Water Poisoning in Man and Animal, together with a Discussion on Urinary Calculi.

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I. INTRODUCTION.

In this paper the following points concerning the harmful effects of drinking water upon man and animal are discussed: (a) Poisoning with excessive quantities of "normal or wholesome water" (III A). (b) Poisoning due to the drinking of excessively cold water (II B). (c) Poisoning due to drinking of distilled water (III). (d) Poisoning due to drinking of excessively mineralised waters (IV). (e) The role played by excessively saline waters in the causation of urinary calculi (V).

Under IV and V only water from bore-holes and wells will be referred to. It might be mentioned that water (effluents) from mines and factories may contain toxic quantities of cyanide, lead, iron (sulphate), manganese, sulphuric acid, zinc (sulphate), aluminium, arsenic, copper, chlorides, etc. Dr. C.S.M. Hopkirk, Officer in Charge, Veterinary Laboratory, Wallaceville, Wellington, New Zealand, verbally informed one of us (D.G.S.) that at a certain place in New Zealand water seeping through a mountain side contains toxic quantities of arsenic. The mountain consists of arsenic-containing ore. In one case where soil and water from a well in South West Africa were submitted for analysis traces of arsenic were found in the soil but none in the water.

Kooymans (1938) referring to the removal of manganese from drinking water states that wholesome drinking water should not contain more than 0.1 mg. of manganese per litre. Water containing excessive quantities of manganese causes brown stains in clothing (textile industries), has detrimental effects on fermentation (breweries), and causes the deposition of manganese in the piping.
In the course of investigations conducted by one of us (D.G.S.) into problems of suspected poisoning of stock in South West Africa, the North-Western Cape Districts (Kenhardt, Gordonia), and the North-Western Transvaal it was evident that both man and animal suffer as a result of drinking highly mineralised water. In a number of cases the water was so poisonous, due mainly to the presence of large quantities of nitrates and chlorides, that the animals died within an hour after having drunk it. Excessively saline waters occur chiefly in the semi-arid and arid regions of South Africa. It should be mentioned that otherwise wholesome water containing harmful quantities of fluorine is of fairly wide occurrence in South Africa (Southern and Western Transvaal, North-Western Cape, South West Africa). Numerous complaints concerning the detrimental effects of drinking water on man and animal have been received from these areas. Many specimens of suspected waters have been analysed and the results are referred to in this article.

Methods of Analysis.

The following methods are being used at Onderstepoort in the analysis of specimens of water:

(a) Total Solids.—The water is evaporated to dryness on a water bath, heated in an air-oven at 100° C. for two hours and weighed.

(b) Temporary Hardness.—The water is titrated with hydrochloric acid using methyl orange as indicator according to Achner’s method (Threadwell and Hall, 1930).

(c) Nitrates.—The method used is that of Caron and Raquet (1936).

(d) Fluorine.—The method is a modification of the method of Willard and Winter (1933) and that of Armstrong (1936).

(e) Chlorides.—The chlorides in the water are precipitated with silver nitrate and the excess silver nitrate titrated with potassium thiocyanate using ferric alum as indicator (Malan and van der Lingen, 1931).

(f) Sulphate.—The method used is that given by Scott (1920).

(g) Calcium.—The calcium is precipitated with ammonium oxalate as calcium oxalate and the latter titrated with potassium permanganate (Godden, 1937).

(h) Magnesium.—Calcium when present is removed with ammonium oxalate and magnesium precipitated as magnesium ammonium phosphate in which phosphorus is determined colorimetrically, (Malan and van der Lingen, 1931, and Holzapfel, 1934).

(i) Potassium.—Potassium is precipitated as potassium cobalti nitrate in which it is determined titrimetrically with potassium permanganate (Malan and van der Lingen, 1913, and Holzapfel, 1934).
(j) Sodium.—Sodium is precipitated as uranyl-zinc-sodium acetate which is dissolved in dilute acetic acid and determined colorimetrically after the addition of potassium ferro-cyanide, (Louw, 1933).

II. POISONING DUE TO DRINKING OF "NORMAL OR WHOLESOME WATER".

A. Poisoning due to Drinking Excessive Quantities of Water.

Davis (1935), Helwig, Schultz and Curry (1935), Kunstmann (1933), Rowntree (1926), Steggerda (1935), and Wolff (1935) refer to water poisoning induced by the consumption of excessive quantities of water. Studies to this effect have been made on human beings and animals. Moss and Brockbank (Helwig, 1935) have observed extreme muscular cramps in workmen who perspired freely and drank large quantities of water. Salt water immediately relieved these cramps. Rowntree (1926) quotes a case in which a man suffering from diabetes insipidus drank up to 40 liters of water on one day.

A number of investigators (Priestley, McCallum and Beeson, Amberg and Austin, Helwig et alia, 1935) produced water intoxication in themselves by drinking up to 3 liters of water in 20 minutes. Helwig and his collaborators (1935) observed a case in which death apparently resulted from water-intoxication wherein the patient absorbed nine liters of tap water by proctolysis.

Rabbits, dogs, cats, guinea pigs and rats develop symptoms of water poisoning within 3 to 5 hours when they are drenched with 50 c.c. of water per kilogram bodyweight at half-hourly intervals, (Helwig and collaborators, 1935).

In water poisoning there is increased excretion of sodium chloride and the blood is diluted. Some authors associate water poisoning with loss of chlorides and alkalosis, whilst others hold that the salt-water balance is disturbed resulting in cerebral oedema, which is the direct cause of the symptoms.

McGange (1936) describes aberrations of flavour, cramps, weakness, lassitude, and severe cardiorespiratory distress on exertion, in experimental sodium chloride deficiency in man.

Symptoms of water poisoning.—Head-ache, dizziness, restlessness, salivation, chills, fullness of abdomen, vomiting, dyspnoea, fibrillary twitchings of the muscles, cramps in the legs and clonic convulsions.

Post mortem appearances.—Helwig and his collaborators (1935) state that there are no gross pathological lesions in rabbits which have died from water poisoning. In some cases there was cloudy swelling of the livers, the cut surface of which was shiny and moist. The brains were swollen and the surface vessels bloodless, and the brain tissue showed vacuolisation. The chloride content of all the organs was reduced except that of the liver whose chloride content had increased by 10 per cent. In the brain the chloride
content was reduced by approximately 50 per cent. They warn against the administration of large quantities of water particularly in post-operative cases as there is a danger of water poisoning.

B. Poisoning Due to Drinking Excessively Cold Water.

Moutax (1937) describes the following symptoms in cattle as a result of ingesting cold water:—(a) temporary atony and tympany of the rumen; (b) generalised vasomotor disturbances; dyspnoea, congested mucous membranes, loss of appetite, low skin temperature, and haematuria (frequently). These symptoms may last for three days after which period the animals may recover; (c) Localised vasomotor disturbances: cerebral congestion with haemorrhage in one case. In one case there was fatal pulmonary haemorrhage. Moutax observed the following symptoms in a two-year old heifer immediately after ingestion of cold water: total loss of muscular coordination, sterterous respirations, loss of consciousness, and coma interrupted by convulsions. The animal took several months to recover completely.

III. POISONING DUE TO DRINKING OF DISTILLED WATER.

From the discussion under II A it is obvious that large quantities of distilled water will be more likely to induce "water poisoning" than tap water owing to the absence of salts from the former.

Straub (1934) reports that the pharmacologist Starkenstein in Prague drank early in the morning on an empty stomach one litre of distilled water within a short time. Diuresis followed and within four hours 900 c.c. of urine instead of the usual 200 c.c. were voided. Starkenstein experienced no ill-effects. After one litre of physiological saline (0·9 per cent. NaCl) was drunk only 250 c.c. appeared in the urine.

Straub states that large quantities of distilled water will cause distension (swelling) of the cells of the intestinal mucous membrane, the cell globuline will be precipitated, the function to absorb water will be retarded and if this were to occur over the whole intestine diarrhoea will follow. Anybody, Straub continues, who quenches his thirst by eating snow is aware of this fact.

IV. POISONING DUE TO DRINKING OF WATER CONTAINING EXCESSIVE QUANTITIES OF SALT.

A. Quantities of Water taken by Human Beings and Animals.

This depends upon the following factors: (a) Humidity and temperature of the atmosphere: The lower the degree of humidity and (or) the higher the temperature the greater will be the quantity of water ingested. (b) Nature of feed or food: the drier the feed or
food the greater the consumption of water will be. (c) Exertion: The greater the physical exertion (work) the more water will be consumed as a result of excessive perspiration. Any condition associated with perspiration will have this effect. (d) Degree of salinity of the water: The higher the degree of salinity of the water the more likely it will be to induce diarrhoea and diuresis. This in turn is partly responsible for the fact that man or animal drinking such saline waters have great difficulty in quenching their thirst. The inevitable result is increased consumption of water. This has been on several occasions the personal experience of one of us (D. U. S.) who was forced to drink saline water in the course of his investigations. In the areas concerned he has seen cattle drinking natural saline water until the abdomen was distended. They would then walk away a short distance from the drinking trough and stand and look back at the trough as if contemplating another drink. Some of the cattle were actually seen to return to the trough and to attempt to drink more water. These animals purged freely and the calves were stunted and pot-bellied. (a) Bingham (1938) in a discussion on the water requirements of surgical patients writes "although each case must be separately considered, the minimal fluid intake in the days following operation should be from 3,000 to 4,000 c.c. a day (approximately 5-7 pints) if necessary by the intravenous route". He continues "if necessary loss from vomiting, etc. occurs the extra volume of fluids so lost must be added to the amount which the patient in any case requires".

In his experiments with water containing calcium chloride or calcium sulphate Heller (1933) found that on some days cows, weighing approximately 375 to 425 Kg., consumed up to thirteen gallons (= approximately 11 Imperial gallons). With 1·5 per cent. salt (NaCl) water and "pure water" he recorded daily quantities of up to almost twenty gallons (= approximately 17 Imperial gallons) drunk by cows.

Ashe and Moseenthal (1937) studied the protein, salt and fluid consumption of a thousand residents of New York and found that the majority of them took a moderate quantity of fluid of one litre or more daily.

Garner and Sanders (1937) found the mean consumption of water per Large White suckling sow to be 43 lb. (= 4.4/10 gallons) daily. The quantity of water consumed by the same animal varied from day to day and was approximately the same in winter and summer.

From all the information at our disposal the authors are of the opinion that the following quantities of water may be consumed daily by man and animal under adverse conditions (dry and hot climates, droughts, exercise): man—one gallon (4·5 litres) or more; cattle—10 to 16 gallons; horses—8 to 10 gallons; sheep and goats—3 to 4 gallons; pigs—3 to 5 gallons.

In certain diseases (diabetes) it appears possible for a human being to drink up to 40 litres (= 9 gallons) of water on one day (see IIA).
B. SALTS COMMONLY FOUND IN EXCESSIVELY SALINE AND "HARD" WATERS AND THEIR EFFECTS ON THE SYSTEM.

The salts most commonly found in highly mineralised South African waters are the following: (a) Carbonates and bicarbonates, (b) calcium, (c) chlorides, (d) fluorides, (e) magnesiuim, (f) nitrates, (g) potassium, (h) sodium, (i) sulphates, and (j) sulphides.

A "soft or fresh water" is one which contains only a small amount of dissolved solids. A "hard water" is characterised by the presence of dissolved salts of calcium, magnesium, iron and to a certain extent also by the presence of sodium and potassium salts. The presence of calcium sulphate (gypsum) in water causes it to be permanently hard and it cannot be softened by boiling. A "temporary hard water" is one containing the bicarbonates of calcium (CaHCO₃) and magnesium (MgHCO₃) and which can be rendered fairly "soft" by boiling. A part of the carbon dioxide is expelled by boiling and the fairly insoluble CaCO₃ and MgCO₃ are precipitated (encrustation in kettles). It is common knowledge that with "hard waters" more soap is necessary than with "soft waters" as a certain quantity of soap must dissolve before a lather is formed. The presence of calcium and magnesiuim determine the amount of soap to be used before the water is rendered soft.

The hardness of water is usually expressed as parts of calcium carbonate per 100,000 parts of water. If a solution contains one part of calcium carbonate in 100,000 parts of water, it is said to possess one degree of hardness (French). In Germany it is expressed in parts of calcium oxide per 100,000, while in England it is expressed as grains of calcium carbonate per Imperial gallon and in the United States of America as grains of calcium carbonate per U.S. gallon, i.e. 1 degree of hardness (French)

- 0.56 degrees on German scale
- 0.70 degrees on English scale
- 0.585 degrees on U.S. scale.

"Saline and alkaline waters" are those containing alkalis like the carbonates, bicarbonates and hydroxides of sodium and potassium and sulphates and chlorides of potassium, calcium and sodium. The term "brak water" or "brackish water" used in South Africa is a very wide term and includes all waters rich in minerals such as the chlorides, sulphates and carbonates of potassium, magnesiuim, sodium and calcium.

Butter (1937) collected and analysed more than a hundred specimens of bore-hole water in South Africa and states that "brak water" forms the sole drinking water of the great majority of South Africa's farmers and small town inhabitants dependent upon bore-hole water.

The presence of salts in underground water supplies is due to the water percolating or flowing through salt deposits containing the abovementioned minerals.
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(a) Bicarbonates and carbonates:

Kobert (1906) states that sodium bicarbonate raises the alkalinity of the tissue fluids and enhances the oxidation processes in the body. Ingestion of excessive quantities of sodium bicarbonate causes dilatation of the stomach, anorexia and anaemia.

Fröhner (1919) reports that a cow which had received 800-900 gm. of sodium bicarbonate aborted, groaned and bellowed, and had to be slaughtered, and that 10-15 gm. of potassium carbonate is fatal for the dog (heart failure and collapse). Dogs fed daily with 15 gm. of sodium bicarbonate for weeks showed vomiting, diarrhoea and loss in condition (Fröhner, 1919).

Reid (1921) describes sodium carbonate poisoning in sheep due to the drinking of effluents from dairy factories. The symptoms were a staggering gait and hurried respirations. The animals soon lay down and died. The following were the post mortem appearances: Hypermemia of the subcutaneous tissues, imperfect clotting of the blood, hyperaemia of the small intestines with subserous haemorrhages, slight congestion of the liver, in very acute cases abomasum filled with dark blood-stained fluid contents, intense hyperaemia of abomasal mucosa with haemorrhages.

Heller and Larwood (1930) conducted experiments upon rats and other small animals with single salts and also with mixtures of calcium chloride, calcium sulphate, sodium bicarbonate, sodium carbonate, and magnesium sulphate. Drinking water containing 20,000 parts of sodium carbonate per million parts (i.e. a 2 per cent. aqueous solution) was found to be decidedly deleterious and reproduction was interfered with at quite low levels. Sodium bicarbonate proved to be less injurious. In subsequent experiments upon rats Heller (1932 and 1933) established that drinking water containing 1 per cent. (10,000 p.p.m.*) of sodium carbonate resulted in unsatisfactory growth of the offspring, while a 1·9 per cent. solution caused a rough coat, red eyes, and diarrhoea in the mature rats and a very high mortality in their young. A 1·5 per cent. of sodium bicarbonate caused undersized adults and impeded growth in their offspring, while there were unsatisfactory growth and appearance with 2 per cent. solutions. Experimenting with 0·5 and 1·0 per cent. aqueous solutions of caustic soda (NaOH) he found practically normal growth with the former solution, the latter causing retarded growth, "dirty animals", marked nervousness, sore eyes and diarrhoea.

Linton and Wilson (1933) refer to sodium bicarbonate poisoning in pigs due to the feeding of "Flour sweepings" containing 33·7 per cent. of this alkali. The symptoms seen were excessive thirst, animals appear to be in pain, stood with their heads lowered and oblivious to their surroundings, and staggered on their front legs. Only one pig died after the sweepings were removed and milk given. Autopsy revealed inflammation of the stomach. Linton furthermore describes alkali poisoning in pigs through accidental discharging into the milk given to the pigs of the alkali used for cleansing the milk utensils.

* Parts per million parts of water.
Witter (1936) added sodium bicarbonate to the drinking water of chicks and found that: “(1) Sodium bicarbonate given in the drinking water in the usual dosage (1 lb. to 5 gallons or 0·6 per cent. solution) caused chicks to drink more water than normal and produce moist droppings. Chicks two weeks old developed pale and swollen kidneys from this dosage, but chicks three weeks old and older were not noticeably injured. (2) A double dose (1·2 per cent. solution) of soda caused chicks to drink more water than those fed the 0·6 per cent. solution and produce watery droppings. Chicks two to eight weeks old were seriously injured by this dosage within one to three days and deaths occurred within this time. (3) Two and four-tenths per cent. solution of soda reduced water consumption below normal for chicks under four weeks of age. The injurious effects of this dosage were noted within a day and deaths occurred within three days. (4) Mature cockerels were injured with a 2·4 per cent. solution of soda, but were not affected by a 1·2 per cent. solution. It was apparent throughout the project that the younger the chicks the more susceptible they were to soda injury. (5) Kidneys from chicks affected by feeding soda became pale, swollen and engorged with urates. The kidney tubules showed degenerative and exudative changes indicating severe injury. (6) Chicks affected by feeding soda showed an increase in kidney weight, and increase of approximately four times in uric acid per gram of kidney and in uric acid in the blood”. He found the injury caused by feeding sodium bicarbonate to chicks similar to the pathology and blood chemistry changes present in visceral gout. Two weeks old chicks consumed from 45 to 113 c.c. of “normal water” daily.

Carbonates, bicarbonates and caustic soda will tend to cause alkalinity of the gastrointestinal juices (change in pH), consequently the continued drinking of alkaline waters will lead to serious digestive and other disturbances. Carbonates are more harmful than bicarbonates.

(b) Calcium:

Shaw (1929) administered to ducks, weighing from 600-800 gm. salts and mixtures of salts either in solution or dry in capsules. He found 1·4 gm. of calcium chloride non-toxic and 4·8 gm. lethal within thirty-five minutes. The symptoms were those of general depression rather than paralysis. In experiments upon small animals Heller and Larwood (1930) found that a combination of 20,000 p.p.m. of sodium chloride (=2 per cent. solution) and 5,000 p.p.m. of magnesium or calcium chloride (=0·5 per cent. solution) inhibits growth. They state that calcium and magnesium ions are more harmful than the sodium ion. According to Heller (1932) growth is normal in rats on water containing 2 per cent. (20,000 p.p.m.) of calcium chloride, but lactation is inhibited. At higher levels the results were similar to those obtained with sodium chloride, 2·5 per cent. solutions of calcium chloride causing death (Heller, 1933). He found furthermore that (1) waters saturated with calcium sulphate (CaSO₄·2H₂O) i.e. a 0·24 per cent. solution (=2,400 p.p.m.) did not interfere with normal growth and reproduction. (2) A
saturated aqueous solution of calcium hydrate \([\text{Ca(OH)}_2]\), i.e. a 0.18 per cent. solution (1,800 p.p.m.), had no apparent ill-effects through four generations of rats with the exception of a somewhat greater mortality of the young.

Katz and Katz (1937) found that Ca and K ions have a direct stimulating action on the adrenals and increases adrenal secretion without acting on the central nervous system. Both ions increase blood pressure and they state that "there is no doubt that both KCl and CaCl\(_2\) have definite vascular actions of their own".

From experiments conducted by Heller and Haddad (1936) with drinking water upon rats it appears that calcium in the form of CaCl\(_2\) is most favourably absorbed and that "excessive amounts of calcium seem to displace magnesium from the body". They state that "the phosphorus in these studies is found in the feces in greater amounts than previously reported: especially is this true when large amounts of calcium and magnesium salts are present."

Gardner and Burget (1938) found that calcium ions retard the absorption of glucose from the intestine.

Glatzel (1938, a) states that normal nerve function appears to be associated with the presence of calcium, and that calcium activates lipase and esterase action, the coagulation of blood and milk, and bone formation. Calcium salts have diuretic effects, but their mode of action is unknown. Infusions of calcium salts are stated to induce hyperglycaemia and this means a stimulation of hormone action by calcium. Calcium is further stated to increase the colloid content of the thyroid. "Does this mean stimulation of the specific action of the thyroid by calcium", Glatzel asks, seeing that in myxoedema there is an inclination towards calcium retention and the thyroid hormone acts "calcium removing" and also because calcium excretion in Basedow disease is very high.

(For further information concerning calcium see magnesium and chlorides.)

\(\text{(c) Chlorides.}\)

In experiments in which chlorides were injected intravenously into dogs Joseph and Meltzer (1909) found the degree of toxicity of the chlorides of magnesium, calcium, potassium and sodium to be in the order in which they are given here. Furthermore they found that Mg. is twice as toxic as Ca, Ca is three times as toxic as K, and Na many times less toxic than Mg, Ca and K. They state that "the smaller the amount of the ion in the blood serum the more toxic it is in the infusion".

In experiments upon dogs Glatzel (1936) proved that the insulin-action in the liver is dependent upon the presence of chlorine. Heller and Haddad (1936) state that approximately 90 per cent. of the chlorides ingested with the water is excreted through the urine, and there is also an increase in faecal chlorides, especially when acid-producing ions accompany the chlorides, probably due to cathartic action of the increased salt content of the intestinal contents.
Buffagni (1936) describes poisoning in pigs, which received large quantities of brine in their food. Five deaths occurred after a number of the animals had exhibited anorexia, inco-ordination of movement and severe diarrhoea. The post mortem appearances were gastroenteritis, cystitis and nephritis. A cow to which was administered 1 Kg. of sodium chloride became seriously ill and was killed. Autopsy revealed intense gastroenteritis. According to Buffagni the toxic dose of common salt for the pig is 1 gm. per Kg. of bodyweight and he considers that cattle should not be given more than 60 gm. of salt daily.

Glatzel (1938) found that the absorption of 1 per cent. solutions of glucose from the intestine of dogs is enhanced by the addition of 0·1 to 0·5 per cent. sodium chloride and is retarded by higher quantities of salt (NaCl).

Rambe (1938) "advanced the theory that a certain form of malnutrition ('torkan') may be due to excess of common salt in the ration of cows, and that the toxic dose of NaCl is smaller than is generally believed". He fed a bovine common salt in amounts increasing from 50 to 250 gm. daily. The animal developed signs of pruritus and abnormal quantities of salt were excreted by the skin. There were also polyuria and attacks of renal haemorrhage lasting for 6-24 hours. During the experiment which lasted for over twelve months the red blood cell count of the animal decreased from 10 to 5·7 million per c.mm. Velu (1938) conducted experiments upon sheep, cattle and guinea pigs in an attempt to determine the optimal amount of salt water compatible with good health. Unfortunately the periodical in which the original article appeared is not available in South Africa and no details of the experiments are given in the abstract. Velu found "that cattle could drink large quantities of salt water without increasing the water content of the tissues, which had been suggested by other authors". (For further information concerning the effects of chlorides see calcium, magnesium and sodium).

*(d) Fluorides.*

As a comprehensive review of the effects of different quantities of fluorine upon man and animal has been published recently by one of us (Steyn, 1938), only the most salient points concerning the effects of the presence of appreciable quantities of fluorine in drinking water will be discussed here.

Underground water flowing through phosphatic and other fluorine containing strata contains appreciable quantities of fluorine. Smith, Lantz and Smith (1931) were among the first to produce evidence that mottled enamel is caused by fluorides in water supplies, as they found that concentrations of fluorine exceeding 1 p.p.m. (parts per million) induced mottled enamel in young rats.

Ostrem, Nelson, Greenwood and Wilhelm (1932) found 10 to 15 p.p.m. of fluorine in samples of water obtained from areas in Iowa where mottling of teeth occurs. Ainsworth (1934) saw mottled teeth in a large number of school children of the Maldon
School, Essex. Their drinking water contains from 4.5 to 5.5 p.p.m. of fluorine. Approximately 90 per cent. of the children who were born and grew up in the affected areas showed mottled teeth. Adults who settled in the affected area after eruption of their permanent teeth were not affected. Also De Beer (1934) refers to the determination of small quantities of fluorine in water and their clinical significance.

In North Africa 4 out of 12 head of range cattle were found to have mottled teeth owing to the presence of fluorine in their drinking water, (Dean, 1935). Dean rightly remarks that their milk may contain harmful quantities of fluorine. Riester, Greenwood and Nelson (1936) found that the feeding to dogs of fluorine levels comparable with those found in some drinking waters produced histologic changes in the small intestine, spleen, bladder, mesenteric lymph nodes and thyroid glands. The experiments lasted from 7 to 12 months.

Dean (1936) states that there are approximately 335 chronic endemic dental fluorosis areas in the United States of America and 175 in the Argentine. Such areas are also to be found in England, Italy, North Africa, India, China and Japan. From the available information in regard to the mottling of teeth in children through the continual use of drinking water containing fluorine Dean compiled the following table:

1. Water containing 1 p.p.m. of fluorine: approximately 10 per cent. of the children will develop a mild form of mottling of the teeth.
2. Water containing 1.7 to 1.8 p.p.m. of fluorine: 40 to 50 per cent. of the children will show a mild form of mottling of the teeth.
3. Water containing 2.5 p.p.m. of fluorine: 75 to 80 per cent. of the children will be affected, with 20 to 25 per cent. of the cases showing a moderate to severe type of mottling.
4. Water containing 4 p.p.m. of fluorine: 90 per cent. of the children will be affected, with 35 per cent. or more of the cases showing moderate to severe mottling.
5. Water containing 6 p.p.m. of fluorine: 100 per cent. of the children will be affected.

He states that clinical observations should be made on children from 9 to 12 years of age in order to obtain reliable figures in regard to the incidence of mottled teeth.

No mottling of teeth is discernible in areas where the drinking water contains 0.6 p.p.m. of fluorine, (Editorial, 1936). Walker and Spencer (1937) analysed 250 samples of water from different parts of the province of Alberta, Canada, where mottled enamel of the teeth is endemic, and found that a relation exists between the fluorine content of the drinking water and the prevalence of mottled enamel. It is of interest to note that Walker and Spencer state that after a considerable amount of work they found that they had to use the following methods of analysis in order to obtain
reliable figures for the amounts of fluorine present in water: (a) a modification of Sanchi's method for amounts of fluorine between 0 and 0.75 p.p.m.; (b) Sanchi's regular method for amounts of fluorine between 0.75 and 3 p.p.m.; and (c) a revision of Armstrong's modification of Burkh and Abbott's distillation method which is based on the macro method of Willard and Winter for amounts greater than 2 p.p.m.

Two specimens of water submitted by Dr. M. Zsehokke, Government Veterinary Officer, Mariental, South West Africa, were found to contain 0.97 and 1.3 parts of fluorine per million parts respectively. Subsequently specimens of water from other parts of South West Africa also proved to contain dangerous quantities of fluorine.

Brown (1935) states that Kenhardt district is unique for the large proportion of children which develop mottled teeth (patchy brown and in some cases black stains). This occurs only on farms where the water is particularly brackish. Arrangements have been made for specimens of water to be analysed as we have good reason to suspect that the mottled teeth are due to excessive amounts of fluorine in the drinking water. In a number of cases these suspicions have already been confirmed.

Shott and his co-authors (1935) describe "mottled teeth" and chronic fluorine poisoning in human beings in the Madras Presidency due to the drinking of water containing fluorine. It is of interest to note that even the milk teeth showed mottling. Unfortunately no mention is made of the quantity of fluorine present in the drinking water. A note-worthy and very important observation made by these authors is that symptoms of chronic fluorine poisoning set in only after approximately thirty to forty years. The symptoms described by them are:—a recurrent general tingling sensation in the limbs or over the whole body. This is followed by pain and stiffness, especially in the lumbar region of the spine. There is ossification of the tendons and gradual synostosis of the entire vertebral column until there is complete stiffness of the back ("poker back"). These symptoms are accompanied by cachexia, slight anaemia, anorexia, signs of pressure on the spinal cord (exostoses), loss of sphincter control, and impotence, which is common. Ultimately the affected individuals are completely bedridden with mental powers unimpaired. Death is usually due to some intercurrent disease.

(c) Magnesium.

Künsenman (Fröhner, 1919) found that the daily administration of 20 gm. of magnesium chloride to pigs, 60 gm. to sheep and 400 gm. to horses had no detrimental effects. Only after the administration of 800 gm. of magnesium chloride did the horses develop symptoms of poisoning, (diarrhoea and heart disturbances.)

Becka (1929) states that (1) magnesium "leads" calcium in the living organism; (2) this does not only apply to the absorption of calcium from the food, but also in its biological use in the body.
and its excretion from the body; and (3) magnesium inhibits absorption of calcium from the food and increases its excretion from the body. According to him each magnesium ion is followed or accompanied by ten ions of calcium and the relation of magnesium combinations to calcium in the body is of a three-fold nature, namely, (i) the magnesium sulphate group which displaces calcium from the body; (ii) the magnesium chloride group which binds calcium for twenty-four hours; and (iii) the magnesium hydrate group which binds calcium for seven to ten days. Magnesium chloride is easily absorbed and also magnesium lactate and magnesium hydrate, hence the increase in calcium absorption from the food for some time. On the other hand magnesium sulphate is absorbed only to a slight degree with the result that calcium is excreted with it. Becka maintains that he has proved the above contentions chemically, biologically and clinically.

Shaw (1929) found 1·5 gm. of magnesium chloride, administered either in solution with a pipette or dry in capsules, toxic for ducks weighing 600 to 800 gm., while 4·5 gm. proved fatal. They exhibit symptoms of general paralysis, being entirely helpless. Heller (1932 and 1933) and Heller and Larwood (1930) conducting experiments upon small animals and domestic animals found that (1) drinking water containing 1 per cent. (i.e. 10,000 p.p.m.) of magnesium sulphate causes poor growth in young rats and emaciation in adults; higher concentrations caused subnormal growth, rough coat and diarrhoea. The harmful effects of similar concentrations of magnesium chloride were slightly less marked; and (2) waters containing sodium chloride do not interfere with normal growth and maintenance of laying hens until the concentration has reached 1·5 per cent or more. Calcium chloride is not tolerated by them (hens) as well as sodium chloride, while ‘ magnesium sulphate is tolerated surprisingly well’. These conclusions drawn by Heller from his experiments are certainly very dangerous in view of the fact that the experiments were conducted over the very short period of ten weeks.

Cunningham (1933) experimenting upon rats found that feeds low in magnesium reduce the normal quantities of this element and feeds high in magnesium raise the magnesium levels in the blood. The extent to which the magnesium level is raised in the blood depends upon the solubility of the magnesium salts. He states that there was a general tendency to a lower blood calcium when the serum magnesium was higher. He fed the chloride, carbonate, sulphate and phosphate of magnesium and the greatest increase in the magnesium content of the bones and blood serum was produced by the carbonate. At the higher levels of magnesium carbonate and magnesium sulphate the ash content of the bones were decreased and the moisture content increased. He states that interpretation of these results is difficult owing to diarrhoea which the rats developed on the diets high in magnesium (1 per cent.). On a diet containing 0·2 per cent. of magnesium the bones were normal. The growth-rates of the animals were not adversely affected by the presence of magnesium in the diets unless catharsis was present. Cunningham states that the magnesium content of blood sera of rats range from 2·1 to 3·0 mg. per 100 c.c. of blood.
Robinson and Rosenheim (1934) readily obtained deposits of salts of barium, strontium and magnesium in hypertrophic cartilage in vitro by agency of the bone-phosphatase in the presence of phosphoric ester, Zwillinger (1935) found that intravenous injections of magnesium sulphate have an effect on the heart and could be used in the therapy of certain forms of paroxysmal tachycardia and also in strophanthid digitalis poisoning. Crittenden and Roth [Crittenden and Roth (1936) and Roth and Crittenden (1936)] studied the effects of saline cathartics on the gastrointestinal tract and found that: (1) "Isotonic solutions of both magnesium and sodium sulphate and hypertonic sodium chloride, when in contact with the intestinal mucosa of unanesthetized dogs, have a marked augmenting effect on intestinal mobility. (2) Isotonic sodium sulphate is less stimulative than isotonic magnesium sulphate thus showing a specific effect of the Mg ion. (3) The Mg ion causes a considerable decrease in the tone of the intestinal musculature, but at the same time augments the amplitude of contractions. (4) All sulphate solutions cause distension of the intestine. (5) The gastric activity is as a rule either unaffected or depressed when the salines are in contact with the intestinal mucosa." (For further information concerning magnesium see sulphates).

(f) Nitrites:

Potassium nitrate is more poisonous than sodium nitrate. According to Fröhner (1919) 50 gm. of potassium nitrate may at times cause serious poisoning in horses; the fatal dose for equines and bovines is 100-250 gm., for pigs and sheep more than 30 gm., and for dogs more than 5 gm.

Shaw (1929) states that in some waters nitrites are reduced to nitrite after two weeks, apparently through the action of calcium, magnesium or bicarbonate ions.

Nitrites, especially potassium nitrate, are fairly active poisons. Potassium nitrate is used as a diuretic in man and animal. Cushny (1918) states that large quantities of nitrites cause nausea, vomiting, and even diarrhoea and urine may be scanty or even suppressed. There are also muscular weakness, apathy, and eventually collapse and death. A number of South African waters were found to contain such quantities of nitrites that they caused death in stock within a few hours after they had partaken of them.

Cushny describes the following post mortem appearances in cases of potassium nitrate poisoning: hyperaemia of the gastrointestinal mucosa with haemorrhages, lesions of acute nephritis and haemorrhages in the kidneys. He warns against its use as a diuretic when there is already gastrointestinal irritation.

A heifer which had received one pound of salt-petre instead of Epsom salt by mistake showed trembling, staggering, and convulsions followed by death within half-an-hour (Clough, 1930). Kaufmann (Clough, 1930) states that the therapeutic dose of potassium nitrate for the ox is 10-30 gm. and for the pig 1-4 gm. Klarenbeek, Veenendal and Voet (1931) conducted experiments upon fowl with sodium and potassium nitrate administered per os either
in solution or in capsule. They found that 1-1.5 gm. of these two poisons per Kg. of bodyweight administered daily over periods varying from a few days to fifteen days caused death after loss in condition, diarrhoea, anorexia, apathy and dry comb. Autopsy revealed caustic ingluviitis, and acute gastroenteritis with haemorrhages in and under the mucosa. They saw no spasms and paralysis as often described by other authors. Potassium nitrate was found to be more caustic and more toxic than sodium nitrate. Seekles and Sjollem (1932) administered 100-200 gm. of potassium nitrate in aqueous solution into the rumen of full-grown cattle and found that they developed characteristic symptoms of poisoning and changes in the blood. The symptoms of poisoning were similar to those seen in nitrates. Most of the nitrate disappeared from the rumen fluid within three to three and a half hours. Excretion through the kidneys commenced soon and lasted for more than twelve hours. Approximately one-tenth of the nitrate administered was reduced to nitrite in the rumen and the latter caused methaemoglobinemia of approximately 20 per cent. of the haemoglobin, which resulted in an increased heart beat. In the first six hours after administration of the nitrate the mineral content of the blood serum changed in that the calcium, inorganic phosphorus, and magnesium levels may be reduced up to 20 per cent. below the normal. After this fall the calcium and inorganic phosphorus levels rise to normal and the magnesium to above normal values. Pincher (1937) reports deaths among cows which drank water containing 6.2 gm. of sodium nitrate per litre (=6,200 parts of sodium nitrate per million parts of water). They were frenzied and exhibited excitement, colic, general cyanosis, symptoms of paralysis, pronounced diuresis, and pulse 150-200. No diarrhoea was noticed. Autopsy revealed: slight gastroenteritis, haemorrhagic inflammation of the brain ventricles, haemorrhages in the cortex of the brain, slight injection of the brain vessels, pronounced cyanosis of the tracheal mucosa, and inflammatory swelling of the mediastinal lymph glands. (For further information concerning nitrate poisoning see chlorides).

(g) Potassium:

Rats fed potassium (0.2 gm. K per day) by Bruman and Finkelstein (1936) showed more or less a clear decrease in the processes of metabolism, both the CO₂ production and the O₂ uptake being decreased. The higher the potassium content of the muscles the greater the retardation of the processes of metabolism. Potassium weakens the muscles hence the above effect. Mathison (Camp and Higgins, 1936) found that potassium salts effect a rise in blood-pressure when they are injected intravenously or intraarterially. His results were confirmed by McGuigan and Higgins. Camp and Higgins (1936) injected potassium salts intravenously into dogs and state that “potassium effects all the changes in the systems studied that are produced by epinephrine”; and that “one of the functions of the adrenal glands is to maintain a constant distribution of potassium”. Dienst (1936) found that: (1) Sodium displaces potassium in the system and increases the retention of water in tissues and potassium displaces sodium and enhances loss of water from the tissues. The ultimate effect depends on the presence of the respective
quantities of sodium and potassium. (2) In excessive doses of potassium its level in the blood serum is raised and it is then excreted in the urine. It has a diuretic action.

From their experiments Gardner and Burget (1938) conclude that potassium ions favour absorption of glucose from the intestine. Glatzel (1938) states that potassium stands in close relationship to muscular action. Isolated striped muscle is paralysed by potassium salts in spite of the fact that they do not penetrate into the fibres. In the heart muscle it causes a small and slow pulse and decreases irritability and enhances diastole. According to Glatzel potassium is very essential for the intercellular activities; it also appears to retard adrenalin action. (For further information concerning potassium see sodium).

(h) Sodium:

Some authors are of the opinion that too much salt (NaCl) in our diet may have detrimental effects on our health and constitution and is the cause of many chronic kidney affections. We have at present no experimental evidence to support this view although such an hypothesis seems feasible with excessive ingestion of salt. We must admit that increased ingestion of salt will result in increased kidney activity as the kidney is responsible to a very large extent for ridding the body fluids of excessive amounts of salt. Whether continuous increased action of the kidney due to the daily ingestion of slightly excessive quantities of salt will result in chronic affections of this organ in healthy individuals is an unsolved problem. Our sense of taste to a very large extent protects us against taking excessive quantities of salt and it is not very likely that individuals will continue taking harmful amounts of salt in their food over long periods. However, some individuals may become accustomed to an excessive salty taste and may ingest harmful quantities of salt. It is known that some individuals use more salt in their food than the average person.

It is an entirely different matter where the drinking of excessively saline waters over long periods is concerned.

Stokvis (Abderhalden, 1923) found 8-10 gm. of common salt administered per os in 25 per cent. solution to be fatal for rabbits weighing 1 Kg.

According to Fröhner (1919) the following quantities of common salt are fatal: 1-5-3 Kg. for bovines, 1-1-5 Kg. for horses, 125-250 gm. for sheep and pigs, and 30-60 gm. for dogs.

Scott (1924) gave a beast salt water containing 1-716 per cent. (i.e. 17,160 p.p.m.) of sodium chloride to drink. Diarrhoea set in within four days and there were loss of appetite, coughing, discharge from the nose and eyes, dull and sunken eyes, grinding of the teeth, dry and hot muzzle, temperature 105-20°F, pulse 80 to 90 per minute, and suspension of rumination. On the ninth day of the experiment there was profuse, foetid and slight haemorrhagic diarrhoea. All these symptoms disappeared after discontinuation of the experiment. In feeding experiments conducted upon pigs
Rasenack (1926) found that these animals apparently suffered no ill-effects from receiving fish meal containing 10 per cent. of common salt. Unfortunately the experiment lasted only a few weeks. On the other hand fish meal containing 15 to 17·5 per cent. of common salt had deleterious effects on the animals.

Legg (1929) describes common salt poisoning in sheep which drank rain water which had collected in salt troughs. They developed dullness, straining, pronounced diarrhoea and pronounced thirst. Autopsy revealed congestion of the entire alimentary tract with liquid contents, moderate congestion of the parenchymatous organs and pronounced hyperaemia of all the subcutaneous tissues.

Shaw (1929) experimenting upon ducks weighing from 600 to 800 gm. established that 5 gm. of common salt, administered either in solution by means of a pipette or dry in capsules, is non-toxic, while 6 gm. or more is lethal. The symptoms exhibited by the ducks were nausea, general depression, and torticollis. In their experiments with common salt upon baby chicks Quigley and Waite (1932) found that mortality was not excessive until the level of salt in the total ration was greater than 5 per cent. by weight: "The minimum lethal single dose of dry salt, with chicks in a "fed" condition, was 4 gm. per Kg. of body weight or 0·4 per cent. of body weight". The normal salt content of mash is 0·5 to 1·0 per cent.

In his experiments upon rats and domestic animals Heller (1933) found that (1) with a 1 per cent. aqueous solution of common salt (i.e. 10,000 p.p.m.) as drinking water for rats their growth was normal while with a concentration of common salt of 1·5 per cent. there were subnormal growth and death, (2) waters containing sodium chloride do not interfere with normal growth and maintenance of laying hens until the concentration has reached 1·5 per cent. (15,000 p.p.m.) or more. Two per cent. sodium chloride was clearly too saline, because the hens' feathers became rough, they lost weight, and some died and egg-production was reduced. (3) Sheep receiving water containing 2·5 per cent. of common salt (25,000 p.p.m.) for a period of six weeks went off their feed at times. (4) Small pigs receiving water containing 1·5 per cent. of common salt (15,000 p.p.m.) died within thirty days and the larger ones "were somewhat stiff when walking". "The food consumption was greatly decreased and the general appearance of the animals was not good. They were removed from the salt water and given pure water and were practically normal in 10 days." (5) Cattle can consume 1·5 to 1·75 per cent. (i.e. 15,000 to 17,500 p.p.m.) solutions of common salt over periods of a few months without serious results. "For cows in heavy production, 1·5 per cent. seems to be slightly more than can be consumed with normal maintenance." (6) The appearance of rats receiving water containing 1·5 per cent. (15,000 p.p.m.) of sodium sulphate was satisfactory.

"Sodium metabolism is intimately connected with the activity of the cortex of the suprarenal gland", (Editorial, 1934). Glatzel (1935) states that common salt stimulates diastase action on polysaccharides and induces the secretion of a very active fermentative
saliva. The administration of common salt to pigs may cause slight fever and lesions in the central nervous system (Michnevitch, 1933). According to Vegh (1935) a diseased liver retains a portion of the common salt taken per os and renders this organ prone to the development of oedema. Schmid (1935) describes common salt poisoning in silver foxes due to the eating of salted ruminal walls of bovines. They showed vomiting, foaming at the mouth and died with spasms within one to two days. Autopsy revealed hyperaemia of the gastrointestinal mucosa, oedema of the lungs, and haemorrhages in the urinary bladder. Schmid calculated that each fox had ingested at least 50 gm. of salt. According to Fröhner (Schmid, 1935) the toxic dose of common salt for carnivora is 3:7 gm. per Kg. of body weight. Tocher (1935) added salt to the feed of poultry for a period of six to seven days and concluded that "poultry can tolerate salt to the extent of 2·5 per cent., but higher proportions affect their health, while proportions amounting to 7·5 per cent. or over cause death". The drawing of this conclusion is rather unwarranted as the experiment was of very short duration. Glatzel (1936) states that sodium chloride through its chlorine content is an important factor in carbohydrate metabolism. It is essential that the salt first reach the stomach before the fermentative (diastatic) action of the saliva is enhanced by it. High concentrations of sodium chloride retard the breaking up of carbohydrates. Battaglino (1936) states that two pounds (= ± 1 Kg.) of salt caused excessive thirst, dullness, diarrhoea and weakness in the hindquarters of a cow. It is known that muscle cells absorb practically no sodium, consequently it will retard absorption of fluid into the muscles (Farkas, 1936). He states that oedematous fluid is not in the muscles but in the interstitial tissues.

Frey and Glatzel (1936) injected 0·9 and 1·0 per cent. solutions of sodium chloride into the blood stream of dogs and found that: (1) chlorine activates the action of insulin. (2) All insulin action is associated with the presence of a certain quantity of chlorine. (3) The insulin secretion of the pancreas is only slightly increased by the direct action of sodium chloride. (4) Under certain conditions sodium chloride, because of its chlorine, stimulates the action of diastase in the liver. (5) Sodium chloride also indirectly enhances the secretion of insulin in the pancreas. Lasch and Roller (1936) conducted experiments upon rats, rabbits, dogs and human beings with inorganic and organic (chlorine-free) sodium salts and found that these salts induced in most cases an accumulation of calcium in the skin and internal organs. In no case could they find an accumulation of sodium in the organs or in the blood. In man there was an increase in the alkali reserve and an increase in the excretion of uric acid and in the mineral ions administered. There was also an increase in the cholesterol content of the blood. Messini and Scalabrino (1936) state "the action of one litre of plain water as a control and of various mineral waters on the dilution and chlorides of the blood and on diuresis was studied in one hundred and twenty experiments on thirty subjects. Water produced in half-an-hour a slight dilution, followed by a more prolonged concentration. Hypotonic sodium chloride water of low concentration produced a slight dilution of the blood, slight increase in chlorides
and greater diuresis than plain water. Concentrated and hypertonic waters tended to concentrate the blood.” Pigs, which had received 400 gm. of brine (60-80 gm. of sodium chloride) each for eight days developed blindness, obstinate constipation and absence of reflexes two days after the feeding of brine was discontinued. The animals went down with legs stretched out stiffly. They recovered after injections of calcium gluconate (Wautie, 1936). Brine contains sodium chloride, potassium nitrate, propylamine and trimethylamine. Wautie (1936) administered to each of two pigs in their food 50 gm. of sodium chloride daily for five days, 75 gm. daily for five days, and 100 gm. daily for twelve days. The only symptom noticed was increased thirst. The pigs then received 200 gm. of salt daily for eight days and 250 gm. daily for three days. At the end of this period they showed acute thirst, diuresis and diarrhoea.

Bourdillon (1938) administered ammonium chloride, potassium chloride and sodium chloride orally to a human subject and found that after the administration of potassium chloride there was a reduction in serum bicarbonate. However, after the ingestion of sodium chloride the serum bicarbonate was not appreciably affected. Greenwood, Hewit and Nelson (1938) found that the degree of toxicity of the chlorides of potassium, ammonium and sodium is in the order KCl, NH₄Cl and NaCl.

Oehme (Glatzel, 1938 a) found that sodium chloride added to milk food caused a retention of calcium and phosphorus and the processes of metabolism are pushed to the acid side, while with potato food excretion of calcium and phosphorus was increased and metabolism pushed to the alkaline side. Glatzel and Glatzel-Schmidt (Glatzel, 1938 a) found a clear difference in the mineral excretion after administration of sodium chloride, depending upon the acid or basic nature of the food, and its sodium chloride and water content. Glatzel (1938 b) states that sodium is altogether indispensable for the irritability of muscles and nerves. Different sodium salts stimulate peristalsis of the excised intestine and also the secretion of fluid. Calcium chloride counteracts these stimulating effects of sodium chloride and sodium sulphate. Glatzel (1938 b) furthermore states that: (1) It is not known why a few grams of sodium chloride induces fever in babies. (2) Sodium chloride diuresis can be counteracted by calcium salts (calcium chloride). (3) The same quantity of sodium chloride may at times cause diuresis and at other times not have this effect in the same individual. (4) Sodium chloride enhances amylase action and from the chlorine the hydrochloric acid of the stomach is formed and the gastric hydrochloric acid produces the necessary pH for pepsin action on proteins. (5) It is known that thyroid hormone deficiency leads to accumulation of sodium chloride and water in the body and that administration of this hormone causes absorption of oedematous fluid and increase in water and sodium chloride excretion. Glatzel asks whether the reverse action can take place, namely, whether sodium chloride administration stimulate thyroid activity. (For further information concerning sodium salts see magnesium and chlorides.)
(i) Sulphate.

Sulphide-, sulphite- and sulphate-combinations administered per os cause transient hyperglycaemia in rabbits. This effect was most pronounced with sulphuretted hydrogen, less with sulphite and least with sulphate (Kojima, 1933).

From experiments conducted upon rabbits Stransky (1934) concludes that sulphates have a de-ionising effect on the calcium present in blood serum. Drenching with Karlsbad mineral water causes changes in the mineral composition ("Zusammensetzung") of the blood serum. However, the calcium content of the blood remains fairly constant. According to Heller and Haddad (1936) the sulphate ion appears to enhance magnesium and inhibit calcium elimination in the urine. They state that "the presence of an ion with which the sulphates form insoluble compounds increases the fecal phosphorus output". (For further information concerning the actions of sulphates see calcium, magnesium and sodium.)

(j) Sulphides.

Alkali sulphides (sodium, potassium and calcium sulphides) are decomposed by the carbon dioxide in the air and sulphuretted hydrogen is liberated (Lewin, 1928). It is for this reason that underground waters containing alkali sulphides become potable when left in an open vessel or when boiled for a while (tea and coffee). Lewin states that alkali sulphides cause irritation of the gastrointestinal tract (vomiting and diarrhoea) and kidneys and have a paralytic effect on the nerves and muscles. Eventually coma sets in. When taken in large quantities sulphides cause sulphaemoglobinæmia and dizziness. Alkali-sulphides are broken up by the acid gastric juice. If the water is alkaline the sulphides will be decomposed at a very slow rate and will be more irritant and less poisonous than hydrogen sulphide. According to Lewin 4 g.m. of potassium sulphide is fatal for dogs. (For further information concerning sulphides see sulphates.)

The following are remarks concerning the general effects of saline waters on animals. In his experiments upon ducks Shaw (1929 a) "found the greatest toxicity in sodium chloride and sodium sulphate mixtures containing in addition either magnesium or bicarbonate together with nitrate ions". Heller and Larwood (1930) state that "it is interesting to note that as the salt concentration increased the amount of water consumed by the animal daily also increased up to the point where the animal preferred to die of thirst rather than drink the necessary amount", and further that "animals which have received the salty water for some time seem better able to stand such water than do animals which are suddenly changed from distilled water to salty water". Heller and Paul (1934), conducted experiments upon rats, chickens, pigs, sheep and bovines with drinking water containing any one of the following salts: calcium chloride, sodium chloride, calcium sulphate, potassium chloride, calcium hydrate, sodium phosphate and magnesium sulphate. They found that there is an increase in the
inorganic (Na, K, Ca, Mg, and Cl\textsubscript{2}) content of either blood plasma or cells in animals drinking water with a high salt content. However, marked changes took place only as death approached. They state that there are very noticeable increases in the sulphate content of the blood of animals consuming the more concentrated solutions. The increase in the salt content of the blood is always found in animals partaking of saline waters. "The change, while small, is significant and increases with the quantity of salt consumed". In rabbits drinking Karlsbad mineral water Stransky (1934) found that trypan blue remains longer in their blood serum than in normal rabbits. However, there was no difference in this respect in the case of sodium fluorescin and trypan red. The rate of precipitation of erythrocytes in the serum of rabbits which drank Karlsbad water was clearly reduced. In the course of experiments conducted upon rats Heller and Hadid (1936) established that "an increase of the mineral content of the drinking water to the maximum amount which will not cause serious injury to the animal produces an abnormal mineral content of the urine and feces and at the same time alters the normal paths of excretion".

Kern and Stransky (1937) state that: (1) Drinking of Karlsbad mineral water for four weeks increases the action of liver sulphatase in rabbits. (2) Drinking of this water for a few weeks stimulates glycogen formation in the livers of rabbits, guinea pigs and rats. (3) Drenching rabbits with this water causes a moderate increase in blood amylase and serum lipase. The glycolytic blood enzymes and the blood glucose content are not effected by this mineral water. (4) Mineral water stimulates liver function. According to Grafe (1937) the effect of the drinking of mineral water on the water balance of the body is not understood. There is no decided effect on the salt balance, but the total production of energy and the sugar balance can be influenced by different mineral waters. Protein metabolism is apparently not affected. According to Glatzel (1938 a) mineral substances may stimulate or retard processes of metabolism in the cells, also enzyme action may be affected in the same way. He states that biochemistry recognises general mineral action (osmotic action), collective or group specific action and individual actions. As a rule a mineral substance acts in all three ways at the same time. There appears to be no doubt, according to Glatzel (1938 b) that the functions of minerals, enzymes, vitamins and hormones are closely associated.

Fried (1938) administered Karlsbad mineral water to rabbits \textit{per rectum} and \textit{per os}. He found that: (1) Three hours after infusion into the rectum of 50 c.c. of the water there was a fairly pronounced diuresis, which was not noticed when it was administered orally. (2) Equimolecular solutions of sodium chloride and sodium sulphate in the same amounts given \textit{per os} produced no diuresis. (3) One hundred c.c. of Karlsbad water given \textit{per rectum} caused pronounced diuresis, which was also seen when solutions of the above salts were given. (4) Rectal infusions of Karlsbad water had a pronounced cholagogue effect, which commenced slowly and lasted for many hours. Liver function was enhanced as the excretion of bile pigments is increased. Oestreich (1938) administered Karlsbad mineral water orally to rabbits and found that it enhances liver
function. Arsenic is detoxicated by more rapid deposition in the liver and quinine by an increase in the rate of destruction in the liver. Detoxication through combination of the poison with sulphuric acid, as in phenol poisons or with glucuronic acid, as in camphor poisoning, is not enhanced by Karlsbad water as these processes are already maximal. Rabbits drenched with Karlsbad water tolerated phenol and quinine better than those drenched with tap water.

C. Safe Limit of Degree of Salinity of Drinking Water.

Klut (1932) states that: (1) In order to prevent the unpleasant salty tastes and the disturbance of appetite, drinking water should not contain more than 0.0168 per cent. (168 p.p.m.) of magnesium chloride, 0.05 per cent. (500 p.p.m.) of calcium chloride, and 0.04 per cent. of sodium chloride (400 p.p.m.). (2) Water with more than 0.034 per cent. (340 p.p.m.) of sodium bicarbonate, or whose salt content is above 0.1 per cent. (1000 p.p.m.), or which contains 0.00001 per cent (1 p.p.m.) of sulphur as sulphuretted hydrogen or sulphides is considered to be a mineral water. (3) Drinking water usually contains from 0.02 to 0.05 per cent. (200 to 500 p.p.m.) of salts. According to the British Pharmaceutical Codex (Editorial, 1934) from 5 to 12 gm. of sodium chloride is taken daily by man in his food and a corresponding amount is excreted in the urine.

In his excellent article on "Aufgaben und Bedeutung der Mineralstoffe" Glatzel [1938 a] states that the optimum mineral requirements depend upon the individual, sex, age, profession or trade, surroundings (climate) and the mineral content of the food taken. Glatzel and Glatzel-Schmidt (Glatzel, 1938 a) found the following to be the mineral requirements per day for an adult person weighing approximately 70 Kg.:—Na: 4 to 5 gm., K: 2 to 4 gm., Ca: 0.5 to 7 gm., Mg: 0.5 gm., Cl: 6 to 9 gm., and P: 0.9 to 2.2 gm.

In a study on the consumption of salt by range cattle Aldea (1935) found that over a period of a year each beast consumed daily approximately 32 gm. of the following mixture: NaCl—91.17 per cent., CaSO₄—1.55 per cent., MgSO₄—3.9 per cent., P-trace, Fe and Al oxides—0.003 per cent., insoluble residue—0.61 per cent. According to Hart and his collaborators dairy cows should receive at least 28–35 gm. of salt per head daily as crops and feed are very low in chloride. Aldea states that his figures agree with those prescribed by Morrison, Beaucamino and Sales, Chapline, and Talbot in different parts of the world.

The following is the conclusion drawn by Heller (1933) from his experiments with saline waters on rats, chickens, pigs, sheep and cattle: "Sheep were more resistant than cattle and cattle more so than hogs. The fact that the sheep were raised in a hard water country might have been a factor. Sheep have been able to exist on 2.5 per cent. solution of sodium chloride and 2 per cent. magnesium sulphate. Cattle not in milk production have maintained themselves on 2 per cent. sodium chloride solution. As a safe rule, however, it can be said that 1.5 per cent. total salts should be considered the upper limit under which maintenance can be expected. For lactating
animals the limit is lower." We cannot agree with Heller's conclusions as according to our investigations conducted into water poisoning in stock over large areas in the North-Western Cape Province and South West Africa concentrations of salt much lower than 1 per cent. (10,000 p.p.m.) are harmful to stock if they partake of it daily over long periods. Facts in support of this statement will be evident from the contents of this article. It is unfortunate that Heller's experiments were conducted over such short periods (a few weeks to a few months) and it is mainly for this reason that the results of his experiments by no means warrant his conclusion quoted above. The effects upon man and animal of drinking saline waters over long periods is a very involved problem and definite conclusions can only be drawn after extensive experiments have been conducted over periods of years with waters containing not only different concentrations of total salts but in which the relative proportions of the different salts have also been varied. It is obvious that it will only be after a large number of experiments have been concluded and after extensive observations in the field have been made that reliable results will be obtained. The effects of saline waters on man and animal depends upon: (a) The concentration of salts in the water; (b) the nature and relative proportions of the salts present; (c) the species of animal, and (d) the quantity of water drunk daily. This depends on various factors as explained under IV A.

Hardman and Miller (1934) classify water for domestic use as follows:—

1. Very good: 0 to 100 p.p.m. (= 0·01 per cent.) total solids, free from organic matter, clear, odourless, tasteless. Lightly mineralised.
2. Good: 100 to 500 p.p.m. (= 0·01 to 0·05 per cent.) total solids. Moderately mineralised.
3. Fair: 500 to 1,000 p.p.m. (= 0·05 to 0·1 per cent.) total solids. Sodium or calcium bicarbonate waters passing sulphate waters. Highly mineralised.
4. Poor: 1,000 to 5,000 p.p.m. (= 0·1 to 0·5 per cent.) total solids. Rejecting sodium sulphate and calcium waters. Very highly mineralised.
5. Unfit: Over 5,000 p.p.m. (= 0·5 per cent.) Excessively mineralised.

According to the older authorities in England and the United States of America the extreme permissible limit of the mineral content of drinking water should be 570 p.p.m. (= 0·057 per cent.) total solids.

It appears that also in some parts of Australia saline waters constitute a serious problem to stock farmers. Allen (1936) quotes a case where well water contained approximately 1·5 per cent. (15,000 p.p.m.) total solids (CaCO₃, CaSO₄, MgSO₄, MgCl₂, and NaCl) and which killed horses, cattle and sheep if they drank it over a period.
Specimens of Water Analysed at Onderstepoort.

Specimens A to P (Table I) were collected by one of us (D.G.S.) in the course of an investigation into the problem of poisonous bore-hole and well water in the Gordonia and Kenhardt districts (North-Western Cape Province). In addition to these specimens a large number of suspected poisonous waters which were submitted by farmers and stock inspectors in the North-Western Cape have been analysed and valuable information obtained in regard to their effects upon stock. With the exception of specimen 0 all were taken from underground water supplies (bore-holes and wells).

From Table I it is evident that in some of the water supplies all the ions, except potassium, occur in very large quantities. Sodium, potassium, calcium and magnesium are usually present as chlorides, sulphates, carbonates and (or) bicarbonates. Nitrates are probably present as sodium and potassium nitrate, and fluorine as calcium and (or) sodium fluoride and (or) in combination with other bases. It is however impossible to state definitely in what combinations the above ions are present. The salt concentrations are very high in some specimens. Sea-water contains approximately 3.5 per cent. of salts and has caused fatal poisoning in cattle (Fröhner, 1919).

The owners of the stock on the farms from which the above specimens of water were collected supplied one of us (D.G.S.) with the following information:

**Specimen A:** Both human beings and animals drink this water with no apparent ill-effects. Human beings not accustomed to the drinking of saline waters develop diarrhoea from this water. Whenever available both human beings and animals drink open (rain) water.

**Specimens B and C:** Both the bore-hole (B) and the well water (C) are entirely unsuitable for man as it causes serious gastrointestinal disturbances (nausea, vomiting, headaches, severe diarrhoea). Animals drink this water when there is no "open water" (rain water) but seem to drink more of it than of wholesome water and develop diarrhoea. Both sheep and cattle chew bones to a remarkable extent and losses from lambsiekte (botulism) in both sheep and cattle are at times very severe. A certain amount of bone meal is fed. The bore-hole water causes extensive rusting of the iron piping.

**Specimen D:** This water is unsuitable as drinking water for human beings as it causes the same symptoms as those described under specimens B and C. This bore-hole was sunk about six months before the specimen was collected and sheep and cattle have been drinking this water since that time. At the time the specimen of water was taken all the animals were suffering from severe diarrhoea and it remains to be seen what the effects of drinking this water over long periods will be. The owner of the animals stated that the animals have to drink more of this water than of less saline waters in order to quench their thirst.
WATER POISONING IN MAN AND ANIMAL.

**Specimen E:** According to the owner of the farm the bones (spinal vertebrae) of sheep slaughtered for domestic use could be very easily cut with a knife before he commenced feeding bone-meal. Both cattle and sheep chew bones extensively and "flamsiekte" (botulism) is rife at times. Unfortunately no reliable information as to the effects of the water on the stock and human beings could be obtained from the owner as he is trying to sell the farm.

**Specimen F:** On this farm five wells and two bore-holes have been sunk and in each case the water was undrinkable (bitter, salty and burns the mouth and throat). This specimen of water was taken from bore-hole water which the stock have to drink when there is no "open water". They however suffer from diarrhoea and other ill-effects and both sheep and cattle suffer from a very severe form of pica in spite of having constant access to bonemeal licks. The owner is a progressive farmer. The human beings on this farm always drink rain water collected in tanks.

**Specimen G:** This specimen was taken from a shallow well in the bed of the Maloppe River, Gordonia district, and it was stated that stock have been drinking this water for almost twenty years without any apparent ill-effects. The water in the well was only twelve to eighteen inches below the surface of the river bed and it is obvious that its salt content will vary considerably at different times of the year depending upon the rainfall. After rains the stock drink open water.

**Specimen H:** This water causes mottled and bad teeth (caries) in children and gastrointestinal disturbances in man and animal (nausea, diarrhoea, hoven). Young stock do not grow out to normal size.

**Specimen I:** This water has been drunk for years with no detrimental effects.

**Specimen J:** This water kills plants and animals die from within half-an-hour after having drunk it. They develop severe hoven and vomiting and diarrhoea if they survive for a number of hours.

**Specimen K:** This water is drunk by man and animal if no "open water" is available. It appears to be wholesome excepting that it causes severe motting of the teeth in children.

**Specimen L:** When rain water is not available both man and animal in Kenhardt town have to drink water from this spring. Dr. Viviers, district surgeon, informed me that in 70 to 80 per cent. of the children drinking this water there is severe motting of the teeth, which are also notoriously bad (caries).

**Specimen M:** According to information supplied it appears that this water is drunk in the absence of rain water, by both man and animal with no apparent ill-effects apart from severe motting of the teeth of children who grow up on the farm. If too much of the water is drunk gastrointestinal disturbances set in.

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### Table I. Results of Water Analysis in Parts per Million Parts of Water.

<table>
<thead>
<tr>
<th>Specimen No.</th>
<th>Total salt content</th>
<th>Sulphate (SO₄)</th>
<th>Chlorine (Cl₂)</th>
<th>Fluorine</th>
<th>Calcium</th>
<th>Magnesium</th>
<th>Sodium</th>
<th>Potassium</th>
<th>Degree of hardness</th>
<th>Nitrate (NO₃)</th>
<th>pH</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1430-0</td>
<td>94-5</td>
<td>454-7</td>
<td>1-05</td>
<td>107-0</td>
<td>79-5</td>
<td>190-0</td>
<td>13-5</td>
<td>27-85</td>
<td>20-68</td>
<td>7-5</td>
<td>Fairly saline water (especially NaCl). Will cause slight mottling of teeth in ± 10% of children.</td>
</tr>
<tr>
<td>B</td>
<td>12588-0</td>
<td>1277-0</td>
<td>4801-0</td>
<td>2-1</td>
<td>999-1</td>
<td>502-3</td>
<td>1538-0</td>
<td>29-4</td>
<td>26-86</td>
<td>202-0</td>
<td>7-0</td>
<td>Poisonous water—too much salt. Mottled teeth in 10-20% of children.</td>
</tr>
<tr>
<td>C</td>
<td>12581-0</td>
<td>1277-0</td>
<td>4829-4</td>
<td>2-7</td>
<td>999-1</td>
<td>486-1</td>
<td>1670-0</td>
<td>29-0</td>
<td>26-86</td>
<td>206-1</td>
<td>7-3</td>
<td>Poisonous water—too much salt. Mottled teeth in ± 80% of children.</td>
</tr>
<tr>
<td>D</td>
<td>7997-0</td>
<td>2316-0</td>
<td>1581-9</td>
<td>4-2</td>
<td>356-8</td>
<td>185-8</td>
<td>1060-0</td>
<td>23-3</td>
<td>50-75</td>
<td>122-0</td>
<td>7-5</td>
<td>Poisonous water—too much salt. Mottled teeth in ± 80% of children.</td>
</tr>
<tr>
<td>E</td>
<td>5256-0</td>
<td>2214-0</td>
<td>980-4</td>
<td>4-6</td>
<td>535-2</td>
<td>52-1</td>
<td>888-0</td>
<td>25-7</td>
<td>18-91</td>
<td>trace</td>
<td>7-6</td>
<td>Poisonous water—too much salt. Mottled teeth in ± 80% of children.</td>
</tr>
<tr>
<td>F</td>
<td>9111-0</td>
<td>2110-0</td>
<td>2717-0</td>
<td>5-3</td>
<td>590-2</td>
<td>137-5</td>
<td>1063-0</td>
<td>85-9</td>
<td>34-82</td>
<td>444-4</td>
<td>7-9</td>
<td>Poisonous water—too much salt. Mottled teeth in ± 90% of children.</td>
</tr>
<tr>
<td>G</td>
<td>1620-0</td>
<td>270-1</td>
<td>412-0</td>
<td>0-75</td>
<td>142-8</td>
<td>46-7</td>
<td>237-0</td>
<td>36-9</td>
<td>27-38</td>
<td>96-6</td>
<td>8-1</td>
<td>May be harmful when drunk daily over very long periods.</td>
</tr>
<tr>
<td>H</td>
<td>4464-0</td>
<td>1125-0</td>
<td>1289-0</td>
<td>7-2</td>
<td>356-8</td>
<td>182-21</td>
<td>666-0</td>
<td>39-1</td>
<td>29-35</td>
<td>3-704</td>
<td>7-6</td>
<td>Poisonous water—too much salt. Mottled teeth in ± 100% of children.</td>
</tr>
<tr>
<td>I</td>
<td>796-0</td>
<td>73-14</td>
<td>63-93</td>
<td>2-7</td>
<td>108-8</td>
<td>18-2</td>
<td>53-6</td>
<td>25-7</td>
<td>7-96</td>
<td>negative</td>
<td>7-8</td>
<td>This water will cause mottling of teeth in ± 10% of children.</td>
</tr>
<tr>
<td>J</td>
<td>15925-0</td>
<td>4994-0</td>
<td>3485-0</td>
<td>7-2</td>
<td>579-8</td>
<td>599-9</td>
<td>2668-0</td>
<td>47-8</td>
<td>56-2</td>
<td>1529-9</td>
<td>7-8</td>
<td>Very poisonous water. Mottled teeth in ± 100% of children.</td>
</tr>
<tr>
<td>K</td>
<td>1195-0</td>
<td>149-6</td>
<td>277-1</td>
<td>7-6</td>
<td>79-4</td>
<td>39-2</td>
<td>222-0</td>
<td>17-9</td>
<td>39-80</td>
<td>negative</td>
<td>7-9</td>
<td>This water is fairly harmless, except that it will cause mottling of teeth in ± 100% of children.</td>
</tr>
<tr>
<td>L</td>
<td>810-0</td>
<td>107-3</td>
<td>195-4</td>
<td>6-8</td>
<td>67-1</td>
<td>27-2</td>
<td>138-0</td>
<td>21-2</td>
<td>27-36</td>
<td>10-32</td>
<td>7-6</td>
<td>Fairly mineralised water. It will cause mottling of teeth in ± 100% of children.</td>
</tr>
<tr>
<td>M</td>
<td>2946-0</td>
<td>540-0</td>
<td>753-0</td>
<td>8-3</td>
<td>169-4</td>
<td>128-0</td>
<td>440-0</td>
<td>36-9</td>
<td>29-84</td>
<td>261-72</td>
<td>7-9</td>
<td>Fairly highly mineralised water. It will cause mottling of teeth in ± 100% of children.</td>
</tr>
<tr>
<td>N</td>
<td>33425-0</td>
<td>1988-0</td>
<td>8467-0</td>
<td>negative</td>
<td>2301-0</td>
<td>709-4</td>
<td>2860-0</td>
<td>21-2</td>
<td>7-96</td>
<td>2212-4</td>
<td>7-5</td>
<td>Extremely poisonous water.</td>
</tr>
<tr>
<td>O</td>
<td>283-0</td>
<td>71-91</td>
<td>28-42</td>
<td>0-38</td>
<td>44-6</td>
<td>9-0</td>
<td>62-5</td>
<td>6-0</td>
<td>14-92</td>
<td>4-2996</td>
<td>7-5</td>
<td>Wholesome water.</td>
</tr>
<tr>
<td>P</td>
<td>1850-0</td>
<td>345-6</td>
<td>451-1</td>
<td>4-9</td>
<td>44-3</td>
<td>48-8</td>
<td>460-0</td>
<td>38-0</td>
<td>35-82</td>
<td>16-0</td>
<td>7-7</td>
<td>Fairly highly mineralised water. It will cause mottling of teeth in ± 80-90% of children.</td>
</tr>
<tr>
<td>Onderstepoort water supply</td>
<td>530-0</td>
<td>28-77</td>
<td>39-07</td>
<td>0-3</td>
<td>64-2</td>
<td>54-4</td>
<td>30-8</td>
<td>6-0</td>
<td>32-82</td>
<td>3-496</td>
<td>7-6</td>
<td>Wholesome water.</td>
</tr>
<tr>
<td>Brits Agricultural School water supply</td>
<td>687-0</td>
<td>48-9</td>
<td>39-07</td>
<td>0-07</td>
<td>77-6</td>
<td>47-9</td>
<td>91-0</td>
<td>6-0</td>
<td>50-75</td>
<td>3-125</td>
<td>8-0</td>
<td>Although this water is to be regarded as wholesome, some new-comers to the agricultural school complain that it causes digestive disturbances for a few months after their arrival.</td>
</tr>
<tr>
<td>Hope Town Water Supply</td>
<td>590-0</td>
<td>80-1</td>
<td>56-83</td>
<td>0-16</td>
<td>61-6</td>
<td>45-7</td>
<td>91-0</td>
<td>6-0</td>
<td>30-34</td>
<td>4-85</td>
<td>8-0</td>
<td>Wholesome water.</td>
</tr>
<tr>
<td>Lagersdrift Agricultural School</td>
<td>174-0</td>
<td>negative</td>
<td>trace</td>
<td>negative</td>
<td>13-6</td>
<td>9-6</td>
<td>15-4</td>
<td>10-0</td>
<td>9-55</td>
<td>negative</td>
<td>7-5</td>
<td>Wholesome water.</td>
</tr>
</tbody>
</table>

*Parts of calcium carbonate per 100,000 parts of water.
### Therapeutic and Acute Treatment

<table>
<thead>
<tr>
<th>Salt</th>
<th>Man Therapeutic</th>
<th>Man Toxic</th>
<th>Horse Therapeutic</th>
<th>Horse Toxic</th>
<th>Cow Therapeutic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium nitrate</td>
<td>0.5-1 gm.</td>
<td>5 gm.</td>
<td>8-15 gm.</td>
<td>50 gm. may cause serious symptoms</td>
<td>8-15 gm.</td>
</tr>
<tr>
<td>Sodium nitrate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulphides</td>
<td></td>
<td></td>
<td>CaO: 1-2 gm.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbonates</td>
<td>Na₂CO₃ + KOH + O₂: 0.5-1.5 gm.</td>
<td>Li₂CO₃: 15 gm. fatal within a few hours</td>
<td>Na₂CO₃: 8-25 gm.</td>
<td>K₂CO₃: 2-4 gm.</td>
<td>Na₂CO₃: 8-25 gm.</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>2-4 gm.</td>
<td></td>
<td></td>
<td>1-2 kg.</td>
<td>250-300 gm. as cathartic</td>
</tr>
<tr>
<td>Sodium sulphate and magnesium sulphate</td>
<td>2-16 gm. (Na₂SO₄·1 OH₂O; MgSO₄·7H₂O)</td>
<td>50 gm. Epsom salt fatal ad 30 gm. may cause symptoms</td>
<td>250-500 gm.</td>
<td></td>
<td>500-1,000 gm.</td>
</tr>
</tbody>
</table>
### Table II.

**Toxic Doses of Mineral Salts.**

<table>
<thead>
<tr>
<th></th>
<th>Sheep,</th>
<th>Dog,</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Toxie.</td>
<td>Therapeutic.</td>
<td>Toxie.</td>
</tr>
<tr>
<td>240 gm.</td>
<td>3–4 gm.</td>
<td>30 gm. fatal</td>
<td>0.3–2 gm.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>240 gm.</td>
<td></td>
<td>30 gm. fatal</td>
<td>6.0 gm. fatal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>K₂CO₃:—0.3–1.3 gm. as</td>
<td>K₂CO₃:—10–15 gm. fatal</td>
</tr>
<tr>
<td>2–3 kg.</td>
<td></td>
<td>NaHCO₃:—4–15 gm.</td>
<td>NaHCO₃:—0.3–1.3 gm. daily over</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>long periods, toxic</td>
</tr>
<tr>
<td></td>
<td>30–60 gm. as cathartic</td>
<td>120–240 gm.</td>
<td>10–60 gm.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>60–120 gm.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Specimen N: Stock drinking this water die from within a few hours to a few days. Symptoms seen were hooven and diarrhoea.

Specimen O: This specimen was taken from the Upington town supply, which is filtered water from the Orange River. It is very wholesome water.

Specimen P: As the owner had sold this farm no reliable information regarding the effects of the water on stock was obtainable.

It should be pointed out that the salt content of the waters in Table I will vary at different times of the year and in different years depending upon the rainfall and the depth of the wells and bore-holes.

No cases of mottling of the teeth of stock were seen on the farms visited. This should not be taken as proof that the high fluorine content of some of the water supplies does not affect the teeth of animals, as it is a very general practice in the area concerned to move stock about, especially on account of droughts. The result is that the same animals very rarely or never drink from the same water supplies for long periods.

In discussing the results of the analyses given in Table I, the contents of Tables II and III are of great value.

The approximate equivalents of sodium sulphate (Na₂SO₄·10H₂O), magnesium sulphate (MgSO₄·7H₂O) and calcium sulphate (CaSO₄) to sulphate (SO₄) can be calculated by multiplying the figures in the sulphate column (Table I) by $\frac{3}{2}$, $\frac{2}{3}$, and $1\frac{1}{2}$ respectively. Other equivalents can be calculated on a similar basis by utilising the information supplied in Table III.

A full-grown beast which drinks daily 45 litres (=10 gallons) of water which has a total salt content of 0·5 per cent. (5,000 p.p.m.) will consume 225 gm. (=7½ oz.) of salts daily. This quantity of salt is, according to figures of salt requirements for cattle given by authorities in different parts of the world (Alden, 1935), approximately eight times the amount of salt required for growth, maintenance and production. In a very dry and hot climate the daily consumption of 45 litres of water by a beast which had to walk a long distance to the water, as is usually the case, is moderate. In addition it should be considered that stock are inclined to drink larger quantities of saline waters than they do of water, which contains much smaller quantities of salt. It is very difficult with the limited information which we have at our disposal concerning the effects of highly mineralised waters on man and animal to suggest a definite limit of the degree of salinity of drinking water beyond which harm will be done. Experiments have been commenced at Onderstepoort in order to determine the safe limits of the degree of salinity of drinking water for stock. It is realised that these experiments will have to be continued for periods extending over a number of years before reliable and definite conclusions can be drawn.

It is also realised that it is essential to consider any results which are obtained from experiments with water rendered saline artificially, in conjunction with observations made under natural conditions in the field.
Table III.

<table>
<thead>
<tr>
<th>Component</th>
<th>gm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mg</td>
<td>24·32</td>
</tr>
<tr>
<td>K</td>
<td>39·10</td>
</tr>
<tr>
<td>Na</td>
<td>22·997</td>
</tr>
<tr>
<td>Ca</td>
<td>40·08</td>
</tr>
<tr>
<td>Cl</td>
<td>35·457</td>
</tr>
<tr>
<td>H</td>
<td>1·008</td>
</tr>
<tr>
<td>O</td>
<td>16</td>
</tr>
<tr>
<td>S</td>
<td>32·06</td>
</tr>
<tr>
<td>N</td>
<td>14·008</td>
</tr>
<tr>
<td>C</td>
<td>12·0</td>
</tr>
</tbody>
</table>


24 gm. Mg = 95 gm. MgCl₂ = 246 gm. MgSO₄·7H₂O.


96 gm. SO₄ = 136 gm. CaSO₄ = 322 gm. Na₂SO₄·10H₂O = 246 MgSO₄·7H₂O.

62 gm. NO₃ = 85 gm. NaNO₃ = 101 gm. KNO₃.
From the information at our disposal it is definite that the most harmful and poisonous ions are nitrates, sulphates, sulphides, fluorine, and magnesium. It is especially the relative degrees to which they are present which will determine the effects of saline waters upon stock. A very common constituent of highly mineralised waters is sodium chloride, which is certainly also detrimental to health when it is present in appreciable quantities.

In discussing the safe limit of salts in drinking water we must pay due attention to the possibility of the harmful effects upon man and animal being only noticeable after the water had been drunk for very long periods. These harmful effects may show themselves in retarded growth, decrease in productivity, mottled and bad teeth, head-aches, chronic forms of indigestion and urinary calculi. Hard and alkaline waters undoubtedly play a rôle in the formation of these calculi.

We cannot but agree with the older authorities in England and the United States of America that the extreme limit of total salts in wholesome drinking water should be 0·057 per cent. (570 p.p.m.) especially as far as man is concerned. When the suitability, or otherwise, of water for drinking purposes is considered special attention should be paid to the relative amounts of nitrate, fluorine, sulphate, sulphide, bicarbonate, carbonate, calcium and magnesium present especially in waters where the total salt content exceeds 570 p.p.m. Water containing, for example, 0·1 per cent. of total salt (1,000 p.p.m.) could be used with a fair degree of safety provided one, or more, of the above ions is not present in excessive quantities. Fluorine is a dangerous poison and water containing more than 0·0001 per cent. (1 p.p.m.) of it should not be used as drinking water, especially for man. Even water containing 1 p.p.m. of fluorine is likely to cause slight mottling of the teeth in 10 per cent. of the children drinking it. Stock appear to be more resistant to fluorine poisoning than man, especially as far as the mottling of teeth is concerned.

One of us (D. G. S.) is acquainted with several cases where human beings have lived for years in a town where the underground water supply contains approximately 0·08 per cent. of total solids (800 p.p.m.) and who still suffer severely when they drink a few glasses of this water on a hot day. This water when taken by individuals who are not accustomed to the drinking of saline waters suffer severely (slight nausea, feeling of discomfort over the epigastrum, and diarrhoea) in many cases. However, most of these individuals become accustomed to this water and the above effects disappear in the course of time especially if they limit the quantities of water they drink.

D. Susceptibility of Man and of Different Species of Animals to Saline Waters.

Heller (1933) rightly states that: (1) Pigs are more susceptible to salt water than other domestic animals; and (2) cows in heavy production are more susceptible than steers and cows not in production.
It is a well known fact that pigs and poultry are fairly susceptible to salt poisoning, especially to sodium chloride. Horses are more susceptible than cattle and sheep, and man more so than animals.

There seems to be no doubt that both man and animal develop a certain degree of tolerance to waters which contain excessive, but comparatively low, quantities of salt. However, like in all poisons there is a limit to this tolerance which may break down at any time. One thing should be realised and that is that it is extremely difficult to determine what effects fairly highly mineralised drinking water will have upon man and animal over a period of years. It is very doubtful whether tolerance can be developed to hard waters as far as the formation of urinary calculi is concerned. The disadvantage of saline waters is that both man and animal drink larger quantities of it than of wholesome waters, probably because the former waters are inclined to cause diuresis and diarrhoea. The nature of the food consumed should also be considered in a discussion on the susceptibility to saline waters. It is obvious that the salt content, especially common salt, of the food should be as low as possible in cases where water containing large quantities of salt (common salt) is drunk. Diets containing oxalic acid or oxalates (rhubarb, spinach) will be likely to cause the formation of calcium and magnesium oxalate calculi (urinary) if the drinking water contains excessive quantities of calcium and magnesium. The owner of a farm in a semi-arid region of South West Africa where the water is very hard (calcium) and a large proportion of the grazing consists of species of *Mesembryanthemum* and *Pseudovelutinum*, both of which contain oxalic acid, informed one of us that in no case could they eat the kidneys of slaughtered sheep as these organs were "one mass of grit". The "grit" is probably calcium and magnesium oxalate crystals.

The quantity of saline water drunk by man and animal is obviously also a deciding factor as far as susceptibility is concerned. The factors which determine the quantities of water taken by man and animal are mentioned under IV A.

### E. Symptoms of Poisoning with Excessively Saline Waters in Man and Animal.

The following symptoms may be encountered depending upon the nature and concentration of the salts present in the water.

(a) *Man*: Nausea, vomiting, chronic indigestion, loss of appetite, head-aches, diuresis, diarrhoea, feeling of discomfort over the epi-gastrium, mottled teeth (fluorine), bad teeth (caries), and urinary calculi (see V).

In connection with caries in teeth it should be mentioned that Mills (1935) states that putrefactive activity in the colon (colitis) leads to the absorption of harmful bacterial products into the blood stream. These harmful products are excreted in the saliva lowering the vitality of the gingival tissues and may also be the cause of bad teeth (caries).
(b) Animals: The first symptom usually seen in animals is diarrhoea, although death may occur within a few hours after water containing large quantities of nitrates or sodium chloride have been drunk. Vomiting and hovem, even in ruminants, may at times be present, also clonic muscular spasms. Urinary calculi may develop in the course of time and may cause rupture of the bladder (see V). In the more protracted cases of poisoning the following symptoms appear:—chronic diarrhoea, partial loss of appetite, retarded and stunted growth, anaemia, general weakness, reduction in productivity (milk, wool, eggs) and fertility, and increased susceptibility to worms and to the effects of droughts. It is obvious that, owing mainly to the chronic diarrhoea caused by the salt action on the gastrointestinal mucosa, digestion of the food ingested is defective and this may result in many complications. One of the complications may be a disturbance of the mineral metabolism which may already have been rendered abnormal through the presence of large quantities of calcium, magnesium and sulphates in the water.

Both in South West Africa and in the North-Western Cape Province one of us (D. G. S.) visited several farms where both cattle and sheep showed a severe form of pica (allotriophagia) in spite of the fact that they had constant access to bonemeal licks. The only difference between the conditions on these farms and the surrounding farms on which the animals did not show allotriophagia, was that the drinking water (bore-hole water) on the former farms contained very large amounts of salts, and calcium, magnesium and sulphates were present in excessive quantities.

This disturbance of the mineral metabolism in animals drinking excessively mineralised waters, especially those containing excessive quantities of calcium, magnesium and sulphates, can be explained on the following grounds:—(a) Becka (1929) found that magnesium inhibits absorption of calcium from the food and increases its excretion from the body. (b) According to Cunningham (1933) there is a general tendency to a lower blood calcium when the serum magnesium is higher. (c) Heller and Paul (1934) found that there is an increase in the mineral content (Na, K, Ca, Mg, and Cl) of the blood in animals drinking saline waters. The mineral content of the blood increases with the quantity of salt consumed. (d) Stransky (1934) states that sulphates have a de-ionising effect on the calcium present in blood serum. (e) Heller and Haddad (1936) found that in rats drinking water containing calcium and magnesium in excessive quantities there are large amounts of phosphorus in the faeces and also that “the presence of an ion with which the sulphates form insoluble compounds increases the faecal phosphorus output”. (f) Meulendracht (1938) describes “a case of extreme decalcification of the bones manifested clinically by persistent and progressive pain in the back and loin, by spontaneous fracture and collapse of the spine, so that the patient became 10 to 12 cm. shorter, and by numb sensations in the lower extremities, necessitating the use of bandages and leather corsets, and radiologically by an extreme calcium deficiency of the bones, especially of the spine, the vertebrae showing the typical hour-glass-shape (“fish vertebrae”), some of them having con fused in an irregular manner”. Meulendracht excluded the possibility of a faulty diet. He came to the conclusion that this
WATER POISONING IN MAN AND ANIMAL.

Serious disturbance of mineral metabolism was caused by the prolonged use of Carlsbad salts (one teaspoonful every morning for thirty-five years). The chief constituents of these salts are sodium sulphate and sodium bicarbonate. According to him the calcium in the food was precipitated as calcium sulphate and excreted with the faeces, hence the calcium deficiency. It is obvious from the above information that other factors (diarrhoea, sulphate ion, alkalinity, etc., of the Carlsbad salts) also play a rôle in causing the disturbances in the Ca-P metabolism.

F. POST MORTEM APPEARANCES.

These are apparent from the description of the symptoms given above: In peracute cases no specific lesions may be discernible, while in the more protracted cases there may be acute or chronic gastrointestinal catarrh, cachexia, anaemia, and possibly urinary calculi.

G. TREATMENT.

It is obvious that treatment will be of no avail unless the drinking of the saline water is discontinued. In the majority of cases treatment is not necessary as recovery will take place very soon after discontinuation of drinking of salt water. Olive oil and raw linseed oil should be given to allay gastrointestinal irritation and black coffee and tea as diuretics. If available, the patients should be allowed to drink rain water.

H. PREVENTION.

(a) FLUORINE POISONING:

Alum, magnesium oxide, lime and carbon could be employed in the removal of fluorine from drinking water. However, the efficacy of these substances in removing the fluorine depends on the chemical characteristics of the water to be treated and further research is necessary before definite conclusions can be drawn (Editorial, 1936 c). Adler and Klein (Editorial, 1937) found that 10 lb. of tricalcium phosphate will remove sufficient F from 560 gallons of water to render the small impurity harmless.

Evolve (1937) ascertained that tricalcium phosphate, magnesium oxide and magnesium are very effective in removing fluorine from water and that they do so to a similar degree. From an economic point of view magnesium oxide is to be preferred. From his experiments it appears that 1 lb. of calcined magnesite would suffice to treat approximately 88 gallons of water containing 5 p.p.m. of fluorine. The fluorine binding power of the magnesium oxide will to a large extent depend on the nature and amount of mineral salts present in the water to be detoxicated.

According to Kempf, Greenwood and Nelson (1937) the addition of aluminium sulphate to water reduced the F content of water from 8 parts per million to 1.5 p.p.m.
Adler, Klein and Lindsay (1938) found that tricalcium phosphate, which must be porous, possesses marked absorbent properties as far as fluorine is concerned. In their filtering experiments they employed glass tubes ("towers") which contained 40 gm. of tricalcium phosphate, which had a particle size between 30 and 40 mesh. The column of tri-calcium phosphate was 1·59 cm. in diameter and 36·8 cm. high. Water containing 30 p.p.m. of F was passed through this filter at the rate of 12·5 c.c. per minute. The F content was lowered from 30 p.p.m. to 0·3 p.p.m. on three liters of water. Comparative tests showed that tricalcium phosphate has approximately twice the capacity of activated aluminium in removing F from water. McIntine and Hammond (1938) state that the higher the temperature is the more effective tricalcium phosphate is in the removal of F from water. They found that the different brands of tricalcium phosphate differ in their fluorine-binding capacity. In some of their experiments 1 to 4 gm. of tricalcium phosphate reduced the F content from 6 p.p.m. to 0·3 p.p.m. per liter of water. It is suggested that fluo-apatite [3Ca₃(Po₄)₂CaF₂] is precipitated.

Furthermore it is possible that the permutit or zeolite filters described below (b) will also remove a certain percentage of the fluorine present in water supplies.

(b) Poisoning with salts other than fluorides.

Kooymans (1938) states that manganese is removed with iron quite satisfactorily when the manganese content is not too high. In the latter case potassium permanganate or lime could be added to the water or manganese-permutit could be used. The use of chemical filters is however very expensive.

In industries permutit apparatus is frequently used to render hard waters soft. Its action is based on the alternating action between calcium and sodium. The active ingredient in this apparatus is a hydrated silicate of aluminium and sodium (Na₆O·Al₂O₃·4SiO₂·2H₂O) which is known as permutit, silicatite or artificial zeolite. The reaction with hard water is reversible and takes place as follows: Na₆O·Al₂O₃·4SiO₂·2H₂O + CaCl₂ + aq. \[\rightarrow\] CaO·Al₂O₃·4SiO₂·2H₂O + NaCl + aq. (H. 1938). Depoorter (H. 1938) describes how this method of softening water could be applied to domestic water supplies. He proposes the use of an ordinary glass condenser, which is filled with permutit and through which the hard water passes. He has been able to reduce the hardness from 24°-10° in this way.

The authors wish to suggest that the problem of highly mineralised waters could be partly, if not entirely, solved on the following lines as far as the human being is concerned: (1) By storing rain water in galvanised iron tanks or in dams and using it as drinking water in conjunction with bore-hole and well water which are not too saline. Unfortunately the rainfall in the areas concerned is very low, so that provision must be made for the storage of large quantities of rain water. (2) On many farms with saline waters suitable drinking water was found after a number of wells
or (and) bore-holes had been sunk. It is therefore suggested that Government assistance in regard to the sinking of bore-holes be rendered to farmers in the areas concerned as many of them are in a sad plight. It is furthermore proposed that in the course of time specimens of all the drinking water in the areas concerned be collected and analysed in order to safeguard man and animal against the hazards of drinking excessively mineralised waters. (3) By erecting small filters (perlmutite, magnesium oxide, tricalcium phosphate, and alum) in homes for the purpose of filtering the drinking water in order to remove fluorides and other salts. This could be done at a comparatively low cost.

With regard to drinking water for stock it is obvious that the only recommendation which could be made here is Government assistance for sinking bore-holes and building dams to those farmers concerned. The importance of dams for the conservation of rain water cannot be overstressed. This would go a very long way to solve a very serious problem in the areas concerned as the dam water could be used for both human beings and animals.

It would appear from the extensive investigations conducted by various authorities into the effects of excessive quantities of calcium upon the system and from observations made by us in the field that we have good grounds for recommending that calcium-free licks (mono-ammonium phosphate, sodium phosphate) be given to stock on farms where their drinking water contains excessive quantities of calcium. The reason is obvious. It is well-known that the presence of excessive quantities of calcium in the gastro-intestinal tract is prone to render the phosphorus inabsorbable by converting di-calcium phosphate into the fairly insoluble tri-calcium phosphate. This would naturally reflect itself in symptoms of phosphorus deficiency if the quantity of phosphorus in the feed is already low. It is for this reason that the above suggestion in regard to the use of calcium-free phosphate licks is made in order to limit the calcium intake in cases where the drinking water contains large amounts of this element.

V. HARD AND ALKALINE WATERS AS THE CAUSE OF URINARY CALCULI.

McCarrison (1931) states that urinary calculi are of most frequent occurrence in hot, arid, desert plains, but they sometimes also occur in areas rich in water. According to Woodruff (1934) urinary calculi are most prevalent in cattle where arid conditions prevail. The experience of the authors certainly supports Woodruff’s and McCarrison’s statements, as by far the majority of reports of urinary calculi in stock have been received from the arid and semi-arid regions of the North Western Cape Province and South West Africa.

Urinary calculi are of much more frequent occurrence in males than in females. Castrated males again are much more frequently affected than uncastrated ones. This is obviously due to the inhibited development of the genital organs, especially the urethra. Almost
any affection, including infections, of the genital organs especially the penis, is termed "progoed" by the South African farmer (Steyn, 1930).

De Camp (1936) states that the Negro in all parts of the world is free from urinary calculi. Vermooten (1938) also found renal calculi of extremely rare occurrence in the South African Negro. The Negro diet is low in calcium.

According to Left (1936) urinary calculi are twice as common in the male as in the female in patients admitted to the London Hospital. Licknet (1934) and Rumpel (1936) state that there is a steady increase in the occurrence of these calculi in man. Winsburg-White (1938) reviews 426 cases of urinary calculi and states that the incidence of renal calculi in man is on the increase. The reasons are obscure. Of the 426 cases the calculi were found in the kidneys and ureters in 79.1 per cent, of the cases and in the remaining cases (20.9 per cent.) the calculi were in the bladder and in the urethra.

In sheep urinary calculi are very frequently situated in the pro versa us urethrae as the sigmoid curvature of the urethra of the male sheep offers a mechanical difficulty to the passage of large-sized calculi.

A. Causes of Urinary Calculi.

Osborne, Mendel and Ferry (1917) were able to produce phosphatic urinary calculi in feeding experiments conducted upon rats. "In every instance where calculi developed, the animals were without an adequate source of the fat-soluble vitamin for some time ".

Bruck (1937) states that a recumbent (sleeping) position enhances the formation of kidney and ureteral stones as large quantities of urine in the bladder seriously retard the flow of urine from the kidneys and ureters.

Hagar and Magath (1925) refer to urinary calculi caused by Salmonella ammobacae, which renders the urine alkaline. Calculi can be produced experimentally in the bladder by Proteus ammobacae, and Hagar and Magath (1928) state that Vitamin A deficiency is possibly favourable to the implantation of this infection. McCarrison (1927) was able to produce phosphatic stones in the bladder of rats by feeding them a faulty diet, namely, (a) absence of protein of animal origin, (b) deficiency of vitamin A, and (c) excess of earthy phosphates. He states that "to these faults there may possibly have been added a toxic action of the diet on the urinary tract ".

In a later communication McCarrison (1931) states that faulty diets, infections, and physicochemical disturbances in the urinary tract may cause urinary calculi and that the former two factors may produce the third. In India the diet is the most important factor in the causation of calculi. In that country it is a poor man's disease, as their diet is mainly one cereal grain or another. He proved that milk and butter afford protection against stone. He found that a Ca:P imbalance is a very important factor in the production of certain types of urinary calculi.
According to Barr, Bulger and Dixon (1929) there are in hyperparathyroidism (a) rarefaction of the bone, (b) muscular weakness and hypotonia, (c) abnormal excretion of calcium in the urine and formation of calcium stones, and (d) abnormally high serum calcium.

Blount (1931) states that the following are supposed to be the chief factors which control the formation of urinary calculi: (a) reaction of the urine, (b) presence of a nucleus, (c) excess of foods rich in salts and organic compounds, and (d) metabolic disturbances associated with abnormal excretion of salts.

According to Pontus, Carr and Doyle (1931 and 1932) urinary calculi are more frequent in sheep than in any other species of animal and the cause of their formation has been attributed to (a) the feeding of roots, especially mangels, (b) "hard waters", (c) good condition of the animals concerned, as they are too lazy and do not void urine frequently, (d) lack of exercise, and (e) chilling after shearing. Michael (Pontus, Carr and Doyle, 1932) studied the formation of urinary calculi for five years. He fed various diets to sheep as follows: Group 1—grain and clover hay, group 2—grain, hay and corn (mealie) silage, group 3—grain, hay and mangels, and group 4—grain, hay and sugar-beets. No calculi occurred in groups 1 and 2 and their urinary organs showed no lesions. However, in groups 3 and 4 there were a number of cases of calculi and irritation in one part, or more, of the urinary tract. There were also distended and enlarged gall-bladders, enlarged kidneys, and enlarged hearts. Michael attributed the enlargement of the organs to the large quantities of water ingested. These results point to mangels and sugar-beets being responsible for the formation of calculi. Pontus and his collaborators (1932) fed different diets to forty-two sheep for more than two years in order to determine how it would affect the reaction or composition of the urine. The reaction of fresh urine varied from pH 6.8 to 9.0 depending upon the feed of the animal. Lucerne or clover hay or beet rations produced a very basic urine ash, but when a cereal grain or bran was added to the ration the reaction of the urine was nearly neutral.

Traube, Skumburdis and Goldberg (1932) conducted precipitating tests with calcium salts of oxalic acid, phosphoric acid and carbonic acid in test tubes in an attempt to elucidate the problem of urinary calculi formation.

According to Albright, Aub and Bauer (1934) a severe degree of hyperparathyroidism could be associated with calculi within a short time.

Woodruff (1934) states that urinary calculi cause a lot of trouble in certain areas in America. They occur in cattle and almost exclusively in males of the beef type, particularly among steers raised on the Texas and New Mexico ranges and brought to the corn belt to be fattened for the market.

Gruber (1935) refers to endemics of urinary calculi in boys in Dalmatia and Bosnia; the cause is unknown and may possibly be bacterial infections.
Higgins (1935) conducted experiments upon rats and found that
(a) urinary calculi, chiefly calcium phosphate, develop in rats
sustained on a diet deficient in vitamin A, and alkalinuria and
keratinisation of the epithelium of the urinary tract were constantly
observed. In later stages of the experiments infection of the urinary
tract was frequent; and (b) the chemical conditions necessary for
the formation of calculi are produced by vitamin A deficiency.

Keyser (1935) states that in different laboratories urinary
calculi have been produced in animals in the following ways:
(a) by feeding oxamide, (b) by producing artificial excessive
excretion of calcium oxalate (c) by excessive doses of parathyroid
extract and of viosterol, (d) by the formation of uric acid calculi
in animals with Eck fistulae, (e) by feeding diets deficient in
vitamin A, (f) by infection with urea-splitting streptococci,
staphylococci and Bacillus proteus-ammoniac, and, (g) by
the incrustation of organic or inorganic foreign bodies in the presence
of infection”.

Olpp (1935) mentions twelve causes of calculus formation in
China: (a) constitution—stone families, (b) race and habits of
living of different nations, (c) some races in China stand and others
sit on their haunches when urinating. In the latter case the bladder
cannot be completely emptied and concentrated urine remains in
the bladder, (d) hot climate, (e) heavy work in hot weather,
(f) diet—potatoes, “Nudeln”, beetroot, and cabbage constitute the
main diet in China; boiled water, (g) vitamin A deficiency, (h) in
babies the remains of a persistent infantic may form the nucleus of
a stone, (i) microfilaria-parasitic cause, (j) foreign bodies in the
urinary tract, (k) profession most affected are farmers, “boat
pilfers”, fishermen, and labourers, and (l) bilharziasis—desquama-
tion of epithelium. According to De Camp (1936) (1) deficiency in
vitamin A and D is partly responsible for the formation of urinary
calculi, (2) vitamin A should be of animal origin in order to prevent
calculi, and (3) renal calculi frequently follow fractures of the spine
and pelvis.

According to von Quernher (1939) vitamin A deficiency causes
degeneration and keratinisation of the epithelial system resulting in
the formation of concrements. The hemmorhages in vitamin A
and C deficiency and the fact that these two deficiencies are often
accompanied by various infections, may result in the formation of
urinary calculi. Infections of the urinary tract may occur in all
avitaminooses. In vitamin B\textsubscript{2} deficiency there are disturbances in
the calcium metabolism and this may result in the formation of
urinary calculi. In D-hypervitaminosis there is a mobilisation of
bone calcium and during the process of excretion of the excessive
calcium in the blood by the kidneys urinary calculi may be formed.

In hyperparathyroidism there is an increase in urinary calcium,
which may lead to a change in the colloid-crystalloid equilibrium
of the urine which in turn favours precipitation of certain urinary
constituents, (Editorial, 1936 a). Left (1936) states that urinary
calculi sometimes follow prostatectomy. According to Rumpe (1936)
the state of mind, vegetative centres in the brain and in the per-
ipheral nerves, influence urinary secretion and calculi formation.
WATER POISONING IN MAN AND ANIMAL.

Calculi have been observed to appear after diseases of the nervous system. Also Kielleuthner (1938) refers to osteogenetic and neurogenetic phosphate stones. The latter stones occur in diseases of the nervous system.

Van der Ryst (1936) fed rats on the following diet and produced calculi "within a short time": 90 ground white rice, 3 casein, 3 yeast powder, 2 salts (the mixture used in his laboratory), 1 cod-liver oil and 3 calcium carbonate. The epithelium of the pyramid became stratified instead of single.

Verkoren (1937) states that Polak succeeded in producing kidney and bladder stones in rats by feeding them on a diet containing 3 per cent. of calcium carbonate. It was expected that these calculi would consist of calcium carbonate, calcium oxalate or calcium phosphate or uric acid, xanthin or protein substances. However, they were found to contain 50 per cent. of organic material, no oxalate, and a nitrogen-content of approximately 1 per cent. From 80 mg. of a stone 34 mg. of citric acid was isolated; therefore a large percentage of these kidney and bladder stones of the rats contain calcium citrate.

Newsom (1938) refers to losses in lambs from urinary calculi near Fort Morgan, Colorado. The trouble started after they had been fed on lucerne, maize and linseed meal for five months. Sheep fed on beet tops died from ruptured bladders. He quotes the case of a stock owner who lost many sheep from urinary calculi while feeding wheat whereas the mortality stopped when he changed to corn (maize) and lucerne. Calculi were also found in lambs fed on lucerne, corn, bran, dried pulp and cotton cake. The disease is also common in winter in Eastern Colorado in cattle fed on lucerne, bean straw, beet tops and pulp, corn barley and wheat and in addition limestone and bone meal. When the calcium carbonate was removed and corn and lucerne fed no more cases of urinary calculi occurred. Newsom states that most feed-lots in Northern Colorado "are supplied with a water heavy in alkali salts". At the Ohio Station it was found that sheep fed heavily on phosphatic food were more liable to the formation of calculi. Wheaten bran has a high mineral content, especially phosphorus.

Fürth (1936) in his paper on "Pathologische Physiologie der Steinbildung" (Wien Med. Wochenschr., 1936 Pp. 565-567 and 604-606) discusses various factors concerned in the causation of urinary calculi. Unfortunately details of the paper cannot be given here as the publication is not obtainable in South Africa.

Witter (1936) found that the kidneys of chicks, to whose drinking water sodium bicarbonate was added, became pale, swollen and engorged with urates.

In an Editorial (1938 a) in the Lancet the rôle played by bone disease and bone injury in the causation of urinary calculi is discussed. It is stated that "bone repair involves local decalcification; prolonged fixation of the limbs leads to a more generalised bone rarefaction; and both processes favour excess of calcium in the urine".
Griffin, Ostertag and Braasch (1938) state that "in cases of urinary lithiasis the values for blood calcium, phosphorus and phosphatase exhibit no common change which can be termed characteristic of the group. Minor variations in the value for blood phosphorus, particularly a lowered value, are not unusual but the concentration of blood calcium is very constant. Patients with a high value for blood calcium or phosphatase who have urinary calculi should undergo a thorough investigation for some other coexistent pathologic condition. In our study, hyperparathyroidism was found to be an etiologic factor in less than 2.2 per cent. of the 1,206 cases of urinary lithiasis."

B. **Nature and Composition of Urinary Calculi.**

Urinary calculi may be composed of one or more of the following elements:

(a) **Phosphates**, especially calcium, ammonium and magnesium phosphate. [McCarrison (1927), Blunt (1931), Pontus, Carr and Doyle (1932), Woodruff (1934), Milks (1934-1935) and (1935).]

(b) **Xanthin** (C₃H₄N₄O₂). Easterfield, Rigg, Askew and Bruce (1931) state that xanthin is a rare constituent of urinary calculi. Xanthin is widely distributed in the vegetable kingdom and occurs in human and animal bodies. The amount excreted in the urine is increased during inflammation of the kidneys. According to them urinary calculi consisting of xanthin are very prevalent in sheep on some farms in Waimea County in New Zealand. These calculi occurred only on one particular type of soil which was of low fertility. Milks (1934-1935) also refers to xanthin calculi.

(c) **Silicates** (aluminium silicate). [Blount (1913); Pontus Carr and Doyle (1932).]

(d) **Urates and uric acid**: [Blunt (1931), McCarrison (1931), Woodruff (1934), Milks (1934-35), Bruck (1937).]

(e) **Oxalates.** [Blount (1931), McCarrison (1931), Pontus, Carr and Doyle (1932), Woodruff (1934), Milks (1934-1935), and Bruck (1937).]

(f) **Cystin.** [Milks (1934-1935) and (1935), Green, Morris, Cahill and Brand (1936).]

(g) **Lecin** [Blount (1931).]

(h) **Allantoin.** [Green, Morris, Cahill and Brand (1936).]

(i) **Tyrosin.** [Blount (1931).]

(j) **Lithium salts.** [Blount (1931).]

(k) **Carbonates** of calcium, magnesium, and iron [Blount (1931), McCarrison (1931), Pontus, Carr and Doyle (1932), Milks (1934-1935) and (1935).]

(l) **Lime** [Ca(OH)₂]. [McCarrison (1931).]
The following table is taken from Blount's (1931) publication and gives the chief constituents of urinary calculi as found in man and animal:

<table>
<thead>
<tr>
<th>Animal</th>
<th>Acid urine</th>
<th>Alkaline urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horse</td>
<td>Silicates</td>
<td>Triple phosphates, calcium carbonate, magnesium phosphate, calcium phosphate.</td>
</tr>
<tr>
<td>Ox</td>
<td>Silicates, calcium oxalate, xanthin</td>
<td>Calcium and magnesium phosphates, calcium and magnesium carbonate, triple phosphates, iron carbonate.</td>
</tr>
<tr>
<td>Sheep</td>
<td>Silicates</td>
<td>Triple phosphates, iron carbonate, calcium and magnesium phosphates.</td>
</tr>
<tr>
<td>Pig</td>
<td>Silicates, calcium oxalate</td>
<td>Triple phosphates, calcium carbonate.</td>
</tr>
<tr>
<td>Dog</td>
<td>Calcium oxalate, ammonium oxalate, cystin, uric acid, urates</td>
<td>Triple phosphates, calcium carbonate + calcium phosphate, acid ammonium urates.</td>
</tr>
<tr>
<td>Cat</td>
<td>Cystin, uric acid, calcium oxalate</td>
<td>Calcium carbonate + calcium phosphate, potassium and magnesium phosphates, triple phosphates.</td>
</tr>
<tr>
<td>Man</td>
<td>Calcium oxalate, uric acid, cystin</td>
<td>Triple phosphates, calcium phosphate, lithium compounds.</td>
</tr>
</tbody>
</table>

The reaction of the urine depends to a large extent on the nature of the food ingested (Blount, 1931). Herbivora urine is usually alkaline as their food contains large amounts of organic acids (tartaric and citric acid). These acids are completely oxidised during the processes of metabolism and their alkaline bases are excreted. If herbivora are starved and were to derive their nourishment from their own tissues, their urine will be rendered acid by the excretion of acid sodium and potassium phosphates. This type of urine is derived from proteins and is normally found in carnivora. Blount states that "during the metabolism of animal protein, sulphur and phosphorus compounds are being oxidised with the production of their respective acids; these are later excreted and so tend to lower the pH of the blood".

McCarrison (1931) states that in his laboratory two hundred and twenty-six urinary calculi of human origin were analysed in the course of three years with the following results:—pure uric acid: 15, pure oxalate: 13, pure phosphate: 3, phosphate-oxalate: 23, urate-phosphate: 20, urate-oxalate: 78; urate-oxalate-phosphate: 74.

Milks (1934-1935) describes the following urinary calculi:  
(a) Uric acid calculi—yellowish or reddish-brown in colour, hard brittle, smooth or only slightly granular.  
(b) Calcium oxalate calculi—dark in colour, very hard and heavy, often rough or spinous.  
(c) Phosphate calculi are usually composed of the triple phosphate or ammonia-magnesium and calcium phosphate. They are greyish, friable and lighter in weight than the others.

Pontus, Carr and Doyle (1932) referring to urinary calculi in sheep state that the calculi examined by them were largely composed of calcium phosphate and organic matter. They furthermore state that a survey of the literature indicates that calculi are usually
produced by the formation of calcium carbonate, calcium and aluminium phosphates, and aluminium silicate, together with kidney tissue, urates, epithelium, etc.

Felix (1936) describes tests by which the chemical nature of calculi could be determined.

C. Symptoms of Urinary Calculi.

(a) Man: The symptoms may vary to a remarkable degree. However the following are those most frequently encountered—intermittent pain (renal colic), haematuria, frequent and difficult urination, nausea and vomiting, and with infection of the genito-urinary tract there may be pyuria, Jacobs, (1932).

(b) Animals: The first symptom is restlessness; partial or complete stoppage of the urinary tract; anorexia; arched back; head usually carried low; kicking at abdomen; straining to urinate; dullness and listlessness; wiggling of the root of the tail; in advanced cases the animals may appear very sick; there may be pus and blood in the urine (cystitis); inclination to lie down most of the time, usually on their bellies, and when they get up they stamp their hind feet; the wool or hair around the sheath is always wet or encrusted with salts, or urine may be dripping continually from the orifice of the sheath. There may be necrosis of the urethra due to pressure exerted by large stones with the result that urine finds its way into the surrounding tissues (oedema of subcutis). The animals may show repeated attacks of the disease. Palpation of the penis, urethra, ureters or kidneys is painful. After rupture of the bladder, ureters, or urethra, uraemic poisoning sets in and the following symptoms are seen: subnormal temperature, anorexia, animal lies down and will not rise, abdomen distended with urine. The breath smells of urine. Death inevitably follows rupture of the bladder. (Pontus, Carr and Doyle, 1932; Woodruff, 1934; De Camp, 1936; Newsom, 1938).

D. Post Mortem Appearances.

As is evident from the description of the symptoms urinary calculi will be found in the kidneys, ureters, urinary bladder, or urethra. There may be inflammatory conditions or necrotic areas in the ureters or urethra due to prolonged pressure exerted by large stones or due to infections, (b) oedema of the subcutaneous tissues in cases where there is necrosis of the urethra, (c) ureamia, (d) urine in the abdominal cavity in cases where the bladder, ureters, or urethra has ruptured, and (e) distension of the ureters, bladder, urethra, or pelvis of the kidneys.

F. Treatment.

Blount (1931) states that (a) ammonium benzoate is said to assist in the resolution of phosphatic calculi in sheep; (b) sodium bicarbonate (8-60 gm.) prevented phosphatic urinary gravel in lambs; (c) magnesia renders oxalates more soluble; (d) potassium
citrates is a diuretic and combines with calcium thus preventing the formation of calcium oxalate; and (e) acid sodium phosphate acidifies the urine and dissolves oxalates.

Lickint (1934) describes the following methods of treating kidney and ureter stones: (a) application of warmth, diathermy, morphine, pantothen, papaverin, and spasmalgin, with quite good results. (b) Ureter massage with patient lying on his or her side. (c) Irrigation of the urinary organs by administering large quantities of tea, coffee and water. The results are quite satisfactory. (d) Dilatation of the ureters with instruments (ureter catheters). (e) By the administration of hypophysis extracts, which stimulate peristalsis of the ureters. This method is often employed in combination with other methods. (f) Hip-baths stimulate peristalsis of the ureters and absorption of the water from the intestine irrigates the ureters. (g) The effects of ethereal oils (oil of turpentine, oil of peppermint, etc.) in the treatment of urinary calculi differ. (h) Glycerine administered orally. The following hypotheses are advanced concerning the action of glycerine in cases of urinary calculi: (1) Spasmolytic action. Glycerine relieves the pain and the ureters may therefore relax, or it may directly relieve the spasm in the ureters. (2) It may stimulate peristalsis of the ureters through withdrawal of water from their mucous membrane. However, Lickint rightly states that the percentage of glycerine in the urine is very low. (3) Ureter peristalsis may be brought about reflexly through intestinal peristalsis caused by glycerine. However, according to Lickint no diarrhoea follows upon the administration of large quantities of glycerine. (4) Views differ in regard to the diuretic action of glycerine. Lickint saw no diuresis in human beings who received 50 gm. of glycerine three times daily. (5) Removal of small calculi through an increase in the "thickness" of the urine due to the presence of glycerine. According to Lickint's experiments this does not occur as the amount of glycerine excreted in the urine is too small. (6) Removal of small stones through an increase in the viscosity of the urine. Lickint states that this is impossible as there is only an increase in the viscosity of urine when one pint of urine is mixed with three pints of glycerine. (7) Glycerine may act as a lubricant of the ureters. Also this is impossible as the concentration of glycerine, administered orally, is too low in the urine. (8) It may reduce the calculi in size or dissolve them. Previously it was held that glycerine dissolves calcium salts and uric acid deposits. However, Lickint found that glycerine in urine does not dissolve oxalate calculi and uric acid stones. He is of opinion that glycerine removes calculi through its spasmolytic action and (or) increase in the peristalsis of the ureters. He agrees with a number of urologists in that glycerine removes ureter calculi in many cases. His treatment consists of administering three times daily 50 gm. of glycerine up to a total of 450 gm. It is given neat and he has seen no detrimental effects. No additional fluid is given, only the normal quantity of tea, coffee or milk (1$\frac{1}{2}$ litres).

Stevens (1935) discusses the operative removal of calculi. Higgins (1935) conducted experiments upon rats and found that it was possible to dissolve by adding vitamin A to their diet, urinary
calculi which had formed as a result of feeding them a ration deficient in this vitamin. Cook (1936) refers to cases in which bilateral renal calculi disappeared after treatment of the patient with diets high in vitamin A, an acid-ash diet and acidification of the urine by the administration of 4 gm. of ammonium chloride daily for one month. The measures were applied singly and in combination.

De Camp (1936) states that "an increased alkaline content of the urine is useful in dissolving uratic calculi and cystine calculi, while acidification of the urine is indicated in eliminating calcium oxalate and calcium and ammonium magnesium carbonate and phosphate calculi". He states that the urine can be rendered alkaline by the administration of magnesia, potassium citrate, potassium acetate, or sodium bicarbonate, while the administration of a 10 per cent. aqueous solution of concentrated nitro-hydrochloric acid, ammonium chloride, and ammonium nitrate will render it acid.

Hermann (1938) claims good results in the dissolution of calcium phosphate and calcium carbonate calculi by rendering the urine acid by the oral administration of gluconic acid. He administers 80 gm. in a 3 per cent. solution daily. He states that Lohmüller, Karschulin and May had similar experiences. He explains that not all phosphatic calculi can be dissolved in this way as their dissolution depends upon (a) their chemical composition, (b) their age and (c) their structure most resistant are those with organic layers. Carbonate stones and mixtures of phosphates and calcium carbonate are the most soluble ones. Sometimes calculi take months to dissolve and acidification of the urine should be continued daily. Hermann states that in gluconic acid we have a very effective remedy to dissolve phosphate concretions. Tziritsch (1938) failed to dissolve calculi in patients by oral administration of "Extin" (an acid adipinic acid hexamethylenetetramin combination).

Keyser (1935) warns against the overzealous administration of urinary acidifying agents as it may lead to acidosis and nephritis. He rightly states that extreme care should be exercised where the total amount of salt administered in twenty-four hours exceeds 6 to 8 gm.

According to Fränkel (1937) the use of morphine is contra-indicated in spasm of the ureters as it increases the spasm as was proved experimentally by Boeminghaus. Fränkel states that atropine and its derivates relieve ureteric spasm. He maintains that eucodal and eupaverin are the best drugs to relieve spasm of the ureters. He administers per os three tablets on an empty stomach at the rate of one every five minutes, and twenty minutes after the last tablet 750 c.c. of weak tea. This treatment could be repeated in the evening and on the following day. Fränkel furthermore states that it is essential to allay colic due to renal calculi and to relieve spasm of the ureters. He has been doing this for years successfully with intravenous or intramuscular injections of 0·04 gm. of eucodal + 0·06 gm. of eupaverin. This dose can be repeated after one hour.
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Vermooten (1938) refers to the removal of kidney and ureter calculi by means of instruments ("ureter stone extractors"). The disadvantage is that these instruments sometimes break in the ureters. Vermooten and other urologists have great success in dilating the ureters by injections of avertin into the ureters by means of inlying ureteral catheters. They use 15 c.c. of a sterile 2 per cent. solution of avertin. Also Rumpel (1936) describes the various methods of removing urinary calculi.

F. PREVENTION.

According to Blount (1931) the formation of urinary calculi can be prevented by (a) avoiding the drinking of "hard waters" and (b) avoiding an excess of foods containing large quantities of inorganic salts like bran, grains, cereals, cotton seed meal, and fish meal. All these foods are rich in phosphorus. Peas, beans, clovers and fish meal contain much lime. Certain grasses are rich in silica. Animal proteins are rich in sulphates and phosphates. Blount states that acid sodium phosphate and calcium or ammonium chloride administered per os render the urine acid, while cereal grains and bran and the administration of magnesium salts, potassium citrate, alkali carbonates, tartrates, lucerne or mangolds tend to render it alkaline. Fresh fruit check high acidity.

In cases of cystine calculi (cystinuria) the patient should be placed on a low protein diet and the urine rendered alkaline by administration of alkaline salts, (Evell, 1932). Proteins of a high cystine content should be avoided. Diets containing adequate amounts of vitamin A should be fed or taken (Higgins, 1935; Editorial, 1937 a). In an editorial (1937 a) in the British Medical Journal the following recommendations concerning the prevention of urinary calculi are made: (a) avoid the retention of urine and infection of the urinary tract as the presence of urinary calculi is a not infrequent complication in retention and infection of urine, and (b) orthopaedic cases need protection from the formation of urinary calculi. The urine should be kept on the acid side (pH of 5 to 5.2) by an appropriate diet with a high vitamin A content and if necessary also by the use of acidifying agents like ammonium chloride. Special attention should be paid to the prevention of urinary calculi in orthopaedic patients which are recumbent and immobilised. (For particulars concerning diets see article by Higgins and Schlumberger in Archives of Surgery, Chicago, Vol. 34, 1937, p. 702).

Hermann (1938) states that in order to prevent the formation of urinary calculi (a) alkaline water should not be taken; and (b) bacterial infections of the urinary tract should be prevented.

Bruck (1937) discusses his own case of urinary calculi. He suffered from repeated attacks of kidney colic which were followed by excretions of urate-oxalate urinary stones of different size. He states that a recumbent position (sleeping) enhances the formation of kidney and ureteral stones as a large quantity of urine in the bladder seriously retards the flow of urine from the kidneys and ureters. After having suffered very much for fifteen years as a result of urinary calculi he solved his trouble by urinating every night between 3 and 4 a.m.
VI. DISCUSSION.

That the ingestion of excessive quantities of ordinary water can cause poisoning mainly through dilution of the body fluids, with a consequent reduction in the salt (mineral) content of these fluids, has been proved by a number of investigators. On the other hand, according to Moutax (1937) the drinking of excessively cold water may cause serious, if not fatal, localised and general vasomotor disturbances. Also the drinking of large quantities of distilled water may have unpleasant and even serious consequences.

It is evident from the foregoing information supplied with regard to the various aspects of the effects of saline and hard waters upon man and animal that the consequences of drinking such waters over long periods may be, and frequently are, very serious. Not only do many human beings in the more arid regions of the Union of South Africa and South West Africa suffer damage to their health and teeth as a result of drinking saline and hard waters but many of them have a severe struggle to make stock farming a payable proposition, and frequently fail to do so as the losses among their stock are so heavy as to impede all progress. Indeed, cases are known where stock-owners had to abandon farms a few years after having occupied them, as they lost practically all the stock they had brought on to them.

With the information we have at present at our disposal it is impossible for us to propose a definite limit of salts (total salt content and limits for individual salts) in drinking water beyond which harm may result. However, a large number of experiments have been conducted by various investigators and extensive observations made in the field. It is obvious that in attempting to suggest a safe limit for salts in drinking water the following points should be given due consideration: (A) The quantities of water taken daily with food and drink. This point is elaborated upon under IV. A. It is unfortunate that the areas where the underground water supplies are highly mineralised are precisely those where man and animal drink the largest quantities of water and where they are forced through a very low rainfall to be almost entirely dependent upon bore-hole and well water. However, matters can be materially improved by the storing of rain water in galvanised iron tanks and dams. (B) It has been pointed out previously that on many farms potable water was found after a number of wells or bore-holes had yielded poisonous (excessively saline) water. Such potable waters were found both at more shallow and much deeper levels than the excessively saline water and in some cases the respective bore-holes or wells were situated in quite close proximity. (C) The degree of salinity of the water varies at different times of the year and in different years especially that of the water in shallow wells and boreholes. The general complaint among the stock owners is that they and their stock suffer most during the dry periods of the year (June, July, August, September) and during droughts as the underground waters are then much more poisonous than during periods when rain falls. This is quite conceivable as rain water dilutes the superficial subterranean waters. This is a factor which renders it very difficult to draw reliable conclusions from observations in the field as to
the safe limit of salts in drinking water as the concentration of salts in the bore-hole and well water could vary considerably. In addition the animals drink rain water whenever it is available. Furthermore, the fact that many farmers are reluctant to give correct information concerning the effects of the water upon themselves and their stock as they may wish to dispose of their farms at some future date, renders it very difficult to obtain reliable information from them. The harmfulness of saline waters depends not only upon their total salt content but to a very large extent also upon the nature and quantities of the respective salts present. As far as direct poisoning is concerned nitrates, sulphides, and fluorides are the most important salts, while the presence of large quantities of magnesium, sulphates and calcium will be mainly responsible for disturbances in mineral metabolism, especially calcium and phosphorus metabolism (pica). It is true that in addition the chlorides, sulphates and nitrates of sodium, potassium, calcium and magnesium will all tend to cause diarrhoea through their salt action. Of the utmost importance is a consideration of the synergistic effects of the different salts in the water. Both pharmacologically and toxicologically the combined effects of the above salts are obvious. In most cases they will be multiplied and not added. In more ways than one, they will act synergistically especially with regard to their salt action on the gastrointestinal tract, the liver and kidneys. It is recognised that both man and animal develop to a certain extent a resistance to the effects of mineralised waters, especially as far as the causing of diarrhoea is concerned. However, we should not lose sight of the fact that after an apparent tolerance had been developed man and animal may after months and years exhibit the more chronic effects of drinking highly mineralised water, for example, retarded growth, stuntedness, decrease in productivity and reproduction, and urinary calculi. Shaw (1929) in referring to his experiments upon ducks states that "the greatest toxicity in these experiments was found in sodium chloride and sodium sulphate mixtures containing in addition either magnesium or bicarbonate together with nitrate ions". The presence of alkali carbonates (potassium and sodium) will induce digestive disturbances mainly as a result of changing the pH of the gastrointestinal juices. Their presence will also cause the accumulation of urates in the kidneys which will result in damage to the organs. It is known that the enzymes function normally only at certain degrees of acidity or alkalinity (pH) and it is obvious that either excessive acidity or excessive alkalinity will inhibit their actions or render them abnormal, and consequently disturb digestion. On the other hand the alkali carbonates will assist hard waters (containing calcium and magnesium carbonate, bicarbonate and sulphate) in the production of urinary calculi in that they are inclined to render the urine alkaline and consequently facilitating the precipitation of phosphates, calcium oxalate, and carbonates. Hard and alkaline waters undoubtedly play a rôle in the causation of urinary calculi (see discussion on urinary calculi). Dr. Viviers, medical officer of health, Kenhardt, informed one of us (D. G. S.) that slightly enlarged thyroids (goitre) (in many cases the enlargement can only be ascertained on palpation) are of quite frequent occurrence in the Kenhardt district.
Phillips and Hart (1935) fed 20 to 30 mg. of fluorine as sodium fluoride or rock phosphate per Kg. of body weight and petechiae in noticed fibrosis, mild parenchymatous proliferation and petechiae in the thyroid glands of some animals. May (1935) reports that he is making use of the iodine-fluorine antagonism in his sanatorium in that he applies the fluorine therapy to cases of hyperthyroidism and Basedow's disease. He observed this antagonism in hundreds of cases. He states that iodine stimulates the thyroid follicles to increased colloid secretion and also causes an increase in the size of the follicles, whilst fluorine in small doses induces a decrease in the size of the follicles with epithelial hyperplasia and reduced colloid content. Michaelis (1935) states that there are a number of facts which point to a fluorine-iodine antagonism in the system. He refers to Goldemberg's hypothesis which states that goitre and cretinism can be caused by a deficiency of iodine as well as by a superabundance of fluorine. Phillips, English and Hart (1935) found that growing chicks have a high tolerance to sodium fluoride and that the ingestion of fluorine enhances the toxicity of desiccated thyroid. Seegers and Braun (1935) determined the effect of sodium fluoride on experimental thyroid poisoning and state "these findings do not lend support to the hypothesis of an in vivo thyroxine inactivation and a concurrent inhibition of the ferments concerned in metabolism provided a constant supply of thyroxine is available by thyroid feeding". According to Biester, Greenwood and Nelson (1936) small amounts of fluorine fed to dogs have a tendency to increase colloid withdrawal from the thyroid glands. Kraft (1936) studied the antagonism of fluorine and thyroxin using the rate of growth of tadpoles as a criterion. Thyroxin, fluorobenzoic acid, sodium fluoride and 3-fluor-tyrosin were added to the water in which the tadpoles were immersed. He found that all three these fluorine combinations counteract the effects of thyroxin. In his tests 3-fluortyrosin proved less toxic than the other two fluorine combinations. Litzka (1936) states that fluortyrosin (a combination of fluorine and an amino-acid) has an increased specific fluorine action whilst it does not possess the disadvantages of the inorganic fluorine preparations. He (Litzka, 1936 a) considered that both fluorine and tyrosin are antagonists to thyroid hormones. Fluortyrosin, he states, has a pronounced antithyreotoxic action, that is, it is capable of partially or totally paralysing the metabolic actions of the thyroid hormones (Inukrete) which are circulating in the blood. According to him fluortyrosin is not capable of inducing histologic changes in the thyroid which could be held responsible for the inhibition of its glandular activity. Evans and Phillips (1938) found that in cases of hyperthyroidism fluorine occurs in the thyroid gland in widely varying amounts. They observed no relationship between the iodine and the fluorine content of thyroids in these cases. They state that "the data obtained gave no definite evidence that fluorine in any way played a part in human hyperthyroidism by its action on the thyroid gland".

According to Glatzel (1938 a) calcium is stated to increase the colloid content of the thyroid, and he asks whether this means a stimulation of the specific action of the thyroid by calcium, seeing that in myxoedema there is an inclination towards calcium retention and the thyroid hormone increases calcium excretion and
also because calcium excretion in Basedow disease is very high. Furthermore he (Glatzel, 1938 b) states that it is known that thyroid-hormone deficiency leads to accumulation of sodium chloride and water in the body and that administration of this hormone causes absorption of oedematous fluid and an increase in water and sodium chloride excretion. In view of the above information concerning the possible connection between thyroid action on the one hand, and fluorine, calcium and sodium chloride action on the other hand would it be unreasonable to suggest that there is a possibility of the mineral constituents present in the drinking water of human beings playing a role in the causation of goitre in certain areas where the water is excessively mineralised?

Karlsbad mineral water enhances the action of liver sulphatase and increases the blood amylase and serum lipase in rabbits, (Kern and Stransky, 1937).

According to Stransky (1934) the sedimentation rate of erythrocytes is clearly reduced in rabbits drinking Karlsbad mineral water. Glatzel (1938 b) states that the function of minerals, ferments, vitamins and hormones are closely associated. Common salt activates insulin and under very special circumstances also the diastase in the liver (Glatzel, 1936). Sodium metabolism is intimately associated with the activity of the cortex of the suprarenal gland, (Editorial, 1934). A portion of the common salt taken per os is retained by a diseased liver and renders this organ prone to the development of oedema (Vegh, 1935), and Karlsbad mineral water stimulates liver function and enhances glycogen formation in this organ (Kern and Stransky, 1937). Sodium chloride plays a role in mineral metabolism, especially calcium and phosphorus metabolism, (Glatzel, 1938 a). In experiments conducted upon bovines, sheep, pigs and chickens, Heller and Paul (1934) found “that there is an increase in the inorganic content (Na, K, Ca, Mg and Cl) of either plasma or cells in animals drinking water with high salt contents, but marked changes take place only as death approaches”. They state that there are very noticeable increases in the sulphate content of the blood of animals consuming the more concentrated solutions.

From the information we have at our disposal we cannot but agree with the older authorities in the United States of America and England that the extreme safe limit of the total salt content of drinking water, especially for the human being, is 570 parts per million parts of water (=0.057 per cent. of salt). The authors wish to point out that in the case of not too excessively mineralised waters their harmfulness depends not so much on their total salt content as on the degree to which they contain the more toxic or harmful elements. It is therefore obvious that the harmlessness, or otherwise, of mineralised waters should be regarded not so much from the point of view of their total salt content as from the amounts of the respective minerals present, especially in cases where borderline cases are to be considered.

With regard to the prevention of poisoning of man with highly mineralised waters the following methods could be used: (1) installation of small filters containing tricalcium phosphate, magnesium
oxide, aluminium sulphate, activated alumina, or permutite (hydrated sodium aluminium silicate) in the homesteads. These filters will remove fluorine and salts from the water to a certain extent (see IV II). A large number of tests are being conducted by one of us (N.R.) in order to ascertain what type of filter would be the most suitable for rendering highly mineralised waters potable and harmless. (2) By storing rain water in tanks and in dams. And (3) by means of sinking a number of bore-holes, as it was frequently found that the water from different bore-holes on the same farm varied to a marked extent in their salt content. It is suggested that State assistance be rendered to farmers with regard to the making of dams and sinking of bore-holes.

The authors are conducting experiments with saline waters upon sheep at Onderstepoort in order to determine the safe limits of different salts in drinking water.

**Urinary calculi.**—From the extensive literature on the different aspects of urinary calculi it appears that the following factors play a role: (1) Locality. (2) The drinking of hard and alkaline waters. Various stock-owners in hard water areas informed one of us (D.G.S.) that their oxen suffered from urinary calculi within a few months after “ open waters” (rain water collected in dams or rivers) had given up and they were forced to drink hard water obtained from bore-holes or wells. (3) The eating or feeding of oxamide, foods deficient in vitamin A and other vitamins, large amounts of calcium carbonate, plants containing oxalates, cereals, etc. (4) Bacterial infections of the genito-urinary tract, especially of the kidneys and bladder. (5) Hot and arid climates. (6) Hyperparathyroidism or excessive doses of parathyroid extract or viosterol—large quantities of calcium excreted in the urine and serum calcium is very high. (7) Diseases or fractures of the bones (osteogenic calculi). (8) Diseases of the nervous system (neurogenic calculi). (9) Stone families are recognised by some authorities. (10) An abnormal Ca : P ratio (Ca : P imbalance) in the system definitely plays an important role in the causation of calculi (see V A).

Urinary calculi may be composed of one or more of the following substances: Calcium phosphate, magnesium phosphate, ammonium phosphate, calcium carbonate, uric acid, urates, oxalates, lime [Ca(OH)₂], cystine, citrates and xanthin (see V B). Full particulars concerning the symptoms, post mortem appearances, treatment and prevention of urinary calculi are to be found under V C, D, E and F.

On the grounds of disturbances, especially in the processes of mineral metabolism, caused in the system and the role played by alkaline, saline and hard waters in the causation of urinary calculi, would it be unreasonable to suggest that these waters may also play a role in the causation of some types of bile stones?

**VII. SUMMARY.**

A. Poisoning due to the drinking of (a) excessive quantities of ordinary tap water, (b) excessively cold water, (c) distilled water and (d) highly mineralised water is discussed in all its aspects.
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B. The role played by saline, hard and alkaline waters in the causation of urinary calculi is discussed. The causes and nature and composition of urinary calculi and also the symptoms, post mortem appearances, treatment and prevention are described.

C. The ingestion of excessive quantities of ordinary tap water ("normal or wholesome water") or distilled water can cause poisoning mainly through dilution of the body fluids with a consequent reduction in the salt (mineral) content of these fluids.

D. The drinking of excessively cold water may cause serious, if not fatal, localised and general vasomotor disturbances.

E. In the more arid regions of South Africa both man and animal frequently suffer severely as a result of being forced through circumstances to drink highly mineralised waters. The main symptoms are bad teeth (caries), mottled teeth, gastrointestinal disturbances associated with nausea, vomiting and head-aches, diuresis and urinary calculi in man; and in animals sudden death, chronic diarrhoea, loss in appetite and condition, diuresis, urinary calculi, stunted growth, anaemia, and decreased productivity and reproduction. The nature and degree of the above symptoms may vary to a marked extent as they depend not only upon the total salt content of the water but also to a large extent upon the nature and quantities of the respective minerals present.

F. The factors concerned in the determination of the quantities of water drunk by man and animal are discussed.

G. The degree of salinity of subterranean waters, especially those obtained from shallow wells and boreholes, may vary considerably at different times of the year and in different years as their salt content is influenced (reduced) by rainfall.

H. The effects of the different minerals and their combined (synergistic) effects upon the system are discussed.

I. From the results of experiments conducted by various investigators and the analysis of specimens of water and observations made by us, the authors cannot but agree with the older authorities in England and the United States of America that the extreme limit of the total salt content of drinking water especially for human beings, should be 570 parts per million parts of water (=0.057 per cent. salts). The authors fully realise that this limit depends to a large extent upon the nature and quantity of the respective salts present and that the suitability of each mineralised water for drinking purposes should be considered on its own merits (analysis). The most poisonous ingredients of mineralised waters are nitrates, sulphides and fluorides, while magnesium, calcium and sulphates are inclined to upset the normal processes of mineral metabolism. The carbonates and bicarbonates of sodium and potassium render the gastrointestinal juices abnormally alkaline thus disturbing digestive processes and also cause the deposition of urates in the kidneys.
As far as the prevention of poisoning with highly mineralised drinking water is concerned the following methods are proposed. With regard to man (a) the water could be filtered through filters containing tricalcium phosphate, magnesium oxide, aluminium sulphate, activated aluminium, and permutite (hydrated sodium aluminium silicate). However, it should be realised that the efficacy of the above chemicals in removing fluorine and salts from water depends to a large extent upon the type of mineralised water (nature and quantities of the respective minerals present) the physical and chemical nature of the chemicals used and the temperature at which "de-salting" occurs. (b) Rain water should be stored in galvanised iron tanks and dams. And (c) attempts should be made by sinking several bore-holes to find less mineralised waters. On some farms with wells and bore-holes which contain poisonous saline waters, fairly wholesome water has been obtained by sinking a further number of bore-holes. As far as animals are concerned the only solution of the problem is that of sinking a number of bore-holes in an attempt to find wholesome water and to build dams. It is suggested that government assistance be rendered to farmers in the areas concerned, in the sinking of bore-holes and the building of dams.

It is in the interest of man and animal living in the more arid regions to make a detailed survey (analysis) of the types of water they are drinking, as many of them are in a sad plight.

VIII. ACKNOWLEDGMENTS.

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IX. REFERENCES.


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