Clinical Notes, Suggestions and New Instruments

ASPERGILLOSIS: A CASE OF POSTOPERATIVE SKIN INFECTION

LOUIS FRANK, M.D., AND O. M. ALTON, B.S.
LOUISVILLE, KY.

Since our student days we have been familiar with the fact that molds may at times be pathogenic in their action. Attention had been called to this pathogenicity even before Virchow's work in 1856 describing the infectious process and identifying the organism. Baumgarten in his "Mykologie," published in 1890, describes the lesions resulting from experimental injections of Aspergillus niger and discusses very fully the pathologic changes and the microscopic observations.

Myers and Dunn[1] reported a case of aspergillosis in which the infection was located on the dorsal aspect of the hand of a farmer. The lesion was in the nature of a granuloma.

Most often this infection is seen in the auditory canal and in the lungs. In the lung it may run a very chronic course and defy accurate diagnosis for a long time. In the auditory canal it is a question whether the mold acts as a true pathogenic organism or is present as an epiphyte. In the lung, however, it is truly parasitic or pathogenic in character.

Recently our attention has been called to a postoperative dermatosis due to Aspergillus and, having seen two previous cases, we have thought the matter of sufficient interest to record; also, we have noted no similar postoperative skin infections reported in the literature.

A woman, aged 40, was operated on for abdominal tumor, the operation being devoid of any feature worthy of comment. The usual preoperative local preparations were made and the usual dressings applied. At the end of about sixteen days, the dressings were removed and revealed what has been observed on two other occasions; namely, the dressing had the appearance of being studded with black powder, and at one end of the wound, near the site of one of the lower stay sutures, there was a spot that had the appearance of a large ulcer, about 1½ inches (3.7 cm.) in diameter, with sharply defined edges, slightly elevated and filled with a yellowish-black material resembling pus. In addition, at various points in the skin under the gauze dressings covering the wound were pustules varying in size from one-sixth to one-fourth or three-eighths inch in diameter. They were elevated, contained a purulent looking material varying in color from yellowish, in the smaller, to almost black in the larger pustules. They were quite superficial and did not penetrate through the true skin except for the large ulcer-like area at the stay suture, which showed the black discoloration not only over its entire base but also in the depths of the suture tract. The edges of all were sharply defined with the slightest margin, possibly a line in thickness, of redness circumscribing the pustule. As stated, the infection did not extend beyond the gauze pad used as dressing and was definitely confined to this area. As a result of this observation, it was at once recognized that we had encountered an implantation of a species of mold fungus, most likely Aspergillus niger. There was no postoperative elevation of temperature nor any other untoward symptoms. Following exposure of the wound field to air and washing with iodine and alcohol, the apparent ulcers and pustules had entirely disappeared by the next morning, leaving dry, slightly scaly, areas outlined by a faint red line to show where they had been.

The history and the appearance is characteristic of three cases observed. The first was seen thirty years ago and the second about twelve years ago, each of them exhibiting similar pustulation confined absolutely to the area of the gauze dressing and healing rapidly after exposure and painting with 3 per cent tincture of iodine followed by alcohol and dressing applied so as not to exclude air. A photograph of the second case, which followed an emergency appendectomy, failed to show the details sufficiently to warrant publication.

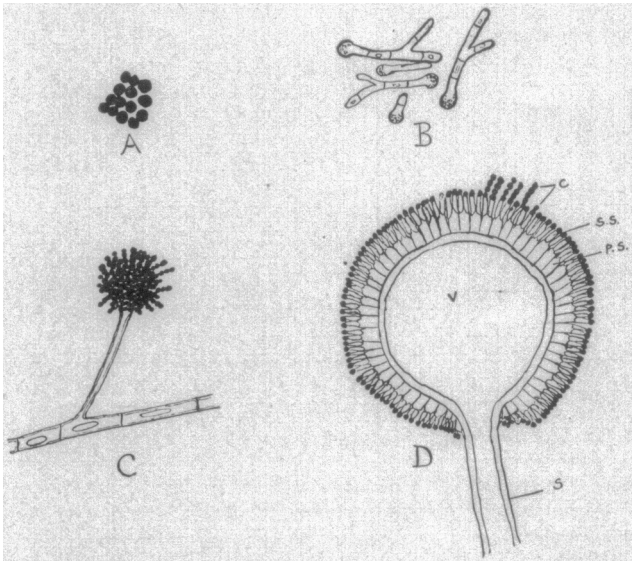
From the Department of Surgery, Norton Memorial Infirmary.

1. Myers, J. T., and Dunn, A. D.: Aspergillus Infection of the Hand, J. A. M. A. **95**: 794 (Sept. 13) 1930.

At first the inclination was to construe the aspergillus found in these cases as truly pathogenic in character, but after consideration one may come to the conclusion that this is not true and that the condition can be called an infection only in the broadest use of the term. The explanation may be that following the preparation of the patient's skin there is in the operating room atmospheric contamination by this organism. It is sealed up by the dressing, skin reaction ensues, blebs are formed under the adhesive plaster or any other dressing that may be used, and the serum in these blebs furnishes a most desirable pabulum for the growth, or there may be a bit of oozing from a stay suture stitch hole or from the lips of the wound, and such would act as an excellent culture medium.

Culture of other packages of dressings put up at the same time as those used in this case proved absolutely sterile, nor was there any evidence of any skin infection in any other clean case in which operation was performed the same day or on previous or subsequent days.

Of the 375 species of Aspergillus, 57 are pathogenic, and 40 are pathogenic for man. The majority of pathogenic species have been found in the ear. These organisms have also been found in the lungs, bronchi and throat, about the nails, in an ulcerated cornea, and in the feces. The organisms were isolated from the beards of two Africans by Castellani.



Aspergillus niger: *A*, conidia; *B*, twenty-four hour growth showing young mycelium; *C*, mature organism; *D*, cross-section of conidiophore (*c*, chains of conidia; ps, primary sterigmata; *ss*, secondary sterigmata; *s*, stalk; *v*. vesicle).

The specimen sent to the laboratory consisted of the surgical dressings covered with a dark powder. This powder was planted on Sabouraud's maltose agar and potato. A rich growth was obtained on the agar in twenty-four hours and on the potato in seventy-two hours. Spores were then planted in Sabouraud's maltose agar between a coverslip and slide and the growth was followed under the microscope from a single spore to maturity. This microscopic slide culture method has been invaluable to us in the study of fungi.

The organism has been identified as one of the strains of Aspergillus niger but differs somewhat from any of the strains already described, as will be seen from the drawings. The characteristics of these organisms are as follows: colonies growing rapidly and becoming very black on the surface after several days; with abundant submerged mycelium; mycelium colorless; aerial hyphae scantily produced; globose, superficial conidia; stalks mostly arising directly from the substratum, some uncolored and some yellow to brown only near the vesicle, smooth, with walls thick and without pits but frequently uneven on the inner surface. The mycelium is septate, each hypha having a distinct nucleus. The vesicle is globose, thick walled and a yellow brown. The sterigmata are both primary and secondary.

Large numbers of calcium oxalate crystals were found in Sabouraud's maltose agar near the growing organisms. The disaccharide maltose is hydrolyzed by the enzyme maltase produced by this aspergillus and is broken down into two molecules of the monosaccharide dextrose:

$$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O_6$$

Citric acid is then fermented from the dextrose as an intermediate product:

$$C_6H_{12}O_6 \qquad C_6H_8O_7 + 2H_2O$$

This reaction is not fully understood. Buchanan thinks that possibly the acid is synthesized from some of the decomposition products of the sugar.

Oxalic acid is formed from the citric acid. When the acid formed is neutralized by the addition of chalk, one half of the calculated theoretical yield is obtained.

This is an interesting phenomenon. The finding of large numbers of calcium oxalate crystals in the mediums may give one an immediate lead as to the type of organisms present.

614 Heyburn Building.

REPORT OF CASES OF CARBON MONOXIDE POISONING TREATED BY METHYLENE BLUE INJECTION

A. W. CHRISTOPHERSON, M.D., HERMISTON, ORE.

I wish to report further confirmative evidence of the value of methylene blue (methylthionine chloride U. S. P.) in the treatment of carbon monoxide poisoning.

Recently five men were brought to me for emergency treatment following a "mysterious" poisoning. They had been working with a road construction crew and were blasting rock in a tunnel measuring 6 by 10 by 115 feet. The blast was set at the depth of the tunnel and ten minutes later two of the men entered the tunnel to commence work. After a few moments one of them sensed the danger and warned the other to run. The latter collapsed almost immediately and the former ran but collapsed at the mouth of the tunnel, where he was dragged to safety. One man ran into the tunnel and rescued the fallen man, but he also collapsed when safely within reach of others. These three were rushed to the hospital, where I attended them.

Within thirty minutes two more men were brought to the hospital. One had entered the tunnel with an air hose to blow the tunnel clean and in a few minutes he collapsed. Another witness rushed in and placed the victim on a belt conveyor and both were brought to safety.

I immediately diagnosed the cases as carbon monoxide poisoning and put all to bed with high elevation of the foot of the bed, external heat, and pure oxygen inhalation. Three required caffeine sodiobenzoate and two, atropine sulphate for cardiac and respiratory stimulation.

Two of the men were profoundly comatose and required artificial respiration, as their voluntary respirations varied from three to five per minute. Their pulses were weak, rapid and irregular. Their color varied; the younger man, about 28 years of age and robust, was flushed pink from head to foot; the other, a man of 55 who had dissipated heavily, was cyanotic and in convulsions.

An attempt was made immediately to obtain ready prepared methylene blue, 1 per cent, for intravenous injection, but as it was not available, a solution was prepared locally. An hour had elapsed when the solution was ready and as the two severely affected patients appeared unimproved, they were both given 50 cc. of the solution. Before the injection was completed, they became conscious and talked rationally. Both made rapid, uneventful recoveries and, while more cautiously handled, seemed to have recuperated sooner than the three remaining patients.

The remaining cases responded promptly to the oxygen and the dye was not used. One of these patients later had the stormiest recovery of the lot and is the only one remaining under my care at this time, having a local systolic murmur over the heart apex, which may or may not be organic.

It would appear that the methylene blue had a remarkably specific action in these cases of carbon monoxide poisoning.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.

PAUL NICHOLAS LEECH, Secretary.

NAÏODINE NOT ACCEPTABLE FOR N. N. R.

"Naïodine" is a product of the Emile Logeais Laboratories of Boulogne sur Seine, France, distributed in the United States by E. Fougera and Company. It is proposed for subcutaneous intramuscular or intravenous injection for the relief of pain from whatever cause.

The advertising material for Naïodine, widely promoted to the medical profession, is pernicious. Rarely today can one read claims of therapeutic usefulness more imaginative in conception or less supported by fact.

Naïodine is claimed to be a "one per cent solution of hyperactive sodium iodide (NaI) . . . stabilized by a special process, exclusive of any other active principle, toxic or otherwise."

There is no chemical method known to the Council whereby a simple, highly ionizable salt like sodium iodide can be rendered "hyperactive," whatever that may mean. The implication in the advertising circulars that this iodide preparation is of a special order of therapeutic effectiveness is highly improbable. It is well known that the addition of small amounts of alkali, preservation in hard glass, and protection from light may tend to prevent the decomposition of iodide solutions.

The following are some of the claims made for this preparation:

"NAÏODINE is indicated for the relief of pain, and distress, *whatever the organ affected, whatever the site of pain, and whatever the nature of the pain or distress present, whether it be due to neuralgia, neuritis, spasm, inflammation, sympathetic pain, anguish or anxiety* [Italics ours].

"NAÏODINE is as powerfully effective against the anguish accompanying the withdrawal treatment in cases of toxicomania as it is against the so called 'essential' sciatica, the crises of asthma, sinusalgia, the tarsalgia affecting adolescents, uterine or ovarian pain in dysmenorrheal patients, pain present in advanced cancer, myalgia, rheumatic or rheumatoid pain and the like.

"In brief, NAÏODINE constitutes a type of sedative preparation, a faithful antispasmodic, and an antalgic. It may be added that the injection of NAÏODINE is painless."

"The sodium iodide present in NAÏODINE, when introduced parenterally, possesses a veritable neuronotropic effect. When absorbed by the capillaries, it progressively impregnates the nerve centers, somewhat as bromides impregnate them, diminishes and suppresses promptly their sensitiveness to pain . . . large doses must be employed from the very first, and must be repeated without hesitation. There is no reason whatever for hesitating, since Naïodine is atoxic and since it produces no modification whatever of the respiratory or circulatory centers . . ."

"Injectable NAÏODINE permits atoxic treatment of all algic states. *It replaces morphin and other analgesics, all of which are toxic . . . Naïodine is Atoxic and Painless.* Any dosage may be injected, without the least difficulty. It has no contra-indications."

"Use and dosage: The Treatment of Attack, by massive doses: 20 to 30 cc. daily, given in one or several injections. Maintaining Treatment, with diminishing dosage: 10 to 5 cc. daily." "Injections . . . in any muscular mass, deep subcutaneous, or intravenous."

Naïodine is further recommended for "sciaticas, lumbagos, shingles, trigeminal neuralgias, syphilitic and rheumatismal iritis . . . dyspnea, angina pectoris, asthma, pulmonary emphysema, toxicomanias . . . phlegmons, burns, acute arthritis, painful chronic arthritis, acute otitis, etc."

A brochure also is distributed, composed about a photograph of a woman's head in marble reproduction; at the bottom appears "Naïodine—cure atoxique"; in one margin, "ne plus souffrir," repeated several times in type of diminishing size.

Naïodine is claimed to be absolutely atoxic; nowhere is there mention of the possibility of iodism, of anaphylactoid reactions from intravenous injection, or of the possibility of inducing serious or even fatal pulmonary edema in susceptible individuals, particularly in the pathologic pulmonary conditions for which Naïodine is recommended. The routine use of injections of sodium iodide to replace "morphine and other analgesics" as