EMERGENCIES IN GENERAL PRACTICE

ACCIDENTS WITH INJECTIONS

BY

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Treatment involving injections is universally employed in all forms of practice and in most specialties. The drugs given in this way are legion, and the number of injections given every year reaches astronomical figures. Indeed, there can be few patients who escape injections for therapeutic or diagnostic purposes; many require numerous injections or courses of such treatment. In spite of the vast numbers involved, reports of accidents are relatively rare, but occasionally the consequences may be grave, and so it seems permissible to discuss the various hazards and to cite examples of reported disasters; to be aware of the possibility of a particular accident is the first step to its avoidance.

Infection

Mild inflammations and infections following inoculation or various types of injections are reported to be not uncommon; abscesses and severe infections sometimes occur and may occasionally prove fatal. Accidents following injection are especially serious when they occur in the course of mass inoculations or in hospital practice. Infection may have its source in the apparatus used or in the solution injected, or it may be introduced by a breach in aseptic technique during the process of injection. The risk of overt infection varies considerably with the type of injection. Obvious infection following intravenous injection is rarely encountered, but cellulitis or abscess formation may occur after hypodermic or intramuscular administration; and the subarachnoid space is extremely susceptible, the gravest results following infection introduced by intrathecal injection. Though serious infections after injections are comparatively rare, that is no excuse for lowering the standard of aseptic precautions before any injection is given. In this connexion the opinion is often expressed fallaciously that a particular method of sterilization (which in the light of present knowledge is inadequate) must be "safe" because no infections have been seen in the practitioner's experience covering a number of years. In the case of syringe-transmitted cross-infective jaundice following intravenous injection, the incubation period is likely to be so long that the disease is unlikely to be recognized as a sequel of the injection. In the practice of self-medication by patients (for example, insulin for the diabetic, adrenaline for the asthmatic) careful education is necessary to reduce the risk of infection.

Sterilization of Syringes and Needles

The M.R.C. memorandum (*Medical Research Council War Memorandum No. 15: "The Sterilization, Use, and Care of Syringes,"* London, H.M.S.O., 1953) on this subject points out that spirit is used more than any other chemical disinfectant for sterilizing syringes; after careful deliberation the committee which prepared the memorandum decided that this practice cannot be recommended except with reservations which largely deprive it of its convenience. Chemical disinfection is likely to be particularly inefficient if syringes have not been thoroughly cleaned, and so contain traces of blood, serum, or other protein material. These conditions are especially likely to occur when syringes are used for intravenous injection—syringes used for aspiration must be kept separate from injection apparatus.

The memorandum states that the only chemical disinfectant that can in any way be recommended for syringe disinfection is 70–75% v/v alcohol: immersion in it of the separated parts of all-glass syringes for at least five minutes

will destroy vegetative bacteria but not spores. This method is not certain when used for glass-metal syringes. The report later points out that spirit in surgical use may undoubtedly be contaminated with spores of pathogenic bacteria.

The only recommended method of sterilization involves the use of heat, the assembled and wrapped syringes and needles being placed in the hot-air sterilizer and maintained at 160°C. for not less than one hour. If syringes and needles are sterilized by autoclaving, a temperature of 120°C. (at a pressure of 15 to 20 lb. per sq. in.—1 to 1.4 kg. per sq. cm.) must be maintained for 20 minutes. If an autoclave or hot-air oven is not available, or if glass-metal syringes are to be used, "sterilization" by boiling for not less than five minutes in water is the method of choice, although this cannot be relied on to destroy all spores. Careful cleaning to remove all protein material is necessary before sterilization is undertaken.

Dry-heat sterilization can be performed only on syringes designed to withstand the high temperature involved—for example, the ordinary glass-metal types are unsuitable. The organization of heat sterilization of all syringes and needles may involve difficulties in certain types of practice; also larger numbers of syringes are required to provide such a service. It must be taken as proved, however, that no other method gives acceptable efficacy.

The Injection Solution

"Killed" vaccines have on occasion proved to contain living organisms. Accidents of this type have occurred with the Salk poliomyelitis vaccine and other prophylactics. Contamination of injection solutions is readily possible; one of the best-known accidents was the Bundaberg disaster, in which diphtheria prophylactic was contaminated with a pathogenic staphylococcus.

Practitioners must rely on manufacturers and dispensaries for the sterility of injection solutions supplied. Fortunately high standards are usually maintained, so that accidents of this type are rare. If multi-dose containers (rubber-capped bottles) are used, however, bacterial contamination may occur after issue, especially if high standards of syringe sterilization are not practised. As many solutions provide a rich pabulum for bacteria, and the "shelf-life" of the multi-dose bottle may be long, gross infection is possible. For this reason solutions should contain an antiseptic preservative to prevent bacterial growth. But the incorporation of such a bacteriostatic cannot be relied upon as a 100% safeguard, and storage at low temperature is advisable. It is far safer to provide individual ampoules for each dose of a drug, and multi-dose containers should be discouraged. The use of drugs dispensed from such containers cannot be accepted at any stage in the administration of a spinal anaesthetic—for this all equipment, drugs, etc., should be autoclaved together in one pack.

Aseptic Technique

Contamination of syringes and needles may occur after sterilization by contact with fingers, etc., or from droplet infection. Clean dry hands and the use of sterile forceps for assembly should abolish these risks. So-called "sterile" water is often supplied for rinsing syringes before injections. This fluid has often proved to be contaminated, and therefore this step should be avoided if possible. Sterile water or saline can be accepted as such only if dispensed from an ampoule or other sealed container freshly opened

for the occasion. The risk of infection of this type is very serious when intrathecal injections are involved.

The chance of infection is increased if syringes are served up wet in a dish or bowl containing saline or other liquid. This procedure can be avoided if the methods of sterilization advised above are adopted.

To cleanse the skin before injection the selected site should be rubbed with a small quantity of spirit or tincture of iodine on a swab, the area then being allowed to dry. Injections should not be made into or through an infected area.

When intrathecal injections are planned full surgical asepsis is essential. The operator scrubs up and is masked, gowned, and gloved as for surgery. Careful skin cleaning is performed and the area is surrounded by sterile towels. All drugs and equipment, as already noted, must be heat-sterilized.

Broken Needle

This accident is especially likely to occur when deep injections are being made—for example, intramuscular or intrathecal. Careful preparations may reduce risk of this unfortunate incident (which has often been the grounds for litigation). Evidence of suitable care in this respect should provide satisfactory defence in case of accident. Before any injection the point of the needle should be examined and its patency checked. When any viscous solution is injected a needle of adequate calibre should be used: the risk of breakage is increased if fine needles are used for deep injections (by means of a special introducer very fine needles may be used for intrathecal injections, thus reducing the incidence of "spinal headache"). The needle should be carefully examined for flaws, cracks, or bends along its length, and discarded if not satisfactory in this respect. The usual site of breakage is at the junction of the needle with its hub; for this reason a needle of adequate length should always be chosen, so that insertion to the depth of the hub is never necessary. Should breakage occur at the junction the situation is easily retrieved if a portion of needle is left above the surface. In addition to the danger resulting from defective needles, breakage may occur as a result of sudden and uncontrolled movement on the part of the patient; therefore he should be placed in a comfortable position and usually warned of the moment of insertion. In restless individuals an assistant should be present to provide any restraint necessary to avoid needle breakage.

Should a needle break during injection it should be removed at once if it is easy to do so—for example, when a portion remains above the skin surface, or when the fragment is just subcutaneous and easily secured. An extensive search for deeply lying fragments should not be carried out under unsatisfactory conditions. Full surgical facilities, x-ray localization, etc., will often be necessary, and even with these aids removal of a portion of needle deeply placed may be very difficult. If the patient sustains damage as a result of injudicious searching, he may be successful in a legal action against the doctor.

Errors in the Solution Used

The Wrong Solution

Confusion is all too easy: iodated oil for bronchography has been confused with intravenous pyelography media, cocaine has been injected in mistake for procaine (the assonance being responsible for mistaken verbal instructions), local analgesic solutions have been confused with 1 in 1,000 adrenaline solutions or have contained excessive adrenaline—such and similar errors have been responsible for many deaths.

Some drugs exist in solution in widely differing strengths, the stronger being intended for topical application and the weaker for injection—for example, various local analgesic and certain cholinergic drugs. Dispensing errors are fortunately rare, but on the metric system decimal-point errors have occurred, resulting in tenfold dosage with, for example, atropine; similarly, confusion of the "drachms" for the "ounces" sign in prescriptions has led to overdosage of paraldehyde with fatal results.

Drugs differing widely in action are of necessity dispensed in ampoules which are not greatly dissimilar. The danger is increased if such ampoules are stored mixed in a common container. There are limits to the differences in colour, labelling, shape, and size of ampoules which can be used to assist discrimination. Expert opinion is that no useful purpose can be served by the colouring of injection solutions. However, fluids for skin preparation, which are usually highly dangerous if injected in error, should always be coloured and should also be served in a distinctive container or gallipot on an injection trolley. Similar precautions are necessary with local analgesic solutions for topical application. The subject of injection routine is well discussed and many useful suggestions made in a recent report.* Accidents due to use of the wrong drug are not confined to injections made with a needle: on one occasion a solution of thiopentone for rectal injection was prepared with spirit instead of water, the result being fatal. Another fatal accident resulted when a cleansing powder was used in error to prepare "a barium enema."

From these considerations it follows that dispensing of drugs should always be requested on a *written* order. The ampoule or other container must be directly checked before the injection by the person giving it. The label should be carefully read to check both identity and dosage. There is no substitute for this precaution, and the responsibility is directly that of the individual performing the injection.

Contamination of Solution

Bacteriological contamination has already been considered. Chemical contamination can also occur and has been considered responsible for several disasters after the injection of spinal anaesthetics.

The possibility of traces of antiseptics from syringes gaining entry to multi-dose containers is obvious. Certain labile drugs may thus be rendered ineffectual and irritant, or necrotic effects may follow the injection of solutions containing substantial amounts of antiseptic or disinfectant agents. If ampoules are soaked in antiseptic solutions to sterilize their surfaces, the antiseptic may penetrate minute and invisible cracks, molecular migration finally resulting in a state of equilibrium, so that high concentrations of the antiseptic agent are attained in the injection solution. It has been accepted in the courts that phenol, or spirit, can in this way gain access to solutions used in spinal anaesthesia and cause permanent neurological damage. Colouring of the antiseptic solution has been suggested, it being implied that absence of colour in the injection solution would be a guarantee of safety. In view of differences in molecular size and other factors this view is not acceptable. Soaking of ampoules in antiseptic solutions must be regarded as an unsafe procedure; apart from the risk of contamination, the labels may be soaked off, resulting in confusion of the identity of various drugs.

Errors in the Site of Injection

Many solutions are irritant and can only be tolerated by the intravenous route. Extravenous injection usually causes pain and is often followed by necrosis. Such accidents are commonly the basis for litigation. Conversely, drugs intended for relatively slow absorption into the blood stream from the tissues may cause dangerous effects if accidentally injected into a blood vessel; oily solutions and suspensions intended for intramuscular injection are particularly harmful in this respect. Before subcutaneous or intramuscular injections are made the aspiration test should always be used to make sure that the needle point is not in a blood vessel. Some drugs intended for intramuscular administration are irritant and not well tolerated by more superficial tissues—for example, chlorpromazine and various "depot" solutions. An area with an adequate mass of recipient muscle should be selected and a needle of ample length must be chosen.

* "Injection Routine in Operating Theatres," Dimond, W. E. R., Pollard, A., and Adamson, A. C., *Lancet*, 1951, 1, 410.

Damage to Nerves

In the course of intramuscular injections in the gluteal region the sciatic nerve has been damaged; such injections should be made as far away as possible from this nerve, and therefore the upper and outer quadrant of the buttock is chosen. It is suggested that the antero-lateral compartment of the mid-thigh is free of the risk of nerve damage, and, furthermore, in the recumbent patient less discomfort results from any "irritant" injection. Damage to certain nerves of the forearm has also followed intravenous anaesthesia with thiopentone, and careful and vigilant technique is necessary when such injections are given.

Accidental Extravenous Injections

As pointed out, the veins are used for the injection of strongly acid or alkaline solutions, or other irritant preparations (including vein-sclerosing agents). The injection or escape of such fluids into perivenous tissues is likely to result in pain or necrosis; serious sloughing may occur if a substantial amount is wrongly injected in this way. Leakage of a noradrenaline infusion has been known to cause extensive skin necrosis. For intravenous injection the arm is placed on a support, hyperextension being avoided, and a vein of suitable size is then chosen—commonly in the antecubital fossa. In view of the possibility of accidents, it is wise to choose a vein as far removed as possible from nerves, arteries, and other vulnerable structures; for this reason the lateral part of the antecubital fossa is preferable (some anaesthetists choose a vein on the back of the hand for thiopentone injections). The region is carefully inspected in a good light and palpated to determine the presence near by of any arteries. A light venous-occlusion tourniquet may then be used to promote filling of the veins and facilitate venepuncture. (If the veins are small and collapsed, the application of warm packs to the whole limb for ten minutes may help to increase the blood flow and induce prominence of the veins.) The needle is then inserted into the vein and the aspiration test used to check its correct position. The tourniquet is released and a small amount (1 to 2 ml.) of the solution is injected. A pause of several seconds is then made before proceeding. During this pause the patient is likely to complain of severe burning pain if a solution such as thiopentone has been accidentally injected into an artery—if the injection is halted at once, dire results are unlikely to follow. During the course of the injection the region of the needle point should be kept constantly in view so that extravenous injection will be at once apparent. The risk of extravenous leakage or displacement of the needle point is increased if a long-bevel needle is used for intravenous work. A short (45°) bevel should be chosen for intravenous injections. The diagram illustrates the increased

risk of leakage and vein penetration with a long-bevel needle (1); it is seen that these risks are reduced when a bevel of 45° is used (2)—this type of point also assists the operator to perceive the penetration of various anatomical planes. Many advocate venepuncture with the needle in the "bevel-down" position (3), which further reduces these dangers, but unless the needle is really sharp the puncture may be more difficult to accomplish.

In intravenous work it is important that a needle of adequate calibre (e.g., No. 15) be used. With a very fine needle the aspiration test may be uncertain, and unperceived penetration of the far wall of the vein can more easily occur during the injection. If only very small veins are available a fine needle may be permissible, but it should not then be too long or bending will occur, making the insertion difficult.

Should extravenous injection of thiopentone occur, immediate infiltration of the area with 10–15 ml. of 1% procaine hydrochloride will neutralize the alkaline solution and promote vasodilatation, thus reducing tissue damage to a minimum. The limb should be rested till signs of inflammation subside and heat applied if there is a marked local reaction.

Thiopentone is usually employed in this country as a 5% aqueous solution. The danger of necrosis is greatly reduced with 2½% solution, and it is advocated that this weaker strength should be used routinely. Hexobarbitone does not appear to have the intense necrotizing effect of thiopentone, and for this reason some prefer it.

Apart from damage to extravenous tissues, venous thrombosis is not an uncommon sequel of thiopentone (and certain other solutions) correctly administered. Fortunately this does not often lead to serious after-effects, but the possibility should discourage the injection of thiopentone into leg veins and supports the use of the 2½% solution.

Accidental Intra-arterial Thiopentone

The injection of thiopentone solutions into an artery in the antecubital fossa is usually followed by gangrene of the hand and fingers, and amputation through the forearm is the almost inevitable sequel. Not only are these results tragic for the patient, but very heavy damages may be awarded against the practitioner responsible for the injection. Despite increasing knowledge of the possibility several examples of this accident continue to be reported annually. The whole subject has been reviewed by Cohen* in a paper which should be consulted by all whose work involves giving this type of injection. It appears that the danger is not confined to thiopentone, similar disasters having followed the injection of iodoxyl, mephenesin, ethanolamine, quinine, and other agents. Arterial thrombosis is the essential pathological lesion, damage to the intima being the precipitating factor. In addition to gangrene of the fingers, a varying degree of ischaemic damage to the muscles and nerves of the forearm has been observed.

Once a substantial quantity of thiopentone solution has been injected into an artery and intimal damage has supervened, it is unlikely that subsequent treatment can do much to mitigate the effects. For this reason every precaution must be taken to eliminate the possibility of injection into an artery. Whenever feasible the antecubital fossa should be avoided as the site for intravenous injection: if veins in the elbow region must be used, then the lateral part should be chosen (accidents have been reported even in this area, however, and also at the wrist). Careful inspection and palpation of the chosen site is made to locate any arteries, it being borne in mind that in over 10% of subjects the course of arteries at the elbow may be abnormal. The course of an aberrant ulnar artery may be very superficial, and such a vessel has been accidentally injected on a number of occasions.

After the "venepuncture" has been accomplished, the tourniquet should be released and a test dose of 2 ml. of thiopentone solution injected, and this followed by a pause: an agonizing, scalding pain gives warning of intra-arterial injection. This warning is not available if the patient is under general anaesthesia, and especial care should be taken under these circumstances not to displace the needle into an artery or to make an incorrect reinsertion.

The gravest results from this accident have followed the use of 5% and 10% thiopentone. It is certain that the danger would be greatly reduced with a 2½% solution, and many feel that this weaker strength should be routinely adopted.

Treatment.—If the needle is still *in situ* when the accident is recognized, 10 ml. of 1 or 2% procaine hydrochloride should be injected at once. Brachial plexus (or stellate ganglion) block is then performed to reduce arterial spasm and improve the circulation in the limb. Full heparinization is instituted to prevent thrombosis so far as possible.

* Cohen, S. M., *Lancet*, 1948, 2, 361.

and this should be maintained for 5 to 7 days. It follows that in view of the danger of haemorrhage the operation should be postponed if possible; and the sympathetic block should not be repeated during anticoagulant therapy. If operation is essential the commencement of heparinization must be delayed for safety. The affected limb should be moderately elevated and wrapped in a sterile towel and cotton-wool, and its colour, pulse, and temperature must be carefully recorded at frequent intervals. General measures and drugs to promote vasodilatation are also advisable. The results of arteriotomy and other surgical treatment are disappointing. Late surgery is hopeless. If gangrene results amputation will be inevitable.

Damage to Blood Vessels

Ecchymoses and haematoma-formation are not uncommon, especially if the needle-point is imperfect. Serious effects are unlikely unless infection occurs. Firm pressure with a swab after withdrawal of the needle should serve to prevent extravasation of blood following intravascular injections. Damage to blood vessels by the needle does not usually have dangerous results, but sympathetic block undertaken during anticoagulant therapy (for example, paravertebral block for femoral thrombosis) has been complicated by serious haemorrhage, leading to the formation of vast haematomata and even ending fatally.

Accidental Intrathecal Injections

Large doses of local analgesic solutions have been accidentally injected into the subarachnoid space during the course of caudal, epidural, or paravertebral block procedures. The aspiration test for cerebrospinal fluid should help to prevent this error, and injection of a small test dose of the solution should not produce the effects of a spinal anaesthetic—for example, motor weakness. Total spinal block is likely to follow this mistake, but correct treatment should prevent a fatal outcome. Respiratory paralysis is combated by artificial respiration, a clear airway being ensured by intubation if necessary. The circulation is supported by the head-down posture and the injection of pressor drugs. If these measures are maintained until the effects of the analgesic wear off (1 to 3 hours, depending on the agent), complete recovery is likely.

With paravertebral injections the precautions outlined do not eliminate the possibility of the solution tracking along the nerve sheath. Spinal cord destruction has thus resulted from paravertebral injection of certain solutions intended to produce prolonged nerve block, and this practice must therefore be condemned. Alcohol injected into the Gasserian ganglion may spread in the subarachnoid space and so involve other cranial nerves; special precautions are necessary to reduce the risk of this disaster.

Reactions on the Part of the Patient

Fainting may occasionally occur when injections are performed on a sensitive or nervous subject. Should the patient fall, an injury may be sustained; to minimize this risk injections should always be made with the recipient in the recumbent or sitting position.

Accidental intravenous injection may cause serious collapse, the nature of this reaction depending on the substance injected. For example, opiates may cause respiratory depression or arrest; local analgesics may produce convulsions, loss of consciousness, and respiratory failure. (A similar sequence follows injection of analgesic solutions into the vertebral artery during nerve block procedures in the cervical region.) The general treatment of such reactions involves providing adequate oxygenation by artificial respiration if necessary. The circulation is assisted by adoption of a head-down tilt, and pressor drugs may be helpful. Convulsions must be controlled by a small dose of barbiturate given intravenously.

Sensitivity to drugs may lead to anaphylactic reactions causing bronchospasm and respiratory difficulty, massive urticaria, or acute hypotension. If such a possibility is suspected, a small test dose is advisable. Antihistaminic drugs may reduce the severity of such reactions; injection

of adrenaline is suitable emergency treatment. Dangerous reactions may follow intravascular injection of various contrast media (for example, for angiography), and these procedures must be regarded as carrying an inherent risk.

Overdosage.—Collapse and convulsions may follow overdosage with local analgesic drugs. The risk of such incidents is reduced by the incorporation of adrenaline in high dilution (for example, 1 in 100,000) in local infiltration solutions, the resulting ischaemia retarding absorption of the local analgesic drug into the blood stream. The risk of overdosage is greatly increased by the use of concentrated solutions of local analgesics; $\frac{1}{2}$ % lignocaine or 1% procaine is usually strong enough for most purposes; 2% solutions of these drugs are only rarely indicated for injection purposes—for example, epidural or caudal block. In one reported fatality, overdosage with cinchocaine resulted because evaporation had led to an increase in concentration of the solution used (it had been stored in a flask stoppered with cotton-wool and "cellophane"). Disasters have followed overdosage with adrenaline. The total dose of 1:1,000 adrenaline given by injection should never exceed 1 ml. (the rare exceptions being asthmatic patients, who are tolerant of this drug). In the shocked state subcutaneous or intramuscular injections are very slowly absorbed because of the poor local circulation. Repeated doses of opiate have thus been given to secure an effect; when absorption finally occurs (for example, after circulatory improvement) overdosage results. For this reason the intravenous route is preferable in the shocked patient.

Air Embolism.—It is unlikely that sufficient air could enter the circulation to produce dangerous effects if an ordinary syringe and needle are used for injection. When air pressure is used to facilitate intravenous infusions the risk is high and constant vigilance is essential. Safety-traps have been devised to reduce this danger. Accidents of this type have resulted from the entrance of air via needle-holes into the tubing of transfusion sets; this accident can only occur if the holes are made at a high level in the set so that the dependent column of fluid creates a negative pressure at the puncture site. Air embolus can also result on rare occasions from needle punctures in the region of the lung, and this occurrence may be the explanation of some examples of "pleural shock."

Cardiac arrest may occur as the ultimate result of several of the reactions listed above, or, according to some authorities, as a result of vagal inhibition. Accidental intravenous injection of adrenaline solutions, especially during certain types of anaesthesia, may cause ventricular fibrillation and death. The only treatment for cardiac arrest is to initiate cardiac massage so as to provide an effective circulation within five minutes of the moment of arrest. Should circumstances render this impossible, the only slender hope is that cardiac puncture with a long needle may stimulate the heart beat to recommence.

Conclusion

From this review of the various accidents, it seems reasonable to formulate a set of simple rules to reduce the risks attached to the performance of an injection.

- (1) *Asepsis*: Check the condition and sterilization of the apparatus and ensure efficient aseptic technique.
- (2) *The Drug*: Check the identity, strength, and dosage of the drug.
- (3) *The Site*: Check the site of injection and confirm the correct location of the needle-point.
- (4) *The Patient*: Have the patient in a sitting or recumbent posture and observe him carefully during and after the administration.

Not only should errors be eliminated by such a routine, but, should any accident occur, evidence that a careful procedure had been followed would provide satisfactory grounds for defence if negligence is alleged and proceedings ensue.

Next article on Emergencies in General Practice.—"Acute Osteomyelitis," by Mr. A. W. L. Kessel.