the femur will not produce a typical reaction in the skin, and no vesicles or pustules will appear beyond the affected or infected areas. The aluminum-potassium nitrate compound is apparently selective in its action because it produces no reaction where no organisms are present. This reaction apparently definitely outlines the area of infection. The vesicles and pustules show culturally in practically every instance the same organisms that are isolated from the deeper tissues.

In every case a hyperplasia of blood-vessels in the treated area is noted, evidenced both by the active hyperemia, and also from the histologic study of sections of deep tissues taken at the time of operation, many of which were done for the removal of large sequestræ.

Another observation of importance is the increasing bacterial count of the exudate during the initial period of treatment due to the application of a cultural dressing tending to stimulate the dormant bacteria of a chronic state into activity, reducing their virility and vitality in proportion to the increased rate of propagation, and at the same time increasing the resistant elements of nature by a local leukocytosis and phagocytosis in much the same way that natural forces deal with an acute infection.

In almost every case a marked improvement in the general physical condition of the patient is noted almost at once, making it seem that the aluminum-potassium nitrate compound was absorbed and had produced a direct systemic effect. Extensive investigation has not been able to support this theory, and

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on the other hand, investigations by Professor Kahlenberg of Wisconsin University, failed to disclose any traces of either base in the blood or urine. Continuous observation of this effect, together with the constancy of the condition leads me to believe that the systemic reaction is more apparent than real, and is the result of a rapid autolysis producing local exudation at the site of the lesion where prior to institution of this treatment absorption had obtained, carrying the toxins through the system and imposing an abnormal load on the organs of elimination. The aluminum-potassium nitrate compound treatment simply maintained the case within localized limits permitting the eliminatory organs to resume their normal full functions without this excess load.

TECHNIC

The technic of application consists in applying a plastic dressing directly to the affected area, made up of a vehicle into which the aluminum-potassium nitrate compound is incorporated. Ordinary rolled oats has been used for this purpose, and it has been suggested that same be sterilized for two hours in an autoclave, under about fifteen pounds pressure, for the purpose of destroying the proteolytic enzymes, which would otherwise



FIG. 1.—Cutaneous reaction in aluminum-potassium nitrate therapy.

tend to invert or sour it, besides introducing various other bacilli, tending to complicate the microscopic picture. Should an autoclave not be available it is suggested that practical sterilization of the rolled oats can be accomplished by heating for twenty to thirty minutes in an ordinary oven. Rolled oats is suggested as meeting the best average of the ideal requirements of availability, cost, cellular structure and, above all, being physiologically inert, thereby eliminating the irritant properties of many other available materials. The vehicle is made by adding approximately 50 c.c. of boiling water to the ounce of dry rolled oats, and stirring until a uniform mass is produced, after which

the aluminum-potassium nitrate compound is added and thoroughly mixed through. Experience has shown that the average dose is approximately thirteen grains of the aluminum-potassium nitrate compound per ounce of dry rolled oats. The dressing is applied about one-eighth of an inch thick directly to the skin well beyond the limits of the affected area, and is covered over with some waterproofing material such as wax paper, gutta percha, etc., in order to retain the moisture. This is an important procedure, which, if omitted causes the dressing to solidify and to become hard and shrink away



FIG. 2. —Cutaneous reaction in aluminum-potassium nitrate therapy.

from skin contact. This dressing should remain in absolute contact with the skin continuously and be changed *as often as it becomes saturated with the exudate*, and in any case should be changed at least once in thirty-six hours, on account of loss of moisture to tissues. No gauze should be interposed between dressing and skin.

The definite dosage for individual conditions cannot be accurately plotted, as the individual peripheral nerve sensitivity largely governs the limit of nitrate content, excesses expressing themselves by burning sensations. The safe and rational clinical procedure would be to start with a relatively small

dose and gradually increase it to the point where irritation appears, and then reduce it slightly below that point. This amount may be as low as five grains per ounce and may run as high as forty grains per ounce, varying with individual sensitivity and also with the part of the body treated.

It is of interest to note that an aqueous solution of aluminum-potassium nitrate compound applied in a non-plastic vehicle, such as a gauze pack, does not produce any of the typical reactions or effects of the above described procedure, but on the contrary induces a cessation of all reactions and promotes a rapid epithelization of the abraded surfaces resulting no doubt from imperfect skin contact retarding dialyzation.

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Reaction.—The typical reaction manifests itself within about forty-eight hours with the appearance of an erythema very much like that of an erysipelas, and this is followed within a few days by vesicles and pustules over the affected area (see Figs. 1 and 2) containing purulent fluid, many of which continue to discharge after rupture, presenting the umbilicated appearance of a small-pox lesion without the crater and bluish edge. This definite reaction continues as long as the infection in the underlying tissues persists. The dressings become saturated with exudate, which renders them ineffective, at which time they must be renewed. A good practice is to change the dressings at least once in twenty-four hours.

The area of reaction during the course of treatment gradually reduces in size even though the original area is still being treated. This is perhaps an indication that the area beyond is free from the infecting organisms. This unusual and peculiar reaction in the case of chronic infections, both of soft tissue and bone, seems to be due to the passage through the skin and into the deeper tissues of some of the elements of the aluminum-potassium nitrate compound.

Indications.—In the course of several hundred cases treated successfully by this method, over one-half were of the mixed infection type with staphylococcus aureus predominating. One-third of all the cases cultured staphylococcus aureus alone, and the balance including streptococcus, pyocyanus and saprophytes. The lesions treated included osteomyelitis, both traumatic and hematogenic, bone tuberculosis where secondary infection was established, furunculosis, various post-operative wound infections, and some forms of gangrene.

This method of treatment was found to be contraindicated in the presence of malignancies because of the greatly increased local vascularity which seems to accelerate their growth.

CASE REPORTS

Tuberculosis of the Spine.—Male, twenty-four years of age, Polish. Admitted to the hospital August 10, 1922, with a diagnosis and typical manifestations of acute appendicitis (pain at McBurney's point 15,000 leukocytes, high temperature, tenderness, etc., in right lower abdominal quadrant). Appendectomy; usual technic, Battle-Kammerer incision. Appendix found inflamed, thickened, not containing pus.

Operation did not afford relief, patient continuing to complain of vague pains, heightened temperature and general malaise. X-ray examination of kidney and ureter as well as of hepatic region proved negative.

Aluminum-potassium nitrate compound was then applied over the entire right side. Within four hours a definite area of fluctuation was manifest, which ruptured spontaneously the following day, discharging thick pus, which yielded in culture an almost pure strain of staphylococcus aureus. The area of reaction extended to the lower dorsal spine and a stereoscopic radiogram, made at this time, disclosed a beginning tuberculosis of the first lumbar vertebra.

In this instance the aluminum-potassium nitrate treatment not only afforded excellent relief from pain by instituting prompt local drainage, but, which is more important, pointed the way to an obscure and unsuspected lesion. The treatment

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was continued for four weeks more, when the patient left the hospital very much improved. He presented himself a month later for examination. The improvement in his condition progressed very favorably, and the patient returned to his usual vocation of a rather strenuous type within a month after the aluminum-potassium nitrate treatment was started.

Osteomyelitis of the Humerus.—Male, thirty-four years of age, American. Observation began April 14, 1922. At that time, the left arm was found very much swollen, painful to touch and motion, both active and passive, and a marked contracture at the elbow. Wassermann negative. Physical examination disclosed nothing of importance, other than the condition of the affected extremity. Radiogram showed an active infectious process, affecting over one-half of the length of the entire humerus, with considerable destruction and evidences of early operative intervention (curettements?). The surrounding soft structures were hard and infiltrated; no fluctuation; scars resulting from previous operative procedures red and angry looking.

Treatment with aluminum-potassium nitrate compound was commenced, changing the dressings every twenty-four hours. After the initial application, a marked softening was discovered overlying the affected area, surrounded with a general hyperæmic blush of the contiguous surface. During the succeeding forty-eight hours, many pustules appeared, discharging pus. At this time, the pain had entirely disappeared from the affected limb; contracture of the joint considerably lessened. After seven days of treatment a remarkable regression of the affected process was apparent, the arm being at this time about normal in size, with full return of function at the elbow. Pustules along the margin of the old scar continued to discharge a small quantity of pus, while those in the areas beyond disappeared under the same dressings.

Patient returned to his work, continuing the daily dressing. About three weeks later he returned, at which time no further reaction could be produced. No definite sinus developed in this case, drainage has evidently been accomplished by capillary absorption. Six months later an examination of the patient discloses him to be in perfect health, the arm to all appearances normal. There is no return of the symptoms and clinically at least the patient is to be considered cured.

Osteomyelitis of the Tibia.—Female, single, twenty-four years of age, American. Anamnesis discloses nothing of importance as far as family history is concerned. Patient states that she observed about three years ago, sharp intermittent pains in the right knee, which pains after a few weeks became continuous. Diagnosed by family physician as rheumatism and treated as such for a month. This was followed by an abscess below the knee, which the attendant opened and irrigated. Pain did not subside and fixation in plaster cast was resorted to. Two months later the cast was removed, but incision had not healed. Wide curettement of the tibia was then done, followed by three more similar operations at three-month intervals. Wound has remained open over three years with much destruction of the upper third of the tibia. Physical examination disclosed a rather poorly nourished individual. Urinary findings showed much indican and a slight trace of albumin. Wassermann negative.

The affected limb was subjected to the aluminum-potassium nitrate treatment for ninety days, applications were made daily, after which time the patient was discharged with sinuses healed. Two months later the patient presented herself for examination. No recurrence of objective manifestations can be noticed and subjectively the patient feels well. Patient gained in weight, is in better spirits and looks upon life with greater cheer. Radiogram made at the last examination shows prolific regeneration of the tibial defect.

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Post-operative Suppuration in Abdominal Wall.—Female, fifty years of age, Austrian, came under observation with suppurative sinuses in abdominal cavity following laparotomy.

Usual treatment instituted by attending physicians without results. Attempts to heal the sinuses by the usual methods proved unsuccessful.

Aluminum-potassium nitrate treatment instituted. The day following the first application the drainage tubes which were left *in situ* were removed. The volume of discharge increased many times, necessitating changing of dressings every four hours. Six days after the beginning of treatment the upper sinus had healed by granulation and three weeks after treatment began the patient was discharged with both sinuses completely healed.

Osteomyelitis of the Femur.—Male, thirty-four years of age, Hungarian, presents himself with all classical manifestations of osteomyelitis.

The history reveals a condition that had been persistent for sixteen years, during which time at least eight or nine curettements had been done, and more than a couple of dozen incisions for relief of abscesses, which had burrowed in various directions. During the past five years the affected limb was never free for one month without discharging pus in some place. Amputation was seriously considered by his attendant; Wassermann negative.

Physical examination disclosed nothing of importance, other than objective and subjective findings of the affected limb. X-ray shows extensive destruction of the lower third of the femur, without tendency to regeneration. There is apparent absence of periosteum from the epiphysis to about the middle of the femur.

Aluminum-potassium nitrate treatment was instituted. Within a few hours after the first application the drainage became so profuse that dressings had to be changed every three or four hours. Five days later several small spiculæ of bone worked their way to the surface and they were lifted out with tissue forceps. At this time the dressings were changed thrice daily. Three weeks after treatment was instituted dressings were changed only once a day. The discharge at this time was markedly serous in character.

X-ray studies made a month after treatment was commenced showed a comparatively clear outline of the femur with beginning osteogenesis at the edges of the defect. The patient was able to note a complete closure of the sinuses, a disappearance of objective and subjective manifestations, three months and four days after treatment was commenced. A subsequent examination, two months later, shows no symptoms that might indicate any recurrence. These findings checked up with X-ray studies disclose progressive new bone formation.

Osteomyelitis of the Radius.—Female, nineteen years of age, American, presents forearm disclosing suppurative sinuses, the result of an open operation for Lane plating for fracture of the radius, the result of a fall. Plate had been removed some time after the operative area disclosed signs of infection. A plaster-of-Paris cast had been applied and antiseptic dressings were made through a large window cut in the plaster-of-Paris. A radiogram shows good apposition of fractured fragments, and a small quantity of spongy callus feebly attempting repair.

Aluminum-potassium nitrate treatment was started and continued daily for thirty-four days, at the end of which time the sinus was found healed. With the exception of a week at the hospital the rest of the treatment was strictly ambulatory. Two months later the X-ray examination disclosed new-formed callus welding the broken fragments. Patient has full use of the arm.

Osteomyelitis of the Foot.—Male, fifty-eight years of age, Bavarian. History discloses that patient had suffered from diabetes mellitus, for which he remained under his physician's strict care.

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Physical examination disclosed a fairly well-nourished individual. Wassermann negative. Urinalysis with reference to sugar and albumin negative. His left foot disclosed that two toes had been amputated. A suppurative sinus at the distal end of scar tissue resulting from the amputation which exudes a thin, watery serum. Foot is very much enlarged. Cutaneous circulation poor, foot livid in appearance, suspected of beginning of gangrene.

Radiograph shows absence of the fifth metatarsal and about half of the fourth, the distal end of which seems to be sloughing. Surgical removal of the remaining fragment of the fourth metatarsal bone was performed. Edema did not subside and the aluminum-potassium nitrate treatment was begun. Four days after the commencement of treatment the swelling had receded over one-third of the area affected and within the period of a week it had entirely disappeared. Two weeks later the sinus had healed and the patient was apparently cured, but remains still under observation.

CONCLUSIONS

That the treatment herein described is not in any degree a substitute for rational surgery, but must be considered as a pre-operative treatment in badly infected cases, enabling the surgeon to later work under more favorable conditions.

As a post-operative treatment in infected cases irrespective of whether the case was previously or subsequently infected.

As a procedure in those cases that have failed to respond to previous surgical measures and those patients who persistently decline operation.

Removal of sequestræ is in all cases advisable.

The aluminum-potassium nitrate compound is not an antiseptic, but, on the other hand, is a definite accelerator of bacterial growth, tending by rapid propagation to lower the vitality of the infecting organisms thereby assisting the normal resisting powers of the body to eliminate the invading organism.

Unlike most antiseptics, the aluminum-potassium nitrate compound does not attack normal tissues and does not interfere with granulation or the osteogenetic efforts of nature.

Pain, which in most cases, is the result of infiltration and consequent tension, is very quickly relieved, due to prompt autolysis and liquefaction relieving tension by absorptive elimination through sinus or systemic absorption.

Over 75 per cent. of our cases become ambulatory and are able to pursue their vocations, coming to the clinic for dressings in contrast to the radical surgical procedures of the past, thus eliminating long hospitalization and later invalidism with its attendant expense.

The method is relatively simple, may be used within wide limits, and employs a non-toxic medicament.



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