CORING: THE UNSEEN MENACE*

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CORING is a problem which is met by the average physician in his practice. However, it is relatively unrecognized and only occasionally discussed by the pharmaceutical industry.¹⁻¹¹ Coring is the mechanism by which particles of material are cut away from a pharmaceutical closure or plug upon the insertion of a hollow needle. A core is the actual particle of material cut from the closure material and is usually unseen up in the lumen of the needle. A pharmaceutical closure is any type of plug, usually a combination of elastic material and aluminum, which prevents contamination of a drug contained in a vessel.

Advancing the needle through the stopper, plug, or closure also often abrades the closure material, producing fragmentation and the formation of small, irregular, loose particles which rest upon the top of the closure¹⁰ ready to be pushed into the interior of the vessel and into the solution when the next needle is inserted.

Whenever a hollow needle perforates a pliable membrane such as skin or rubber, coring and fragmentation will probably occur. The production of cores and fragments depends upon two sets of factors, one pertaining to the closure or stopper, the other to the needle. The larger the percentage of inorganic filler in the stopper, the more often will cores and fragments be produced.²

Most stoppers in drug bottles in Canada are manufactured by the West Company of Phoenixville, Pennsylvania, U.S.A. This company has been completely unco-operative in this study and has refused answers to repeated questions over a two-year period.¹² However, on good authority, I am told that the red stopper in xylocaine bottles is about 50 per cent silica by weight, a composition not considered unusual in the pharmaceutical industry.¹³ At the factory the compression of the rim of the rubber-like stopper by the design of the sealing head on the capping apparatus can cause a variation in the percentage of core production.^{1,2} The amount of compression on the rim of the stopper or plug creates forces acting towards the center of the stopper which is unconfined. This causes the stopper to be more compressed in the center and to bulge outwards easily into the bore of a hollow needle.

The principal factors related to the needle are the bore of the needle and the sharpness of the heel.^{1,2} The heel of the needle is that part which is directly opposite the needle point. It has a sharp knife edge, the sides of which slope inward towards the centre of the heel. Thus the sloping sides of the circumference of the needle tip will, upon insertion of the needle, tend to enfold the stopper material, gathering it into the lumen, compressing the material into the bore,

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FIGURE 1 (30X). A1: The superior surface of the plug closure. Uneven surface of plug resulting from bonding of plug to aluminum cap. A2, A3: Uneven surface resulting from bonding after being perforated by a needle.

and making it more rigid and easily cut by the knife edge of the needle heel. As the needle advances into the stopper the cut produced by the point of the needle elongates into an arc and forms a hinged flap, a trap door of stopper material.

The forces created by the compression of the stopper material pushes this flap into the only space available: the lumen of the needle. Depending upon the sharpness of the heel of the needle and the rigidity of the closure, the heel may gouge out that portion of the closure which protrudes into the lumen, thus producing a core. As the needle advances through the stopper, the stopper is distorted, and depending upon its elasticity it produces fragments which break from the surface and the area around the needle. These fragments either are shoved into the drug solution, stick to the side of the needle, or remain on the top of the closure to be pushed through on the next perforation. Generally, the larger the lumen of the needle, the greater the percentage of inorganic filler in the stopper; and the longer and hotter the sterilization process, the greater will be the production of cores and fragments.

To refer to the plug in a pharmaceutical container as "rubber" is erroneous. Some of them contain everything but rubber. Many contain only fifty per cent of latex by weight.¹⁸ The other fifty per cent is mostly a silica clay and compounds which are used in processing the plug such as sulphur, titanium dioxide, barium sulphate, zinc oxide, iron oxide, thiazole, and thiuram type accelerators.

The manufacturer refuses to make the percentage composition of the

FIGURE 2 (30X). B1: The superior surface of the plug closure, showing needle cut, loose flap of plug material, and cavity in plug which has formed a core. The cavity shows a compression bar in its centre. B2: Needle cut and flap of closure material which has not formed a core. B3: Needle cut and core cavity with two compression bars. B4: Flap of closure material with a small amount missing and the end of a paper clip which has been inserted in the needle cut in the closure plug.

pharmaceutical closures known to the medical profession. The doctors who accept responsibility for use of these products are denied knowledge of their constituents. In my opinion this is serious, in view of the fact that the physician may be injecting into the patient a drug contaminated with the soluble products used in processing the plug, with cores or fragments of the stopper material, or with an epoxy-type lacquer used to coat the aluminum cap.

There have been a few articles written on this subject in the past, mostly by the pharmaceutical companies. The article most readily available, because it is supplied by the West Company to the pharmaceutical companies, is entitled "Factors Influencing the Coring of Rubber Closures," by J. H. Hopkins, a research chemist employed by the West Company.² It describes what seems to be a complicated experiment, but I disagree with the method of determining the coring percentages. Page 5 of the article states, "Water was injected through the needle after each puncture. Cores were counted by viewing the bottle under light against a background of contrasting white or black color." On page 7 the author states, "This presently accepted method of counting cores does not take into account those which lodge in the needle, are trapped in the stopper-slit

FIGURE 3 (30X). All four photographs are of the inferior surface of the plug after it has been pierced by a 16-gauge needle. C1: A core of plug material cut from the superior surface of the plug, now caught between the cut edges on the inferior surface. C2: Irregularity and fragmentation of an inferior surface after perforation with a needle. C3: Needle cut on inferior surface, and cavity which apparently was not part of the original form of the plug. C4: A core of plug material which, cut free from the superior surface, was carried down and became caught between the cut edges on the inferior surface.

upon withdrawal of the needle, or are deposited upon the top of the closure after withdrawal." The author also states that "the conclusions reached using the above method of counting cores are unsound"; that coring can be estimated more accurately "if the tops of the closures are examined under low magnification and the actual chips cut out of the rubber are counted." He further states, "It was discovered during the course of the study that a microscopic examination (at 30 X magnification) of the surface of the stopper after coring gave a quicker and clearer indication of the relative coring rate of needle-closure combinations." The author is cognizant of both methods, and he states that one method is better, yet the experiment and the published results are based on an inaccurate method which gives lower readings.

Without the sophisticated equipment of a large industrial organization, the following simple examinations were performed. The obstetrical nurses saved 261 20 c.c., 2 per cent xylocaine bottles after they had been emptied by the anaesthetist performing an epidural injection. In all cases the contents had been

FIGURE 4. Various metallic particles. D1, D3, D4, D5: Metallic particles at 30 $\times$ magnification. D6: A metallic particle at 60 $\times$ magnification. D2 (30 $\times$): The gouge in the inferior surface of the aluminum cap formed by lifting the aluminum cap with a needle point. Encircled is a sliver of aluminum having the characteristics of D6 and attached only at one end.

removed by means of a needle which pierced the "rubber" plugs. Using a bottle opener, the aluminum and rubber closures were removed from the bottles. Each bottle was then filled two-thirds full with warm water. The water was agitated in the bottle and poured into a filter which had been previously examined microscopically. The water was allowed to filter and settle through a very small area on the filter paper. The unfilterable particles remained concentrated on the small area. Sample areas of the filter paper were then removed, examined microscopically at thirty power, and photographed. From the dregs of the xylocaine solution remaining in the bottle five types of particles were obtained: large, red, rubber-like particles, small, red, rubber-like particles, large and small metallic particles, and black particles. Both the superior and inferior surfaces of the red closures of the xylocaine bottles were then examined and photographed. It was decided that to count and classify the different particles would not be useful because one closure could give rise to one or more particles, and the method used would not determine the total number of particles or their exact origin. Nor was there an advantage in counting them, as it is sufficient to prove that this method of obtaining drugs from a bottle will cause particles of aluminum and rubber to contaminate the solution and the lumen of the needle before injection into the patient.

The large rubber particles had all the characteristics of cores: they had a

FIGURE 5 (30 $\times$). Various phases of core formation as seen on the superior surface of the plug closure after perforation with a sixteen gauge straight needle. E1: Needle cut and cavity with two compression bars after core formation. E2: Needle cut and two cavities (which have produced two cores) separated by a compression bar. E3: Needle cut and a flap of closure material which has produced two small cores. E4: End of a paper clip in the needle cut and a flap of plug material. E5: Cut formed by the needle point and a flap of plug material. E6: Cut made by the needle, with a cavity showing two compression bars.

roughly triangular outline with two smooth sharp edges resulting from the cutting action of the needle. A third rough edge was formerly the hinge on the "trap door" that had been partly sheared and torn by the heel of the needle. There was a flat surface which formerly was part of the flat superior surface of the closure, and a convex surface which was formed by the enfolding and cutting action of the needle heel.

The smaller red, rubber-like particles come from two sources. The first was the shredding and abrasive action of the needle. As the needle perforates the closure it pushes the central area of the closure inward into the bottle. This causes distortion and inward flexion of the closure. If the closure material is not flexible enough to withstand this degree of bending, cracks appear in the flexed superior surface of the closure. These cracks and deformities of the superior surface create an irregular surface which rests upon and encircles the shaft of the needle whose abrasive action easily breaks off particles from the area of the closure around the needle.

A second source of fine rubber particles is the apparently oxidized surface of the rubber closures. Occasionally during the investigation rubber closures were

FIGURE 6 (60X). F1: Typical core on a background of millimetre lines. The flat superior surface of this core was formerly the flat superior surface of the plug closure of a drug bottle. F2: The same core after it has been shoved down into view. F3: A loose particle of the plug material which has become attached to the shaft of the needle. These loose particles may be found on plugs which have been perforated often as in multidose bottles. F4: A loose plug of closure material about to be taken into the lumen of a needle as it descends through the plug.

found on which the surface was very uneven and had a whitish colour. This corresponded to that area of the superior surface of the closure which is covered by the removable metal cap. This area was covered with cavities, projections, and irregularities. These defects extended only a short distance into the body of the closure material. In some way, probably owing to the sterilization process, the superior surface of the closure had become bonded to the metal cap; then, when the metal cap was removed forcibly, the superior surface of the closure was torn. This mechanism is probably assisted by an epoxy lacquer which is coated on the aluminum alloy during the manufacturing process. The cap is

FIGURE 7 (60X). G1: Flat superior surface of core which was formerly the flat superior surface of the plug closure. Background is a millimetre rule. G2: The smooth convex inferior surface of the core cut from the plug material by the heel of the needle. Using a stilette this core was shoved into view from higher up in the lumen of a 16-gauge needle. Visible in this view is the smooth inferior surface of the core that has been cut by the knife edge of the heel of the needle tip.

stamped and die cut from sheets of lacquered aluminum.¹⁴ Unfortunately the manufacturer has not supplied any explanation for this observed phenomenon.

When this highly irregular surface is pierced by a needle there can be no doubt that it is an excellent source of small particles which can easily pass through a standard needle and be injected into the patient.

Next, at a magnification of thirty times, the superior and inferior surfaces of the plugs were examined and photographed. Of the 261 consecutive plugs examined, 10 were found unsuitable, so 251 were tabulated. Of these, 77 or 30.8 per cent showed cavitation on the superior surface. Forty nine, or 15 per cent, showed a combination of cavitation and abrasion. There was cavitation which indicated core formation in 49 per cent of the superior surfaces of the plugs examined. Of the 251 plugs examined, 150, or 60 per cent, showed abrasions of the surface in the area of needle penetration. A total of 75 per cent of the superior surfaces showed abrasion. It is interesting to note that of the 251 plugs examined only 2 showed a cavity on the inferior surface. However, 42 of the inferior surfaces, or 16 per cent, showed fragmentation. Eighty-two per cent of the inferior surfaces showed clean cuts from the needle point with no visible abrasion.

It was most disconcerting to find metallic and black particles of various sizes in the dregs of the xylocaine bottles after they were used. Having no knowledge of the manufacturing processes, I have looked for the source of these particles at our hospital and in our techniques. After washing many needles I have concluded that the black specks were formerly skin cores or clotted blood which remained in the lumen of the needle after previous epidural injections. These

FIGURE 8. H1 (30 $\times$): Gouge made in the inferior surface of the aluminum cap by a needle point used to lift the cap. Also seen is a sliver of aluminum attached at one end, having the characteristics of metallic particle in H4. H2, H3 (30 $\times$): Metallic particles. H4 (60 $\times$): Typical characteristics of metallic particles found in the dregs of drug bottles after they were used.

particles then became burnt to carbon by the heat of the steam sterilization processes at the hospital. The particles would not necessarily be dislodged during the cleaning of the needles after use, as the stilettes used are usually smaller than the lumen of the needle.

The source of the metallic particles may be due to bad designing of the bottle cap,⁴ and to anaesthetists who attempt to maintain a scrupulously sterile technique. At our hospital, in order to maintain the best sterile technique, the xylocaine solution is sterilized in the tray with the syringes and needles. The tray is generally not opened until the anaesthetist has donned his sterile gloves. After preparing the skin of the patient, the anaesthetist picks up the capped bottle of xylocaine solution. Now comes the dilemma. To obtain the xylocaine, the anaesthetist must lift a thin aluminum tab off the top of the bottle. In order to raise this tab with his fingers, he must exert pressure against the thin, jagged, sharp, irregular edge of the tab, and while doing this there is danger of tearing the sterile glove. Not wishing to jeopardize his sterility, the physician seeks a small strong, thin-tipped instrument to put under this tab to pry it up so that he may grasp it without the danger of tearing the glove. The closest instrument at hand that can be quickly used as a pry is one of the needles attached to a

syringe giving a good hand grasp. The point of the needle is slipped under the aluminum tab which is quickly flicked up, grasped with the thumb and forefinger, and is then easily removed and discarded. The same needle, still on the 20 c.c. syringe and in hand, is plunged through the rubber-like plug and the contents of the bottle are drawn into the syringe. Easy, quick, and simple; however, 25 of these soft aluminum tabs were examined under a microscope, and all had been scratched by the hard steel needle. Under the microscope the scratch is seen for what it really is, a gouge in the metal with ragged metal particles at the side of the trough in the soft aluminum. Of the 25 16-gauge needle tips examined, 15 contained fine metallic particles. It is quite possible that these particles are washed from the lumen of the needle into the solution as the syringe is filled.

Whenever a hollow needle pierces a semi-rigid material, coring is liable to occur.^{15,16} Skin is a semi-rigid material and when it is pierced with a hollow needle, coring does occur. When a physician makes an injection, the problem of coring is presented on two separate occasions. The first is when he uses a needle to penetrate the closure in order to obtain medication. The second appears when he pierces the skin of the patient to make an injection.

To demonstrate coring when a needle pierces skin, the following punctures were made after the skin had been infiltrated with local anaesthetic prior to an epidural injection. Using an ordinary 18-gauge needle with a pointed end, 71 skin punctures were made. Of these, 61, or 85 per cent, produced skin cores. The cores produced by the 18-gauge needles were characteristic. They were usually a full thickness piece of skin which filled the lumen of the needle. They are not easily seen at first because they have slid up into the interior of the needle, but they are readily demonstrated if a stilette is shoved through the needle to the tip.

Sixty skin punctures were made with a number seventeen Tuohy side-opening needle from which the stilette had been removed. In this series of 60 skin punctures, cores were produced in 45, or 75 per cent. The cores produced by these needles were much smaller, some were full thickness, most were crescent-shaped, and most had slid up into the lumen of the needle above the heel.

The final series of punctures was made with a Tuohy side-opening needle with its stilette in place. In this series of 62 punctures, 54, or 87 per cent, produced smaller cores. However, in this case the size of the core varied according to the fit of the stilette. It was noted that a poorly fitted stilette could produce a large core but still not as large as those produced when there was no stilette filling the opening. A well-fitting stilette, if it produced a core, would produce small particles of skin that usually caught between the heel of the needle and the stilette.

There have been a few articles in the literature on the coring of skin by needles. Dr. Crawford Little¹⁵ states that with a standard, end-opening, 18-gauge needle used to produce pneumoperitoneum, 25 to 50 per cent of the needles used were found to contain a small fragment of skin in the end opening. He did not use any magnification to examine the needle tips. He concluded, "that when open

ended eighteen-gauge needles are used, portions of superficial skin were frequently being carried into the body cavities."

In an article entitled "Skin Fragments Removed by Injection Needles," Gibson and Norris¹⁶ have recorded the following observations, made without the aid of magnification. "No real difference was noted between new and resharpened needles. Although the incidence with different sizes of needles showed no wide variations, the size of the skin fragment was proportional to the size of the lumen." "We found no method of sharpening an open-ended needle which would reliably avoid the excision of skin fragments." "The fate of these (fragments) is of particular interest; they are in effect small skin grafts, and there seems no reason why they should not survive and grow provided they come into the apposition with a suitable bed." "Many thousands of injections have been given every day for many years, and the fact that no harmful effects have been previously attributed to skin emboli suggests that little is to be feared from that source." "The risk of infection subcutaneous, intramuscular, or pulmonary, seems to be real and calls for care in skin preparation before injection." "In a series of three hundred [coring] tests with a wide range of needles the overall [coring] frequency was 69 per cent."

The problem of coring is of particular importance now, with the growing popularity of epidural injections. The epidural space is bounded by a bony canal and has the soft spinal cord and filum terminale in its centre. If foreign bodies such as cores of skin or plugs are deposited in the epidural space there is a possibility of abscess and scar tissue formation. There is even the possibility of skin cores acting like full thickness skin grafts and if deposited on a suitable bed, forming dermoid cysts.¹⁷ Fortunately most epidural injections are deposited in the area of the cauda equina which can stand compression much better than the spinal cord. There are no readily available statistics comparing the incidence of back pain and epidural injections. There are many articles on acquired extradural cysts but they are unavailable in Toronto. A bibliography may be found at the end of an article, "Spinal Extradural Cysts," by Rosenblum and Derow, printed in December 1963.¹⁸

After becoming acquainted with this work, the Astra Pharmaceutical Company has changed its method of closure on bottles of xylocaine for epidural injections. It is now relatively easy to remove the plug and there is no need to pierce it with a needle.

CONCLUSIONS BASED ON TESTS WITH 16- AND 17-GAUGE NEEDLES

1. To eliminate the possibility of injecting a core of skin into the epidural space, the physician should make the actual injection with a needle other, and smaller, than the one used to pierce the skin.

2. To eliminate the possibility of injecting a core of "rubber" into the epidural space, the local anaesthetic drug should not be obtained by piercing a pliable membrane.

3. No drug that has been obtained by piercing a pliable membrane should be injected into a patient.

4. Multi-dose vials should not be used by the medical profession.

RÉSUMÉ

Il est un problème auquel la plupart des médecins ont à faire face mais dont ils méconnaissent généralement l'importance. C'est le mécanisme par lequel des parcelles de matériel sont enlevées d'un bouchon lorsqu'on le perce à l'aide d'une aiguille creuse. Ces parcelles sectionnées du bouchon sont généralement invisibles dans la lumière de l'aiguille.

En poussant une aiguille à travers le bouchon d'une fiole, on écorche souvent le matériel de ce bouchon, ce qui produit des fragments et de petites parcelles libres et irrégulières; ces dernières peuvent être poussées dans la bouteille ou dans un vaisseau à l'occasion d'une ponction subséquente. Dès qu'une aiguille creuse perce une membrane flexible telle que la peau ou du caoutchouc, le phénomène se reproduit probablement.

C'est une erreur de croire que le bouchon d'un contenant pharmaceutique est un bouchon de caoutchouc. Quelques uns ne contiennent pas de caoutchouc du tout. Plusieurs sont fabriqués de 50 pour cent de latex, le reste étant surtout de l'argile de silice et des composés utilisés dans la fabrication du bouchon tels que du soufre, du bioxyde de titane, du sulfate de barium, de l'oxyde de zinc, de l'oxyde de fer, etc. Le médecin peut injecter au malade un médicament contaminé par les produits solubles utilisés dans la fabrication du bouchon, ou par des fragments de matériel ou de vernis utilisés pour enduire le capuchon d'aluminium. L'auteur a examiné 261 bouteilles de xylocaïne de 20 c.c. après leur usage par un anesthésiste pratiquant des injections épidurales; au cours de ces injections les bouchons avaient été percés par une aiguille.

Après avoir soigneusement enlevé les fermetures d'aluminium et de caoutchouc à l'aide d'un ouvre bouteille, chaque fiole a été remplie aux deux tiers d'eau chaude; après l'avoir agitée, cette eau a été passée à travers un filtre préalablement examiné au microscope. Après la filtration, des échantillons du papier filtre ont été examinés au microscope (grossissement 30) et photographiés. On a observé cinq types de parcelles: de grosses parcelles ressemblant au caoutchouc, de petites parcelles ressemblant au caoutchouc, de grandes et de petites parcelles métalliques et des parcelles noires. Les surfaces des fermetures rouges des bouteilles de xylocaïne furent alors examinées et photographiées.

Les grosses parcelles de caoutchouc avaient l'apparence de pièces sectionnées. Les surfaces des bouchons présentaient les défauts caractéristiques de sections par ponctions d'aiguilles. Les petites parcelles de caoutchouc semblaient dues à l'oxydation de la surface des bouchons de caoutchouc.

Parmi les bouchons examinés, 40 pour cent montraient des cavités dues à une perte de substance alors que 60 pour cent montraient des écorchures de la surface dans la zone de pénétration de l'aiguille.

Les parcelles métalliques semblaient le résultat d'écorchures du capuchon d'aluminium par une aiguille, laquelle était ensuite utilisée pour aspirer la solution de la bouteille.

Les parcelles noires trouvées après lavage de plusieurs aiguilles sont considérées comme des morceaux de peau ou de sang coagulé qui demeurent dans la lumière de l'aiguille malgré le nettoyage et l'insertion de mandrins, et qui sont ensuite brûlés par la stérilisation à la vapeur.

La ponction de la peau à l'aide d'une aiguille creuse enlève un morceau de peau,

et ce dans 85 pour cent des cas, si on utilise une aiguille dix-huit. Ces morceaux sont généralement assez gros pour remplir la lumière de l'aiguille, et ils ne sont pas faciles à voir. Sur 60 ponctions de peu pratiquées à l'aide d'une aiguille Tuohy sans mandrin, 45 ont sectionné des morceaux de peau qui ont été retrouvés dans la lumière de l'aiguille. Une ponction de la peau à l'aide d'une aiguille Tuohy munie de son mandrin a enlevé de plus petits morceaux dans 87 pour cent des cas; ces parcelles varient dans leur grosseur selon la qualité du mandrin. Il est vraisemblable que l'introduction de ces parcelles de peau soit l'équivalent de l'introduction d'une petite greffe, et il n'est pas impossible que ces petites greffes de peau s'implantent en un milieu favorable pour produire subséquemment un kyste épidermoïde. Ceci peut être particulièrement important en anesthésie épidurale.

Conclusions

(1) Pour éliminer la possibilité d'injecter une parcelle de peau dans l'espace épidural, le médecin devrait injecter son médicament au moyen d'une aiguille autre que celle qui a servi à percer la peau; l'aiguille pour la peau devrait être plus grosse que l'aiguille d'injection. (2) Pour obvier au danger d'injecter une parcelle de caoutchouc dans l'espace épidural, l'anesthésique local ne devrait pas être prélevé en perforant une membrane flexible. (3) On ne devrait injecter à un malade aucun médicament obtenu en perforant une membrane flexible. (4) La profession médicale ne devrait pas utiliser des fioles à doses multiples.

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