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Review Article

Toxicity, Untoward Reactions, and Related Considerations in the Medical Use of Plastics

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THE FIFTIES ushered into the medical and related professions a host of devices or items of one type or another composed in part or whole of a plastic material. Nearly a geometric increase in the use of these plastic items has occurred each year. The spectrum of uses today defies any ordinary listing, and it now appears possible that with the correct choice of plastic any desired property can be achieved. For the most part the medical and other ancillary professions have accepted these plastic items with a great deal of confidence—a confidence which perhaps is not entirely justified. Part of this acceptance of plastics for any and all uses stems from a lack of knowledge on the subject of plastics by clinicians, nurses, pharmacists, and hospital administrators. Other segments of the population are also finding that certain polymeric materials and their additives might cause harmful effects to the purchaser, as may be witnessed by recent findings in the United States that a plastic molding toy has caused over 1600 skin irritations.[1] It seems logical then that as more information is accumulated by medical and allied professions on plastics, a greater safety feature will be forthcoming, not only to patients but also to the general public. This review attempts to cover some of the problems encountered in the use of plastics in medicine and is intended to alert those interested in them that consequences—from very minor to extremely serious—may fall upon the user or patient if proper safeguards are not taken. Knowledge of this type can help all segments of the public health professions and their suppliers to produce and use only those items which insure absolute safety for intended use.

In this review the author has attempted to

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[1] From a U. S. Department of Health, Education and Welfare, Food and Drug Administration, News Release, May 17, 1963.

cover the general field (without claiming a complete coverage) of toxicity and untoward reactions which have or may have a direct or indirect effect upon the welfare of the patient.

TOXICITY AND UNTOWARD REACTIONS

General

Toxicity or tissue sensitivity reactions in animals can take place by two distinct routes: (*a*) by direct contact of the plastic material or product with tissue and (*b*) by indirect contact with tissue, such as injection or application of a solution (drug product, nutritional product, blood, etc.) which has had previous contact with a plastic. A number of reports have appeared in the past discussing the toxicity of various polymers and the other ingredients which are utilized to prepare a plastic product (1–8). For the most part these reports have dealt with industrial health problems in relation to the manufacturing of a plastic material. As is well known, many of the chemicals used in the synthesis of a polymer are highly toxic if proper care is not taken to safeguard the health of the worker. However, the discussion presented in this section will deal with the finished plastic material. Texts by Rolf (9) and Wesolowski (10) should be referred to for more detailed and specific information on the use of plastics in medicine and surgery.

Direct Effect on Tissue (Acute)

Pure Plastic (No Additives).—It is a natural biological consequence that any material introduced into tissue will show some degree of reactivity, even if this cannot be truly detected with present means of analysis. Results and conclusions must be viewed as relative and in comparison to a standard state. This "standard state," of course, poses a problem since different investigators may use different standards for comparison. Many of the conflicting reports, or at least differing opinions, dealing with plastics should be examined in the light of what has been said. One other additional factor is relevant, however, in regard to plastics, especially when the same generically named plastic has been used by more than one group with varying results. Since there are no standards for plastics to be used in medical practice, it is very probable that the "same" plastic might not actually be the same, even though the difference may not be apparent by visual observation.

A great body of evidence is readily obtainable to support the claim that a pure plastic material is inert when in contact with normal, healthy, unbroken, or untraumatized tissue such as the skin or mucous membrane (11–13). The use of synthetic yarns in various clothing apparel for a number of years by millions of persons with little incidence to tissue reactivity attests to this statement. Unfortunately, less information is available as to the effect of a pure plastic introduced into tissue of ill or diseased patients.

Early reports of tissue sensitivity, dermatoses, or other untoward reactions ascribed to a pure polymer may be—in the light of present knowledge—traced to the presence of monomers or other low molecular weight polymers rather than to the polymer itself. A good example of this may be seen by referring to the literature in both the dental and ophthalmic professions where acrylic resins were used (and, of course, are used) as prosthetic devices. For one reason or another in these early uses of the acrylic resins, the monomer was not completely polymerized and this caused the tissue response. Contact lenses have caused some difficulty to a small number of patients out of the nearly 5 million wearers. Recently, however, a report pointed out that 14 proved cases of blindness or near-blindness were attributed to contact lenses (14). One suspected cause of blindness is the possibility of a chemical impurity in the plastic migrating onto the surface of the eye.

Patty (15), LaVeen and Barberio (16), and Scales (17) have emphasized the importance of the removal of the monomers before actual medical use. There have been instances of tissue response to other polymeric materials, but most of these can also be traced to factors other than the polymeric material. Harris (12) states that the final polymerized chemical (plastic) is inert to tissue and cites the studies by Schwartz (18), Morris (11), Hine *et al.* (19), Zapp (20), and Calnan *et al.* (21), to support his contention. The reader should note, however, that these reports were based upon experiments on the skin.

Introduction of a pure plastic into the tissue (subcutaneous, intramuscular, intraperitoneal, etc.) has been found in numerous instances to be well tolerated by the host tissue (at least for short periods), but it would be incorrect to assume that tissue sensitivity will not appear. There is difficulty in assessing the results from this type of investigation since the reaction or lack of reaction will depend upon such factors as its particular site of implant, the size of implant, the degree of blood supply, the possible trauma effect of implantation, and the time of tissue contact. It is also possible that even here a reaction might have been caused by a contamination of one form or another rather than by the pure plastic.

Some authors have assumed that tissue re-

activity was due to the pure polymer after short contact with tissue. For example, Harrison *et al.* (22) indicated that Dacron, Ivalon, nylon, Orlon, and Teflon did produce some tissue sensitivity when subcutaneously implanted in dogs. In their study nylon was found to be the least acceptable, while Teflon was the most tolerated plastic in the series. Usher and Wallace (23) found that nylon, Orlon, Dacron, and Teflon were less tolerated in dogs (up to 1 week) than Marlex. Longer periods of contact with tissue (perhaps up to a year) might produce further tissue reactions, depending upon the particular plastic.

Little and Parkhouse (24) investigated a number of plastic materials as to their potential tissue reactivity in guinea pigs and noted that a correlation could be established between crystallite size in the plastic or the size of an added filler to the plastic and the incidence to fibroblast reactions. They employed X-ray diffraction methods to approximate the size of the crystallites or fillers. Results of their study demonstrated that the silicones and low-density and medium-density polyethylene produced little incidence to reactions whereas other types of plastics could elicit responses.

Compounded Plastics (Polymer plus Additives).—The propensity of toxic responses in animals and humans would seem to increase for those plastic materials which require the presence of other ingredients to impart a specific desired property. The evidence to support this previous statement is more difficult to find in the literature since little practical use is made of compounded plastics by surgeons as possible prosthetic devices. In recent years, however, more use is being made of compounded plastics such as polyvinyl chloride for tubings and protective coverings. For example, in-dwelling catheters and other types of catheters which are introduced into a natural body orifice or inserted through a surgical procedure will have contact with tissue which might be susceptible to a leached constituent from the plastic material. Actual clinical reports of this occurrence have been rare in the past, but results from several animal studies do indicate that toxicity of leached constituents is a real possibility. The work of Brewer and Bryant (25) may be cited as an example to demonstrate that even certain commercially available plastic devices used in medical practice can cause tissue sensitivity when implanted in various animal tissues for short periods of time.

Lawrence *et al.* (26) conducted a toxicity study on a number of commercially available plastic administration devices and found that out of 48 samples tested by intramuscular implantation in animals, 25 were found to cause a reaction after 1 week of contact. Most of these devices were tubings of the vinyl type and were packaged in sealed cartons ready for use. This particular investigation indicated that one or more ingredients in the tubings were being released to the tissue. Even though the actual offending agent was not ascertained, it was demonstrated that the plasticizers were not the causative agents in producing tissue reactions. Gas chromatographic techniques suggested that the offending agent was one of the additives incorporated in the plastic in minute quantities. Alcoholic extraction of the "toxic" tubings removed the offending agent from the tubing.

The above authors make a very poignant conclusion in their paper. They state the following:

> The question of course may now be raised that the tubings which are reported in this paper were never intended to be implanted either in animals or humans; consequently, for their intended use, they may be quite safe. Questions of this sort can best be answered by stating that good public health practice would seem to dictate that no plastic item should contain an ingredient which has a potential harmful ingredient that might leach into a solution to be administered to a patient.

Autian *et al.* (27) noted that one type of vinyl urinary bag caused tissue reaction in animals, while a similar type of bag from another manufacturer showed no ill effects.

On a number of occasions in-dwelling catheters have caused problems in patients. Bansmer *et al.* (28) documented a number of complications when catheters were placed into the inferior *vena cava*. Some of the complications were local thrombosis, thrombosis with embolism, suppurative thrombophlebitis with septicemia, and chemical necrosis. Derrick, in animal experiments, concluded that intra-aortic catheters cannot be left for a prolonged period of time without precipitating thrombosis and embolism to vital areas (29). Several reports have also appeared indicating that in-dwelling catheters have been severed and lost in the arm of patients (30). The break in the catheter may have been due to a bending action on the catheter with movements of the arm. Urinary catheters have increased the incidence to bacteriuria in patients (31). The exact reason or reasons for these catheters causing the infection is still unclear.

Direct Effect on Tissue (Chronic)—Cancer

Since no evidence has appeared in humans that a certain plastic material is the causative agent

in the production of tumors, there might be a natural tendency to discount these "inert" materials (plastics) as possible carcinogens. At the moment we must be content to view certain animal experimentations which have demonstrated that long implantations of plastic materials cause responses which would rightly be considered as carcinogenic.

Turner (32) appears to have been one of the first to detect the carcinogenic activity of plastics. In 1941 he reported his findings which showed that implanted Bakelite disks in rats gave rise to sarcomas at the site of implants. In the latter part of the forties, Oppenheimer *et al.* (33) observed that cellophane wrapped around rat kidneys for a period of 24 months gave rise to tumors. This was a chance discovery since these investigators were actually experimenting on hypertension. Further work by the Oppenheimer group reported in 1952 (34) that various types of plastic films caused a certain percentage of sarcomas in rodents tested. Druckrey and Schmahl (35) were able to produce sarcomas in rats at the site of implantation with regenerated cellulose film. These authors noted that the tumors were produced in a strain of rats which had shown no spontaneous disposition to sarcomas during a prior 12-year period.

In 1953, Oppenheimer *et al.* (36) reported the testing of a number of films by implantation in mice and rats. They found the production of malignant tumors when films of regenerated cellulose, pure and impure polyethylene, polyvinyl chloride, Silastic, Teflon, Dacron, polystyrene, and nylon were used. Druckrey and Schmahl (37), in a continuation of their earlier studies, reported that they had produced tumors in rats with a number of polymers, while the team of Laskin *et al.* (38) observed a 25% occurrence of fibrosarcomas in mice after implantation of methyl methacrylate film.

Further work by the Oppenheimer group (39–42), reports by Bering *et al.* (43), Nothdurft (44), Hueper (45–47), Russell *et al.* (48), and Bing (49) clearly show the incidence of sarcomas when various types of plastics are implanted in animals.

An analysis of the previous workers' data and conclusions offers two schools of thought concerning the causative mechanism of polymer cancer. A minority group, particularly Hueper (47) and Druckrey and Schmahl (35, 37), have advanced the hypothesis that a chemical or a physicochemical interaction between the polymer and the tissue is the chief causative factor in the production of tumors, while a much larger group of investigators, *i.e.*, Oppenheimer *et al.* (39), Nothdurft (44), and Russell *et al.* (48) support the physical or nonspecific theory of polymer carcinogenesis.

The chemical theory viewers postulate that such factors as end groups, free radicals, complex formation between the polymer and protein, degradation products of the polymer, and/or the presence of impurities in the plastic might initiate cancer production. On the other hand, those of the physical theory approach point out that many chemically unrelated substances cause cancer, but a specific substance in a number of physical forms, *i.e.*, film, perforated film, powder, size of implants, smoothness of implant, etc., may or may not cause cancer.

The physical theory school would seem to believe that induction of tumors by plastics is indirect and may be due, in a large part, to a general interference with normal cell growth at the interface between the plastic and the tissue. The critical factor, either stated or implied by this group, is the total uninterrupted surface contact. For example, films which have induced tumors will show less tendency to do so when they are perforated, and powders of the polymer show little or no tendency to cause tumors. Horning and Alexander (50) have observed a correlation between the size of the surface area of the implant and tumor production, while a recent report by Oppenheimer *et al.* (51) confirms that powdered plastic materials when implanted do not seem to act as carcinogenic agents.[2]

However, Hueper (47) disagrees with the physical theory group and reinterprets the results of other workers, as well as the results of his own study, to support the chemical or physicochemical thesis as the causative factor in polymer cancer. Therefore, it must be obvious that much more experimental work must be done to define clearly the causative factor which is responsible for the production of tumors when various types of plastics are implanted in animals.

In general, there appears to be a minimum induction period, depending upon the animal, before a tumor will develop from an implanted plastic. Oppenheimer *et al.* (41) noted that if implants are removed from their sheath (pocket or capsule which will form around an implant) within a 6-month period, no tumors will develop in rats. If the implants are kept in place for a longer period than 6 months and then removed, tumors will develop. However, tumor response,

[2] It should be noted that for the same unit weight of plastic, a powder will have more surface area than a film, but the powder will not have an uninterrupted contact with the tissue.

may be eliminated after the 6-month period, if both the implant and the sheath around the implant are removed. This would indicate that once the cells have reached a certain point of alteration, the reaction cannot be reversed even when the causative agent (plastic) is removed. Nothdurft (44) also paid attention to the sheath surrounding the implant as a factor to be considered in tumor production.

What has been noted in animals has, up to the present time, not been seen in man. In fact, Harris (52) points out that from his knowledge of 8000 cases of breast plasty in humans, not one case of cancer was noted due to the plastic implant. Several reports (53, 54) have indicated, however, that tumorlike manifestations in several humans could be traced to the use of aerosol hair products which contained polymeric material, but the evidence cannot be considered conclusive. The experiments performed in animals ranged for a period of several years which in man might mean an equivalent of 15 to 30 years. Since implanted prosthetic devices are of comparatively recent vintage, no sure prediction of either noncarcinogenic or carcinogenic activity can be postulated at this time. The surgeon must weigh the merits of implantation in saving or prolonging life with regard for the possible risk involved.

Indirect Effect on Tissue

Leaching of a Constituent into Solutions.—Another problem is the possibility of one or more ingredients from a plastic device leaching into blood, parenteral products, and other solutions during storage, collection, and administration. These will be referred to as "indirect effect on tissue" since the plastic itself will not have actual contact with tissue. Two questions might be raised here: (*a*) is an ingredient or ingredients being leached into a solution which will then be injected into animals or humans and (*b*) is that ingredient or ingredients toxic to the host?

If the answer to the first question is a definite "No," then there may be little need to seek an answer to the second. At first glance, the previous statement would seem reasonable, but a deeper penetration into the plastic problem will reveal a number of factors which will influence the migration rate of a constituent from the plastic into the solution. Of course, it is assumed here that the plastic is a compounded plastic or has been treated with one or more agents to improve the quality of the device. A plastic device in contact with saline solution may reveal no leaching, but in another solvent system or at another pH there may be significant quantities of the leached constituent in the solution. The problem becomes even more complicated when one considers the variety of parenteral products which could come in contact with a plastic device.

Several years ago, Autian and Brewer reported in a study on a disposable hypodermic needle having a plastic hub that a constituent was being released by certain needles from the plastic hub to a saline solution which on intravenous injection caused the death of mice (55). Further work by Brewer and Bryant (25) on various disposable devices demonstrated that compounded plastic materials may or may not cause a toxic effect when first exposed to several parenteral solvent systems and then injected by different routes into animals.

It is pertinent at this point of the review to mention that very little appears to be known concerning the toxicity of a number of agents which can be formulated into certain types of plastics. Certain countries, for example, the United States, have very stringent regulations on food packaging materials. Physical and biological testing must be performed on these packaging materials before they can be employed as food containers. The biological tests invariably involve long oral feeding tests in groups of animals to ascertain the safety of the substance. Unfortunately, this same information often appears to be used to indicate that the additives approved for food packages will also be safe when they are parts of plastic devices to be used in medicine. Of course, this assumption may be true, but on the other hand strict obedience to this doctrine could present possible harm. Documentation of this statement is not easy in regard to humans, but preliminary animal experiments by Meyers *et al.* (56) on a group of citric acid esters used as plasticizers revealed how false oral testing programs can be when they are extrapolated to parenteral administration. The aforementioned workers studied the behavior response to parenteral administration of these esters in rats, mice, frogs, and rabbits. They noted that all of the esters exhibited a marked effect on the central nervous system. A single dose (depending on the particular ester) killed these animals in a period of several hours. Death was not due to citrate intoxication as may have been anticipated, but due to another mechanism not yet elucidated. The question arises regarding what actions other ingredients used in plastic formulations may have on animals and upon sick persons by routes other than oral if they leach out into a solution.

plastic tube into blood can occur. In their study they noted that when they changed from glass tubing to a particular polyvinyl chloride tubing, premature cardiac arrest and ventricular fibrillation occurred on the isolated perfused rat's heart. The important point to be made here is that these authors indicated that some brands of polyvinyl chloride did show this adverse reaction.

Keith *et al.* (70) reported that one batch of plastic tubing enhanced the hemolytic effect on perfused blood. This observation suggested to Hirose and associates (71) that the significant increase in the incidence of renal complications during extracorporeal circulatory bypass in patients in their hospital might be due to the particular plastic and the ethylene oxide method used for sterilization. These investigators noted that ethylene oxide sterilization increased the tendency to hemolysis in blood samples stored in plastics but that the particular plastic would also influence the rate of hemolysis.[4]

There is, therefore, the very serious consequence in extracorporeal circulation in humans that the wrong brand of tubing might release a constituent into the blood and thereby produce one or more untoward reactions.

Another problem has arisen in the use of plastic tubing in heart lung machines. Usually the tubing or tubings are coated with silicone, and if the silicone actually has not been baked on the plastic, which in many cases might be the case, there is the possibility of the blood washing particles of the silicone from the plastic into the circulating blood. A report of this occurring in humans has been given by Lindberg *et al.* (72). In their study 10 patients had died after open heart surgery. On necropsy, clear, refractile emboli were found in the capillaries of the kidney, brain, and heart. The emboli were investigated and found identical to the silicone used in the coating of the tubings. Further work on animals substantiated the human results that silicone coatings can cause embolization and death. Similar results were noted by Helmsworth *et al.* (73), who found silicone emboli in the glomeruli of the kidney of patients and animals. The silicone was traced to the oxygenator pump which had been silicone treated for debubbling.

Here it is important to remember that as new materials are introduced into one or more of the components in various types of extracorporeal apparatus, it is imperative that the material be evaluated biologically to prevent any unnecessary hazard to the patient. Reuse of certain components by specific washing, rinsing, and sterilization should require further evaluation of the component since these treatments may affect the plastic material sufficiently which in turn may produce an untoward effect in the patient. Clearly, more research is needed in this area for better patient protection.

[4] It was found that if the ethylene oxide sterilized plastic was kept for 7 days prior to its contact with blood, the gas had no effect on the blood.

COMPLICATIONS ARISING FROM PLASTIC PROSTHESES

General

The use of synthetic materials as a prosthesis dates back to the year 1890 when Fraenkel repaired a bony defect in the skull by the use of celluloid (74). Since that time and especially within the last 15 years, an array of uses has been found for plastic materials within the body for both physiological and cosmetic needs (10). Many of these surgical procedures with subsequent implantations of the plastic prosthesis have permitted extension of human life or have given certain forms of comfort to the patient. Many problems still need to be studied in detail before an ideal synthetic device becomes possible. The following section attempts to bring some of these problems into focus with past experiences by various investigators.

Vascular Prostheses

The general success of surgical procedures in the replacement of segments of diseased or failing aortas and peripheral arteries with homografts soon made it evident that the supply of these homografts or even heterografts would not fulfill the anticipated needs. Thus, it was quite natural for the surgeon to turn to the various polymeric materials as synthetic vascular replacements.

One need not go too far back into the literature to note that most animal and clinical experiences with synthetic prostheses have occurred within the last 7 or 8 years, even though Deterling (75) refers to Vinylon-N yarn being used as a vessel substitute in dogs in 1951. Since 1957, the two most used plastic materials for synthetic grafts have been Dacron and Teflon; but Ivalon, nylon, Vinylon-N, Orlon, Fortisan, polyethylene, and polypropylene have had some initial success.

Much experience has now been accumulated on Ivalon. It might be of interest to review this material as a synthetic substitute for vessels from its original success to its final demise.

A number of excellent properties such as porosity, compressibility, ease in handling, and ease in molding made this material attractive

as a vessel substitute. Early reports by Shumway *et al.* (76), Ellis and Kirklin (77), Rob *et al.* (78), and Fitch and Denman (79) were extremely encouraging in regard to Ivalon as a vessel replacement; however, Deterling (75), as early as 1956, had some reservations in the use of Ivalon, for he noted that the material could not withstand the pressure in the thoracic aorta unless highly compressed. Creech *et al.* (80), in a report to the Society for Vascular Surgery in 1956, reported some unfavorable results with Ivalon in clinical practice. Rob (81) reversed his earlier impression of the value of Ivalon; in fact, he no longer advocates its use as an arterial replacement. This reversal of opinion also has been enunciated by Fitch *et al.* (82). They now state the following: "The use of Ivalon grafts as arterial conduits in the human patient is unjustified due to the hazards of thrombosis, aneurysmal formation, rupture, and anastomotic disruption." A recent report by Payne and Kirklin (83) on a number of patients having had reconstruction surgery performed on the right ventricular outflow tract with several plastic materials noted that Ivalon was an unsatisfactory material. Further support of the inadequacies of Ivalon is given by Adler and Darby (84), who noted marked changes in physical properties of Ivalon after tissue contact. In the light of present knowledge, it would appear that Ivalon no longer merits a position as a worthy substitute for vessel replacement either in man or other animals.

As early as 1956 an attempt was made to assess actual clinical experiences in the use of synthetic materials as vessel substitutes in humans. This assessment became a preliminary report which has been mentioned previously (80). The report relates the success of aortic replacements with one or more of the synthetic materials (*i.e.*, Ivalon, nylon, Fortisan, Orlon, Dacron, Vinyl-N, and Teflon). Less success was found for synthetic materials when these were used as replacements for peripheral arteries. Critical factors causing the failures of the peripheral vessels were the relatively small diameters of these vessels, the great length, and the crossing of flexion areas.

There appears to be general agreement today that vessels less than 5 mm. in diameter will fail. Most likely these failures will be due to the propensity of thrombi formation. Harrison (85, 86) found this to be the case with nylon, Dacron, Orlon, Ivalon, and Teflon in his studies. Further confirmation of this fact is given by Dale and his group (87, 88), as well as by Cate (89).

Some controversy exists as to the actual causative factor or factors inducing thrombi formation in synthetic vessels. Change in flow rate of blood and turbulence of flow due to the synthetic graft has been believed to be a factor in thrombi formation (90). Szilagyi (91) has viewed thrombi formation in synthetic grafts as possibly due to the nonreactivity of a particular plastic material. The implication here is that arteriogenesis will be delayed and that the intima will not adhere firmly to the synthetic vessel. A recent study of Phillips *et al.* (92) disputes both the turbulent flow and the nonreactivity theories as causative agents; in turn, it postulates that thrombosis formation is a direct consequence of a foreign body—especially if that body is relatively nonporous. They found in their study on Teflon that woven Teflon caused a greater degree of thrombi formation than the knitted material. The knitted Teflon, more porous than the woven form, permitted fibrous tissue to invade the interstices of the fiber, resulting in greater adherence of the fibrin lining in the vessel. Other investigators also have pointed out the importance of porosity in regard to synthetic materials used as vascular substitutes (90, 93–95).

Biogenic conditions will alter physical properties of synthetic materials, even though much still needs to be done to elucidate the actual mechanism underlying such physical changes. It is fairly well established now that polar polymeric compounds such as nylon, Orlon, etc., will show greater changes of properties than the very nonpolar compounds, exemplified by Teflon after long contact with tissue. Tensile strength measurements (for elastic properties) have been conducted for a number of synthetic polymers before and after implantation in tissues. For example, it has been reported that nylon will lose from 20 to 25% of its original tensile strength after 7 to 18 months of tissue contact (80). Other materials also will change significantly, but to varying degrees. This has prompted some to believe that elastic properties might be a critical factor to consider when a decision is made to use a specific synthetic material as a vessel substitute. Present evidence, however, gives little emphasis to tensile strength as a factor in success or failure of grafts (80). A revealing study by Newton *et al.* (96) apparently confirms this fact. In their studies (*in vivo*) they noted that various arterial substitutes showed differing elastic properties within a 6-month period; but after this time period, they all tended to stiffen and reach a constant

elastic value. They concluded that the constant value was due to the formation of scar tissue within the implanted arterial substitute.

As has been mentioned for synthetic materials, a degree of success has been made for grafting of vessels having larger diameters than 5 mm., while, conversely, little success with vessels smaller than 5 mm. A number of investigators recently have observed that homografts have proven more successful postoperatively over synthetic materials when surgical grafts were performed on smaller vessels falling below the inquinal ligament. Irvine *et al.* (97) noted this to be the case in a study of 95 patients who underwent a total of 106 femoropopliteal bypass treatments. Cockett and Maurice (98) in a 9-year observation of direct arterial surgery for claudication and ischaemia of legs, concluded that the synthetic materials were not functioning up to the level of homografts or other surgical techniques not involving synthetic materials.

It should be obvious that for vessels large or small other factors must enter the picture which can give rise to success or failure of synthetic grafts. In this respect it is interesting to note the suggestion of Wesolowski and associates (99), who have contributed a great deal to surgery in techniques and knowledge in regard to vessel and tissue substitutions. These investigators have concluded that the ideal synthetic vascular graft material should meet the following standards: (*a*) no toxicity or no allergenic potential, (*b*) no deterioration of the synthetic fiber upon biological implantation for prolonged periods of time, (*c*) desirable mechanical handling properties of being easily scrunched, crimped, and twisted, (*d*) very low implantation porosity, and (*e*) very high healing porosity or fibroblasting permeability. To achieve the last two requirements (*d* and *e*), Wesolowski *et al.* (99) fashioned compounded prosthetic vascular grafts (a core of resorbable material which has been wrapped with multifilament polymer). These compounded materials were found to be superior (in animals) to the conventional monoplastic material. Similar results with a gelatin-impregnated Dacron prosthesis by Jordan *et al.* (100) also have been reported.

Surgical skill has made it possible to replace faulty or defective cardiac valves in humans. Unfortunately, studies in canines and humans have revealed survival rates not as encouraging as had initially been anticipated. The most serious drawback to the synthetic valves has been the severity of thrombosis formed on the valve. A number of investigators—Frater and Ellis (101), Kolff *et al.* (102), and Muller *et al.* (103)—have observed this serious problem. Gott *et al.* (104) have noted the importance of electrical charge on the plastic (positive charge in comparison to the negative charge on the blood particles) and found that this charge could be reduced or eliminated by coating the valve with colloidal graphite. The coating resulted in producing an extremely smooth surface which apparently dissipated or reduced the positive charge, thereby decreasing the incidence to thrombosis. To date these authors have been able to coat polycarbonate, polyvinyl, and methyl methacrylate; their results appear encouraging. However, final success or failure must wait for long-term studies in both animals and humans.

Subcutaneous Prostheses

Reconstructive surgery on or near the surface of deformatives, either natural or induced by disease, accident, etc., has restored many patients to a normal manner of life. The synthetic materials have been used for this type of surgery for approximately 15 years with various degrees of success. As with other plastic implants, real problems have been encountered which have led to replacement of the original implant or to complete failure after varying periods of time.

Breast plasty has gained some popularity in the past to relieve psychic disturbance caused by actual or imagined hypoplastic breasts. Even though cosmetic acceptance can be achieved by the use of plastic implants behind the breast, the material gradually becomes firm and loses its initial resiliency (105, 106). The implant may also shrink in size or "fall" from its original position, thus creating further psychic disturbance. Hamit (106) lists a number of complications which might result from breast plasty, such as infection, drainage, increasing firmness of the plastic material, disruption of breast function or appearance, development of draining sinuses, and possible carcinogenic activities of the plastic material. Polyvinyl sponge has shown the greatest number of failures up to the present, and it is hoped that newer materials such as silicone rubbers and polyurethanes might prove more satisfactory. Harris (52) appears to be quite satisfied with a special type of polyurethane for breast plasty.

Various other reconstructive procedures on the face and other surface portions of the body have been performed with, in some instances, amazing success. Favorable initial results, however, must be weighed against long-term usage and the possible complications which will be ever

present with a foreign body. It will be interesting to see how plastics such as the dimethyl silicones and the various halogenated carbons will perform over long usage. Encouraging reports on these materials for subcutaneous prostheseis have been given by Brown *et al.* (107).

Synthetic Adhesives

One can see great advantages for adhesive materials which can replace the usual nail, clamp, cast, and other means of closing or holding segments of tissue or bone together. Fruitful progress has been made in this direction in the past 4 years in surgery with the advent of polymeric materials which, when actuated in some fashion, can become a tenacious adhesive for tissue.

In 1958, Manderino and Salvatore (108) were able to restore broken bones by the use of polyurethane material which acted as a very powerful adhesive agent, fixing the break in a very short period of time. Since then considerable use has been made of this material for the same purpose (109–111). To some it is considered as a form of "bone glue," but others are not quite so convinced of this fact (112). Up to the present no definite tissue reactions have been reported (which could be attributed to the polymer), but sufficient time must elapse before a complete evaluation can be made.

A great number of synthetic adhesive materials have been produced in the last decade, but for the most part these had little place in medical practice, since for one or more reasons they were quite noxious to tissue. Then in 1959, Coover and co-workers (113) demonstrated the unusual adhesive properties of alkyl 2-cyanoacrylates, the chief one being that the monomer (as a liquid) polymerizes when spread between two surfaces and pressed. The change from a liquid state to a solid (as the adhesive) takes place with little or no change in volume, enhancing the adhesive quality. Experimental surgical applications, in particular for blood vessel repairs, have been performed by a number of workers using the above-mentioned monomer (114–116). In general, few tissue responses have been noted by most workers, but a word of caution should be noted for these adhesive agents since there appear to be some differences in the compound when purchased from different sources.

Lewers *et al.* (117) have noted that certain of the synthetic adhesives have a distinct toxic effect. For example, in animals they found that both the monomer and the polymer caused death when injected into the liver and peritoneal cavity. Biological mechanism for death still has not been elucidated by these workers, and the possibility of carcinogenic activity is still to be decided. The above workers in their concluding remarks refer to a 1948 paper (118) in which the following sentence was quoted: "Clinical use of cellophane, polythene, or any other plastic carries with it the urgent requirement of knowledge of both the chemical and physical characteristics of the product being used." Lewers *et al.* (117) maintain this statement to be true with the synthetic adhesives.

PLASTICS AND DRUG ACTIVITY

In recent years pharmaceutical scientists have recognized the potential of polymeric materials as vehicles for prolonging the action of medicinal agents. Some success has been achieved in compounding the drug with an insoluble polymeric material which can then be taken by oral ingestion, the drug being released over a prolonged time period as the tablet or pellet travels along the alimentary tract. Similar dosage forms also have been suggested for long-term implantation of certain hormones. Advantages to both the patient and clinician of the above dosage forms are clear (one-time administration instead of multiple-drug administration) if certain unknown complications do not appear. Two hazards, even though they many appear only as remote possibilities, should be considered. The first of these is the release of a greater quantity of the drug than planned due to uncertain biological manifestations on the dosage form. The second is the possible irritating or sensitizing effect the particular plastic might have on the tissue when implantation therapy is employed. It remains to be seen whether these hazards will materialize in the future when more prolonged or sustained dosage forms are used.

Several investigators, in particular Garb (119), Scholtz (120), Sulzberger and Witten (121), and Hall-Smith (122), have noted that plastic films will aid the percutaneous absorption of a number of topical drugs. Such reports have stimulated other clinicians to consider the use of plastic films to decrease the usual concentration of the drug when applied topically. Lack of knowledge of the influence of these polymeric materials on the physical and chemical properties of drugs regarding their rate of penetration and diffusion into the skin may lead to unexpected toxic or untoward reactions. Vickers and Fritsch (123) have documented this fact with several cases where naphazoline was the test drug and Saran the plastic film. These aforementioned authors

give the following warning: "The knowledge of the vast increase in percutaneous absorption due to Saran occlusion might tempt clinicians to try to increase the effectiveness of other topical preparations with possible serious or even disastrous consequences."

DRUG-PLASTIC CONSIDERATIONS

Less recognized as a problem, probably due to the paucity of reports published, is the consequences which might result when a drug or drug product is kept in contact with a plastic material used as a container or administrative device (124–131). These problems may be collectively grouped into five general categories:

(*a*) *Permeation*—Oxygen or other gases permeating the plastic material and causing an incompatibility or, conversely, a volatile constituent in the drug product passing out of the container or device.

(*b*) *Leaching*—One or more ingredients migrating from the plastic into the drug solution.

(*c*) *Sorption* (including adsorption and absorption)—One or more constituents being removed from the drug solution into the plastic by a sorption process.

(*d*) *Chemical Reactivity*—One or more ingredients reacting by covalent bonding with the polymer or one of the additives in the plastic.

(*e*) *Alteration in the Physical Properties of Plastics*—Depending to an extent on one or more of the above or due to environmental effects, the container or device may undergo sufficient changes to no longer function as originally intended.

The above five considerations have been reviewed in some detail in previously published papers (132, 133) and thus will not be discussed any further in this review, except to emphasize that both the manufacturer and the user must share in the responsibility of safeguarding the health of the patient when plastic devices are to function as containers or devices for storing or administering drug products.

NEED FOR STANDARDS

An analysis of what has been reviewed in this paper should note that plastics are not so safe as originally thought. In no manner does this suggest that plastics should be banned or eliminated from medical practice. Such an expression would be ridiculous and certainly is not tenable to the many outstanding advantages to be gained by the use of the synthetic polymeric materials. Rather, a method should be sought which would insure that a particular plastic or plastic device will be safe for intended use. Standards must be created for "medical use" plastics as well as standards for the final plastic device. These standards obviously must include biological, physical, and chemical methods of testing. Finally, these standards must become part of the official compendia to insure legal status.

Autian (58) has published a guide to hospitals in the selection of plastic devices, while The University of Texas Medical Center has undertaken the task of developing its own standards for plastics [see report by Autian and Nicolaides (134)]. Brewer and Bryant were the first in this country to publish biological methods of testing of plastics to be used in medical practice (25). Workers in other countries recognizing the plastics problems have recommended also that stricter controls be maintained on plastics and have suggested a number of testing procedures (135–137). Guess and Autian (138) have presented a tentative protocol for the biological testing of plastic materials. In this country the Pharmaceutical Manufacturers' Association with support from the Society of Plastics Industry has developed a group of biological and physical chemical tests for plastics to be used with drug products.

Much work still remains to be done now and in the future before adequate standards are developed. Certainly, greater emphasis should be given to basic studies on plastics as they are related to medicine. In the past such support from industrial groups interested in plastics has been minimal, but it is hoped that a reversal of this trend will soon be forthcoming. There is also a need for better communication among groups working to manufacture and distribute plastic items to the medical profession. Often one group is not aware of what the other group has done to a plastic item. This point is clearly brought into focus by Bender (139), a consulting engineer, in his excellent article dealing with the trend toward plastics in surgery and medicine.

The plastics problem is such a vital health issue that it no longer can be kept as an "incidental" hazard with the ever-increasing use of plastics in all phases of medical practice. Good public health practice requires as much emphasis on measures to prevent a potential danger from becoming a serious reality as to combat the danger once it has occurred. Perhaps the best example of this in the past years is the pesticide issue brought into shocking public attention by Rachel Carson's "Silent Spring." Even though adverse criticism was given to the author for having overplayed the problem based upon

meager scientific evidence, it was interesting to note that the President's Science Advisory Committee has made a number of recommendations to prevent some of the possible consequences illuminated in the book "Silent Spring" (140). In much the same way, though on a much smaller scale, plastics for medical practice deserve equal attention.

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contain 17 g. NaOH/l., 10 g. Na_2S/l., and 110 g. Na_2CO_3/l.; they were treated by pptn. of the sulfide S (by adding 50 g. of polyacrylamide/m.³ water, followed by the addn. of 7.3 kg. of $FeSO_4$/kg. Na_2S and filtration of the ppt.) or by evapn. to a NaOH content of 25% (the Na_2S and Na_2CO_3 pptd. and were removed by filtration) and utilization of the resulting soln. in the purification of the pyrolysis gas. A. Aladjem

Effect of iron and thiocyanates on the purification of waste from gold extracting plants by the ion-exchange method. I. D. Fridman, L. N. Kuznetsova, and B. L. Serebryanyi. *Zh. Prikl. Khim.* 38(3), 482–7(1965)(Russ). The effect of complex ions of Fe such as $Fe(CN)_6^{4-}$ and of NCS^- on the sorptive capacity, α, of anion-exchange resins for CN^- was studied with resin AB-17 contg. (*a*) 6% and (*b*) 16% divinylbenzene. The irreversible sorption of $Fe(CN)_6^{4-}$ lowered α. The effect increased with the concn. of $Fe(CN)_6^{4-}$ and was higher with (*a*) than with (*b*). Dil. acids did not regenerate CN^- from the complex anion of Fe. Desorption of Fe with 0.5*N* HCl was greater than with 0.2*N* H_2SO_4, and α of AB-17 in the SO_4^{--} form was 1.5-2 times lower than in the Cl^- form. The results were ascribed to the formation of $Fe_4Fe_3[Fe(CN)_6]_6$ and $Fe_4[Fe(CN)_6]_3$. The effect of SCN^- ions was similar to that of the Fe anion. In the presence of SCN^-, α of (*a*) decreased from 5.8 to 1.6% and that of (*b*) from 4.9 to 0.37%. The extn. of cyanide in the process of desorption in every cycle was 80%. GBJR

Monitoring Kraft Mill combustion processes by gas chromatography. F. N. Rhoad (Union Bag-Camp Paper Corp., Savannah, Ga.). *Southern Pulp Paper Mfr.* 28(3), 60, 62, 64(1965)(Eng). CO_2, O_2, N_2, CH_4, CO, and H_2 in lime kiln flue gases are detd. by the use of a modified gas chromatograph. The carrier gas is He for all components except H_2, and H_2 is detd. by using N_2 as carrier on a duplicate sample. The path of the sample is through an 8-in. silica gel column, one side of the thermal cond. detector, a 24-ft. C-22 acid-washed firebrick column, a 6-ft. mol. sieve column, and the other side of the detector. The column temp. was 40°, and carrier gas flow rate was about 100 ml./min. This arrangement has the carrier gas passing one side of the detector while one component passes the other side. Polarity is switched after the CO_2 peak is recorded. The sample is dried by passage over $CaSO_4$ prior to entry into the sample loop. The detection ranges, in % by vol., are: CO_2 0.1–20, O_2 0.1–22, N_2 0.1-80, CH_4 0.1-10, CO 0.1-10, H_2 0.1-10. Several hrs. are required to purge the system of He after changing to the N_2 carrier. F. B. O'Neal

Use of the reaction with diazotized sulfanilic acid to determine phenols in waste waters from rosin-turpentine oil production. K. K. Lebedev. *Sb. Tr., Tsentr. Nauchn.-Issled. i Proektn. Inst. Lesokhim. Prom.* No. 15, 119–22(1963)(Russ). This reaction cannot be used owing to interferences from terpenes. Olaf Thomsen

Purification of sulfite pulping waste by adsorption. D. Ruzickova and V. Secova. *Sb. Vyskum. Prac Odboru Celulozy Papiera* 9, 73–116(1964)(Czech). Pulp mill waste contg. 200–5000 mg./l. org. matter, obtained from $Ca(HSO_3)_2$, $NaHSO_3$ semichem., and Na_2SO_3 semichem. pulps, were purified by adsorption on slag, washed coke (I), waste lignite, and coke fly ash (II). Their adsorption isotherms disclosed max. capacities for II and possibly I. The optimum grain size was 1–2 mm. and the flow rate 0.1–0.2 m.³/m.²/hr. Expressed as O consumed by the waste, II adsorbed 20.9 g. O/kg. when a filter tube was used and 31.16 g. when a continuous filter was used. With intermittent flow, the adsorbent could be partly regenerated because of oxidn. The effluent approached pH 7 after treatment, hence the pH of the original waste was irrelevant. The sulfite pulp effluents were freed from up to 70–95% oxidables and dry matter was reduced ~50%. Advantages of the adsorption method include low space requirements and cheap refuse low-cost raw materials. Biochem. methods require large areas. R. Ripa

Water economics and possibility of agricultural utilization of sewage from sugar factory at Baworow. Piotr Prochal. *Gaz, Woda Tech. Sanit.* 38(8), 271–5(1964)(Pol). It is proposed to use the sewage from a sugar factory contg. an av. of N 62.3, P_2O_5 9.2, K_2O 73.8, and CaO 215.0 mg./l. as a fertilizer. This application would lower the surrounding water contamination. Irena Kloczko

Rate constants in the reaction of biochemical oxygen demand of spent sulfite liquor wastes. Czeslaw Leszczynski, Zofia Skwara, and Jerzy Zielinski (Inst. Celulozowo-Papierniczy, Lodz, Poland). *Gaz, Woda Tech. Sanit.* 38(10), 335–7(1964)(Pol). Overall waste from a paper mill and those from a pulp mill were dild. 1:25, 1:100, or 1:250, and B.O.D. was detd. by diln. and manometric methods. The B.O.D. of the overall waste varied from 57 to 752 mg. O/l., and in wastes from the pulp mill it ranged 74–716 mg. O/l. The rate const. of biochem. oxidn. was in the 2 cases 0.19 and 0.20, resp. Irena Kloczko

The treatment of tannery wastes. I. Properties of the wastes from various parts of the tanning process. Harukazu Toyoda, Tetsuo Yarisawa, Akira Futami, and Masayoshi Kikkawa. *Tokyo Kogyo Shikensho Hokoku* 59(6), 246–56(1964)(Japan); cf. *CA* 62, 6252*b*. Chrome tanning and vegetable tanning of green-salted steer hide were carried out on a lab scale, and the individual wastes from various operations of the processes were collected and analyzed. The individual wastes seemed to be classified into two groups, although they varied widely in characteristics and vol. The continuously discharged wastes, such as the wash waters from mech. operations and washing operations were, in general, the weaker waste, although they were large in vol. The wastes, such as those from soaking, liming, and tanning operations were the stronger wastes, and all of them were discharged intermittently. The wastes from pre-tanning operations were, in general, alk., and were rich in dissolved and suspended org. solids. Their ratio of B.O.D. to chem. O demand (C.O.D.) was much larger than those of the wastes from tanning operations. The wastes from chrome tanning processes were low in pH and contained a large amt. of dissolved inorg. matter and a considerable amt. of toxic Cr salts. The vegetable tanning wastes constituted the worst fraction of tannery wastes, although they were small in vol. The vegetable tanning waste accounted for only 8% of the total vol., but carried about 47% of the total C.O.D. **II. Change of the composition of the wastes by mixing and storage.** *Ibid.* 257–75. A part of the composite wastes was stored for few days and redn. of the pollutional strength of the wastes was examd. Furthermore, a survey of the compn. of wastes discharged from a vegetable tannery was carried out. It was found that the pollutional strength of the composite wastes from pre-tanning operations increased with the amt. of mixed liming wastes, but more redn. of pollutional strength during storage was attained by increasing the ratio of liming wastes. As regards both the composite wastes from chrome tanning, dyeing, and fat-liquoring operations, and the composite wastes from vegetable tanning and bleaching processes, their pollutional strength was greatly reduced by mixing with the combined wastes from pre-tanning operations. The survey of vegetable tannery wastes revealed that the compn. of the wastes varies widely from time to time, and the suspended matter is usually very difficult to settle, but when pH of the wastes was raised above 11, owing to the large amt. of alk. wastes discharged from pretannery, the suspended matter and some of the dissolved matter coagulated and formed large rapidly-settleable flocs. **V. Effect of the treatment with lime.** *Ibid.*(7), 317–28. A study was made of the purification of tannery wastes by flocculent sedimentation by using $Ca(OH)_2$ as a coagulant. The efficiency of the treatment with lime varied with the properties of tannery wastes. Usually the C.O.D. and the suspended matter content of tannery wastes, varying 1300–4500 and 1360–2500 ppm., were reduced by about 50–87 and 60–90%, resp., by increasing the pH value of the wastes to 11.5–12.0 by the addn. of lime and settling for 30 min.–2 hrs. When $FeCl_3$ was used in conjunction with lime, further purification was secured. For the neutralization of the supernatant liquor of lime treated wastes, bubbling of CO_2 into the liquor was very effective, although further purification of the liquor could not be expected by this neutralization. Tannin and Cr salts in the wastes were completely removed by coagulating with lime, but the partial hydrolyzates of protein were difficult to remove by this treatment. **VI. Effect of anaerobic digestion.** Harukazu Toyoda and Akira Futami. *Ibid.* 329–37. When an artificial waste contg. tannin was digested in the anaerobic condition, some C.O.D. components of the waste were gradually accumulated in digesters, and the treatment of the waste became gradually difficult. Treatability of vegetable tannery wastes by the anaerobic digestion process was dependent upon the character of the wastes, and in general the composite vegetable tannery wastes were able to be treated by the anaerobic digestion process, provided an acclimatized sludge was used and loadings of wastes were suitably adjusted. For instance, when the wastes ranging from 880 to 2500 ppm. of B.O.D. were employed, and their loadings were adjusted to 0.2 to 1.0 g. B.O.D./l./day, it was possible to treat the wastes continuously, and a B.O.D. redn. of about 78–90% and a C.O.D. redn. of 50–77% were obtained. **VII. Effect of step-wise treatments by anaerobic digestion, activated sludge, and chemical precipitation.** *Ibid.* 338–46. Effluents from anaerobic digestion of vegetable tannery wastes were further treated by chem. pptn. adsorption, and(or) activated sludge processes, and their effectiveness was compared. Some of the components of the wastes removed by each process differed mutually, and by treating the effluents from anaerobic digesters successively by these processes addnl. B.O.D. and C.O.D. removals were obtained, and a higher degree of purification was attained. For instance, when a vegetable tannery waste having 3784 ppm. of C.O.D. was used as a sample, about 70% of the C.O.D. was removed by the anaerobic digestion process, and when the effluent from the anaerobic digesters was further treated by the activated sludge process about 90% of C.O.D. was removed, and the effluent from the aerators could be further treated with $FeCl_3$ or lime, or with activated C with the results of about 94 to 98% and 99 to 99.6% removals of C.O.D., resp. RCTT

→ **Characteristics and treatment of waste waters from production of vinyl resins.** Boleslaw Kotulski (Zaklady Chem., Oswiecim,

Poland). *Gaz, Woda Tech. Sanit.* 38(10), 336–9(1964)(Pol). Waste waters from the production of CH_2CHCl and from its polymerization by both emulsion and suspension methods are considered. Sewage from CH_2CHCl production contained C_2H_2 <2.5, HCl 15–80, aldehydes <1, and CH_2CHCl 100–400 mg./l. Sewage from emulsion and suspension polymerization *a* plants had, resp.: pH 6–7 and 8; dry residue 1.0–10.0 and 8.8, CH_2CHCl 0.5–9.0 and 1.3, and surface-active agents 0.02–0.2 and 6.6 g./l.; oxidizability 0.1–0.5 and 2.0, chem. O demand 0.2–2.0 and 8.8, and B.O.D. 0.1–0.5 and 2.0 g. O/l. It was found that polymerized CH_2CHCl is most efficiently removed by coagulation and sedimentation. Optimum dose of coagulant $Al_2(SO_4)_3.18H_2O$ for sewage from suspension polymerization is 0.1–1.0 g./l. For sewage from emulsion polymerization thermal coagulation is advisable. Irena Kloczko

Characteristics and purification of waste waters from production of vinyl resins. Boleslaw Kotulski (Zaklady Chem., *b* Oswiecim, Poland). *Gaz, Woda Tech. Sanit.* 39(2), 46–9(1965)(Pol). The phys.-chem. characteristics and toxicity for living organisms (*Daphnia magna*) were studied for waste waters from the production of monomers and polymers of CH_2CHOAc (I) and CH_2CCl_2. Sewage from the synthesis of I had pH ~4, O consumption ~500, chem. O demand ~19,000, and B.O.D. ~2000 mg. O/l., and a Zn content ~80 g./l. The sewage killed living organisms even when dild. 1:10000. The degree of pollution of other sewage studied was much greater. In coagulation with CaO and NaCl, the former was more efficient. The sewage from polymerization and copolymerization of CH_2CCl_2 contained many *c* inorg. salts and had relatively low toxicity. Irena Kloczko

Role of hydroxides and carbonates in the flocculation and sedimentation during the clarification of sewage from viscose production. O. P. Sinev. *Dokl. XV-oi [Pyatnadtsatoi] nauchn. Konf. Novocherk. Politekhn. Inst. Stroit. Sekts., Novocherkassk* 1964, 75–6(Russ). $Fe(OH)_3$, $Zn(OH)_2$, $Mg(OH)_2$, and $CaCO_3$ improved flocculation and sedimentation of hydrated cellulose, which in turn accelerated the hydrolysis of metal salts, coagulation of hydroxides, and crystn. of $CaCO_3$. The optimum pH for the flocculation and sedimentation of suspended solids was 10.5–11.5. From *Ref. Zh., Khim.* 1964, Abstr. No. 23I326. MVRK *d*

Pilot plant denitration of Purex waste with sugar. E. A. Coppinger (Gen. Elec. Co., Richland, Wash.). AEC Accession No. 35243, Rept. No. HW-77080. Avail. OTS, 16 pp.(1963)(Eng). A plant flowsheet was developed and successfully demonstrated in pilot plant equipment. A 1.4*M* sugar soln. was added to 25 l. waste for 12 hr. at 100°, and the mixt. was digested for 18 hr. The initial HNO_3 concn. was 6.14*M*. The residual was 0.94 and 0.90*M* after 12 and 18 hr. of digestion, resp. A residual C content equivalent to 1.9 and 0.4% of the total C fed as sugar was present after 12 and 18 hr. of digestion, resp. About 19 moles HNO_3 were destroyed per mole of sugar fed. Foaming *e* was produced during batch denitration with sugar by adding 0.4 g. dibutylphosphate/l. of synthetic waste. The addn. of 0.2 g. Dow-Corning Antifoam B/l. of waste reduced foam levels by about a factor of 2. An induction period of ~6–9 min. was observed before the reaction started. The length of the induction period increased as initial sugar addn. rates were reduced. Gentle air sparging reduced the induction period by about a factor of 2. The use $NaNO_2$ as a means of decreasing the induction period was not successful. Sugar soln. was added to cold waste, and the mixt. was heated to det. the pot pressures and tower pressure drops that could be developed under abnormal conditions. A decrease in pot vacuum of 30 in. H_2O and a tower pressure drop of 8 in. H_2O were observed when 20 l. of waste and 2.7 l. 2.5*M* sugar soln. were mixed together and rapidly heated to 100°. From *Nucl. Sci. Abstr.* 17(20), 4704(1963). TCNG *f*

Report of invention-solvent extraction process for recovery of strontium, cerium, rare earths, and cesium from radioactive waste solutions. Lane A. Bray (Gen. Elec. Co., Richland, Wash.). AEC Accession No. 5988, Rept. No. HW-75537. Avail. OTS, 14 pp.(1962)(Eng). A solvent extn. process is described which removes Sr, Ce, Cs, and rare earths from acid solns. (pH 3–5) in 1 operation. The process is based on the use of a solvent composed of 4-*sec*-butyl-2-(α-methylbenzyl)phenol *g* and bis(2-ethylhexyl)phosphoric acid in a diluent, such as Soltrol 170. Data are presented on the extn. of Sr, Ce, and Cs under varying conditions. From *Nucl. Sci. Abstr.* 19(4), 681-(1965). TCNG

Equipment for a counterflow sorption using natural sorbent suspensions. V. Vesely, I. Napravnik, S. Gaderka, M. Paar, and L. Mazel. AEC Accession No. 6879, Rept. No. UJV-1108/64. Avail. AEC, 14 pp.(1964)(Eng). A method for countercurrent sorption of radionuclides from aq. waste by using bentonite and tuff was developed on a lab. scale. The tuff showed relatively high extn. coeffs. esp. for Cs. Values for Sr *h* were lower and depended on Ca ion concn. An industrial process carried out in conical-bottomed mixers is outlined. From *Nucl. Sci. Abstr.* 19(4), 792(1965). TCNG

Engineering development of nuclear waste pot calcination. M. E. Whatley, C. W. Hancher, and J. C. Suddath (Oak Ridge Natl. Lab., Oak Ridge, Tenn.). *Chem. Eng. Progr., Symp. Ser* 60(53), 32–40(1964)(Eng); cf. Buckham, *et al.*, following abstr The feeds investigated were TBP-25 solvent extn. waste, Dare waste, and conventional Purex formaldehyde-treated waste The waste was concd. by evapn. and by steam-stripping of th HNO_3. The concd. soln. was then introduced into the heate calciner pot where it was denitrated, brought to a solid cake, an calcined. The process is workable and safe. Albert E. Nugent, Jr.

Development of fluidized bed waste calcination proces: J. A. Buckham, L. T. Lakey, and J. A. McBride (Phillips Petro Co., Idaho Falls, Idaho). *Chem. Eng. Progr., Symp. Se* 60(53), 20–31(1964)(Eng); cf. Tomlinson, *CA* 60, 3866*c*. All mann, *et al.*, *CA* 60, 15584*d*, Whatley, *et al.*, preceding abst A plant-scale, fluidized bed calcination process was constructe to utilize a totally continuous process for the conversion of aq. high-level radioactive wastes into compact granular solids. feed soln. of $Al(NO_3)_3$ waste was injected into a heated bed granular solids, such as sand seed particles. The bed was mair tained at 300–600°, and the thermal decompn. of the feed soln caused its solid reaction products to build up in layers on the be particles. The introduction of fluidizing gases, such as air, ca ried the gaseous products from the bed to scrubbers. Amorphou and α-Al_2O_3 were the chief solid reaction products. The redn. i waste vol. was 17-fold for 80% α-Al_2O_3 of bulk d. 1.6 g./cc. an 10-fold for amorphous Al_2O_3 of bulk d. 0.95 g./cc. Albert E. Nugent, Jr.

Purification of radioactive waste solutions with inorganic na tural ion exchangers. I. **The use of silicate clay as ion exchar** ger. G. Sachse and E. Leibnitz (Zentralinst. Kernphys. Dresden, Ger.). *Kernenergie* 4(8), 633–6(1961)(Ger); cf. *C.* 62, 2442*b*. Clay from the Radgendorf region was analyzed an characterized by electron microscopy, differential thermal analy sis, and x-ray analysis for the purpose of using it for the concn. o the liquid radioactive waste. The stabilization of the clay fo use in the column operation was also examd. by mixing poly acrylate with the clay. IV. **Leaching resistance of radioactiv annealing products of clay from the Radgendorf region.** *Ibid* 5(3), 187–90(1962). The clay samples which adsorbed ^{137}Cs ^{90}Sr, and ^{144}Ce were heated at 120–900° and the leaching of th activity with H_2O was examd. at room temp. and 80°. Whe heat-treated at 700°, 0.02% of ^{137}Cs, 0.4% of ^{90}Sr, and 0.3% c ^{144}Ce were leached, but with the clay treated at 900°, <0.05% c ^{90}Sr and ^{144}Ce were leached; thus leaching of the activity de creased with the heat-treating temp. N. Oi

Removal of cobalt and chromium by precipitation and ion ex change on soil, lignite, and clinoptilolite from citrate-containin radioactive liquid waste. D. B. Hawkins. AEC Accession No 35235, Rept. No. IDO-12036. Avail. OTS, 24 pp.(1964)(Eng) ^{60}Co and ^{51}Cr can be removed from sep. waste streams contg ammonium citrate and alk. permanganate by a combined proc ess of pptn. and ion exchange. The general procedure used wa to neutralize the alk. permanganate with H_2SO_4 and to combin this soln. with the ammonium citrate soln. causing the oxidn. o the citrate. The Co and Cr originally present as complex anion were converted to cationic form by this process and scavenge from soln. by the MnO_2 ppt. formed by redn. of the permanganate The Co and Cr remaining in soln. were then removed by ion ex change on lignite, soil, and clinoptilolite. Distribution coeffs for Co and Cr were 56 and 1.2, 800 and 36, and 24 and 0.1 for soil, lignite, and clinoptilolite, resp. Lignite used in combinatior with the oxidn.-pptn. step resulted in the removal of 99.7% o the ^{60}Co and 95.1% of the ^{51}Cr from the waste streams. From *Nucl. Sci. Abstr.* 18(19), 4713(1964). TCNG

Radioactive wastes disposal. A. N. Marei. *At. Energ* (USSR) 18(3), 268–70(1965)(Russ). A review is given of the reports on the title subject that were presented at the Third International Conference on the peaceful uses of Atomic Energy, Geneva 1964. A. Aladjem

Biochemical research methods of the phenomenon and of the efficiency of the purification of waste by activated sludge. Lydia Vaicum. *Hidrotch. Gospodarirea Apelor Meteorol.* (Bucharest) 9(10), 546–9(1964)(Rom). A review is given of the mechanisms involved in the purification of waste by activated sludge and o the methods used to control them. Edgar Perry

Biological purification of pulp-manufacturing effluents. M. A Evilevich. *Tr. Vses. Nauchn.-Issled. Inst. Tsellyulozn.-Bumazhn. Prom.* No. 49, 111–31(1964)(Russ). Biol. purificatior of effluents of the Svetogorsk pulp and paper mill was studiec in pilot plant equipment with a capacity of 120 cu.m./day. Fundamental principles of the process used and calcns. of the process variables are discussed. To carry out the process, the effluents must be subjected to the following preliminary treatment: removal of coarse fibers; redn. of the concn. of fines to 75 mg./l.; deodorization through removal of H_2S, SO_2, and mercaptans; neutralization; and enrichment with nutrient elements (N and P). Measures must be taken to control foaming, to keep the compn. of the effluents const., and to introduce automation and remote control. The oxidn. capacity of aeration tanks

The effects of soaking seeds in various concns. of gibberellic acid on germination was detd. for different plants. Increased total seed germination was obtained in the case of *Hyoscyamus muticas*, *Lepidium sativum*, *Nepeta cataria*, and *Lithospermum officinale*. However, no effect was observed in *Peganum harmala*, and an adverse effect was obtained in seeds of *Digitalis purpurea*. a
R. L. DeVault

Role of gibberellic acid in the growth response of yeast cells to auxin. Naohiko Yanagishima (Univ. of Osaka, Japan). *Physiol. Plantarum* 18(2), 306–12(1965)(Eng); cf. *CA* 60, 4477*f*. In respiration-sufficient diploid strains of *Saccharomyces ellipsoides*, cells were elongated by auxin when gibberellic acid (GA) was given, together with auxin. When precultured in the presence of GA, cells were elongated by α-naphthaleneacetic acid (NAA) or by indoleacetic acid (IAA); but when precultured with NAA or IAA, cells were not elongated by GA. In a respiration-deficient mutant, whose cell elongation was stimulated by auxin without the aid of GA under special cultural conditions, the response of cells to auxin was not affected by GA under ordinary cultural conditions. b
J. J. Willaman

Effect of merapid on growth of plants. Stefan Peterfi and Edith Brugovitzky (Babes-Bolyai Univ., Cluj, Romania). *Physiol. Plantarum* 18(2), 359–67(1965)(Ger). Several cytostatic effects of merapid (I) (polymethylene glycol) were demonstrated on radish, mustard, lupine, broadbean, beet, corn, wheat, and 2 algae, *Coccomyxa dispar* and *Stigeoclonium variabile*. A given concn. of I inhibited germination of mustard and radish, but greatly stimulated germination of sugar beet. When inhibition occurred, amylase and catalase activities were reduced; when stimulation occurred, these enzymes were increased. I at 0.01–1.0% prevented division and growth of the algae cells. c
J. J. Willaman

Effect of gibberellic acid on elongation and geotropically induced curvature of Avena coleoptiles. W. E. Norris, Jr., and Beatrice Brotzman (S. W. Texas State Coll., San Marcos). *Physiol. Plantarum* 18(2), 403–9(1965)(Eng). Gibberellic acid (I) at 0.1 ppm. stimulated section elongation. Mixts. of I and indoleacetic acid showed no synergistic action on elongation. I at 1.0 ppm. increased the amt. of geotropically induced curvature resulting after stimulation for 90 min., but did not cause a detectable effect on elongation of the intact coleoptile tip. d
J. J. Willaman

Effects of substituted phenols on bud formation and growth of tobacco tissue cultures. T. T. Lee and F. Skoog (Univ. of Wisconsin, Madison). *Physiol. Plantarum* 18(2), 386–402 (1965)(Eng). The tissues were grown on nutrient medium supplemented with 4.6 μ*M* kinetin and 1.1–2.8 μ*M* indoleacetic acid. Compds. tested were *trans*-cinnamic acid, phenylpyruvic acid, L-phenylalanine, 4-hydroxyphenylpyruvic acid, L-tyrosine, 2-, 3- and 4-monohydroxycinnamic acids, caffeic acid, L-3,4-dihydroxyphenylalanine, ferulic and benzoic acids, 2-, 3-, and 4-hydroxybenzoic acids, 4-hydroxybenzaldehyde, 4-methoxy- and 4-hydroxybenzoic, 2,4-, 2,5- and 3,4-dihydroxybenzoic, phenylacetic, 2-hydroxyphenylacetic and 3,4-dihydroxyacetic acids, phenol, catechol, and hydroquinone. In stimulating bud formation, the monohydroxy compds. were more active than the unsubstituted ones, and OH substitution at the 4- or 2-position was more effective than at the 3-position. In the benzoic acid derivs., the presence of both OH and a carbonyl was beneficial, but neither group was essential. 3,4-Dihydroxy derivs. and ferulic and sinapic acids inhibited bud formation. The 2,4- and 2,5-dihydroxybenzoic acids were weakly active, and the 2,3,4- and 3,4,5-trihydroxybenzoic acids were inactive. The evidence with phenylacetic acid derivs. was that their action on bud formation was limited to cultures with the higher kinetin levels. Dihydroxyphenols enhanced callus growth, whereas the monohydroxy phenols and related compds. which induced bud formation tended to inhibit growth. In order of decreasing auxin effectiveness were 2-methoxyphenylacetic, phenylacetic, 2- and 4-hydroxyphenylacetic and 4-hydroxyphenylacetic acids. e
J. J. Willaman

Inhibition of the germination of mustard seeds by saturated fatty acids. N. Le Poidevin (Roy. Vet. Coll., London). *Phytochemistry* 4(3), 525–6(1965)(Eng). Germination of *Sinapis alba* seeds was inhibited by a series of satd. fatty acids when applied at concns. of 0.01–0.1%. The greatest inhibition was with nonanoic acid. f
J. B. Harborne

State of investigations into (2-chloroethyl)trimethylammonium chloride (CCC) and related compounds with special consideration of their effect and possible application in agriculture. Marian Michniewicz. *Postepy Nauk Rolniczych* 11(6), 25–38(1964) (Pol). A thorough review of recent world literature with a bibliography of 58 titles. g
Anna H. Koffler

Keeping quality, flower size, and flowering response of three varieties of Easter lilies to gibberellic acid. James D. Kelley and Allen L. Schlamp (Univ. of Kentucky, Lexington). *Proc. Am. Soc. Hort. Sci.* 85, 631–4(1964)(Eng). Gibberellic acid, 0–1500 or 0–2000 ppm., was applied to buds of the varieties. Croft, Ace, and Nellie White, when from 1–6.5 in. long. The treatments had no significant effect on time of flowering or flower size but prolonged the keeping qualities of uncut flowers by delaying first-petal necrosis and 50% petal necrosis by as much as 35%. h
Lawrence P. Miller

Effects of *N*-dimethylaminosuccinamic acid (B-Nine) on vegetative and fruit characteristics of apples, pears, and sweet cherries. L. P. Batjer, Max W. Williams, and George C. Martin (U.S. Dept. of Agr., Wenatchee, Wash.). *Proc. Am. Soc. Hort. Sci.* 85, 11–16(1964)(Eng). Sprays (for the most part 500 to 2000 ppm. applied 3 times at 10-day intervals beginning 15 to 17 days after full bloom) markedly reduced shoot growth and increased the amt. of bloom the following spring. Reduced growth was accompanied by shorter internodes and 80–100% more leaves per linear unit. Other effects were a redn. in fruit size, larger leaves, delay in blossoming, shorter fruit stems (Golden Delicious), and advanced maturity of sweet cherries.
Lawrence P. Miller

Effects of *N*-dimethylaminosuccinamic acid (B-Nine) on apple quality. Max W. Williams, L. P. Batjer, and George C. Martin (U.S. Dept. of Agr., Wenatchee, Wash.). *Proc. Am. Soc. Hort. Sci.* 85, 17–19(1964)(Eng). Sprays at 1000 to 2000 ppm. applied 3 times shortly after full bloom largely prevented the development of scald on Red Delicious apples in storage and significantly extended the shelf life after removal from storage. There were no significant differences in sol. solids, pH, and total titratable acidity. There was less water-sol. pectin and slightly more total pectin in the fruit from treated trees after storage.
Lawrence P. Miller

Ethylene action and the ripening of fruits. Stanley P. Burg and Ellen A. Burg (Univ. of Miami, School of Med., Miami, Fla.). *Science* 148(3674), 1190–6(1965)(Eng). Mostly a review of reported evidence that C_2H_4 is a fruit-ripening hormone. Kinetic studies of the author are discussed which indicate that CO_2 competitively inhibits the tissue swelling effect of C_2H_4 on etiolated pea stem tissue, and that the effect of O_2 can be explained by postulating that it must be present at the receptor site for the C_2H_4. Their studies on the C_2H_4-like activity of various compds. indicate C_2H_4 binds at a metallic receptor site in tissues. i
John M. Lawrence

Certain physiologic actions of kinetin in small concentrations. Kunihiko Shono and Toshio Yamaki (Univ. Tokyo). *Sci. Papers Coll. Gen. Educ., Univ. Tokyo* 13, 203–11(1963)(Eng). In the presence of 1 mg. of indoleacetic acid (I)/l., 0.1 mg. of kinetin (II; 6-furfurylaminopurine)/l. promotes wt. increase of the callus and that of the original tissue of hypocotyl quantities of *Helianthus annuus;* however, growth is hindered by 0.01 mg. of II/l. In the presence of 0.01–10 mg. I/l. 0.1 and 1 mg. II/l. increase the wt. of carrot root crowns; 0.01 mg. II/l. inhibits the growth. II concns. of >0.1 mg./l. increase the wt. and the growth of the cotyledon crowns of *H. annuus;* the growth is inhibited by about 10 mg. of II/l. The expansion of hypocotyl cross sections is inhibited by 1 and 10 mg. II/l. (in the presence of 1 mg. I/l.); however, it is promoted by 0.01 and 0.001 mg. of II/l. From *CZ* 1964(48), Abstr. No. 1215. j
MNCR

The persistence of two novel methoxyurea preparations in the soil. K. Homburg and F. Mariouw Smit (Farbwerke Hoechst A.-G., Amsterdam). *Z. Pflanzenkrankh. Pflanzenschutz, Sonderh.* 2, 145–50(1964). Linuron (Afalon) and monolinuron (Aresin) were applied to a moor soil that contained 40% humus and to an impoverished sand, at 1, 2, 4, and 8 kg./ha., to a clay sand contg. 20% humus, at 1.5 kg./ha., and to a clay-sand soil contg. 15% humus, at 3 kg./ha. Soil samples were tested for phytotoxicity to oats, by comparison of the wts. of seedlings with those grown in treatments with known amts. of the herbicides applied directly to test pots. One month after the applications, 40% linuron and 60% monolinuron remained and no evidence of residues of up to 2 kg. applications could be found after 3 months. Linuron was inactivated more rapidly than monolinuron. With the same rainfall, the disappearance was more rapid the higher the humus content. Residues of the excessive dosages of 4 and 8 kg./ha. were found after 6 months. No residues were found in the sandy soils in the 15–20-cm. depth. k
E. L. Green

Gas-liquid chromatography of organic herbicides. Jun Kanazawa. *Bunseki Kagaku* 14(5), 481–3(1965)(Japan). A thermal cond. detector and 1 m. × 4 mm. stainless steel columns packed with 4 stationary phase liquids (5%) on 48–60-mesh Celite 545, operated at 190° with a 75 ml./min. He-flow rate were used for analysis of 11 herbicides (2,6-dichlorobenzonitrile, Me 2-methyl-4-chlorophenoxyacetate, Me 2,4-dichlorophenoxyacetate, DNOC, PCP, 3,4-dichloropropionanilide, 2,4-dichlorophenyl-4-nitrophenyl ether, 2-methyl-4-chlorophenoxyaceto-*o*-chloroanilide, propazine, simazine, and prometryn). Fire to 10 μl. sample soln. (10% in $HCOMe_3$ or Me_2CO) was injected into a vaporizer at ~240°. Of the stationary phase liquids used (high-vacuum silicone grease, FS-1265, SE-30, and poly(ethylene adipate) (PEGAE)), PEGAE showed comparatively high resolution. l
Y. Ito

The use of chemical agents for the control of couch grass. H. Ansorge (Inst. Saatgut- Ackerbau, Halle, Ger.). *Deut. Landwirtsch.* 15, 128–30(1964)(Ger). Tests were run on the