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ACCIDENTAL POISONING IN CHILDREN IN CAPE TOWN, WITH SPECIAL REFERENCE TO KEROSENE AND SALICYLATES

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The total number of cases of poisoning admitted to the childrens' wards at Groote Schuur Hospital, Observatory, Cape, during the years 1951 - 1958 inclusive, and to the Red Cross War Memorial Childrens' Hospital, Rondebosch, Cape, from the time of its opening in June 1956 to the end of 1958, was small when compared with other reports, especially those from Johannesburg.[1,2] However, many of the Cape Town cases were treated as out-patients and not admitted to the wards.

There were 127 cases at Groote Schuur Hospital during the 8-year period, being 1·8% of admissions to the childrens' medical wards. There were 80 European, 39 Coloured, and 8 African children. These represented 3·3%, 1·0% and 1·0% of the total admissions for the respective racial groups. Three children died, a mortality of 2·4%.

The Red Cross War Memorial Childrens' Hospital had 39 cases in 2½ years, 18 being European, 17 Coloured and 4 African. The figure is 1·4% of the total admissions to the medical wards during this time. By races, the percentages of all admissions were 2·0%, 1·3% and 0·8% for European, Coloured and African children respectively.

Craig and Fraser[3] reported a continual increase in the number of cases of poisoning in children in 2 Scottish hospitals over a 20-year period up to 1951, and the Johannesburg workers' figures indicated a similar trend. The Groote Schuur Hospital figures for the period under review did not, however, show any such increase.

It is noteworthy that in our series there were considerably more Europeans than non-Europeans, despite the fact that of the patients admitted for all causes, about 66% were non-European. This is also reflected in the figures for children presenting with poisoning at the casualty department of Groote Schuur Hospital during 1958. In this period there were 39 Europeans and 29 non-Europeans. This does not, of course, necessarily mean that there were more cases of poisoning among Europeans in the community as a whole, since it may be that non-European children are not always brought to hospital unless symptoms are severe.

TABLE I. AGE INCIDENCE OF ACCIDENTAL POISONING

Hospital	*Dates*	*0 - 1 Year* %	*1 - 2 Years* %	*2 - 5 Years* %	*Over 5 Years* %
Cape Town ..	1951-1958	5	49	36	10
Scottish	1931-1951	5	37·4	47	10·6
Johannesburg (1) ..	1948-1952	6·4	43·7	39·1	10·8
(2) ..	1953-1955	6·8	48·2	40	10

Age Incidence

Our highest incidence was in the 1 - 2 year group, followed by the 2 - 5 year group. These figures agree with those of the Johannesburg workers,[1,2] while Craig's figures showed the opposite.[3] In the groups under 1 year and over 5 years all 3 centres had similar figures (Table I).

Nature of the Poison

Table II shows the commonest poisons ingested in order of frequency in the Cape Town, Johannesburg and Scottish series and in the childrens' section of Addington Hospital, Durban, as reported by Simson.[4]

In all 3 South African centres *kerosene* was the poison most frequently taken by children. *Barbiturate* poisoning was fairly common in all the reports quoted, but was seldom fatal. All our cases in this group recovered rapidly, though there was often marked ataxia for a few days. In only 1 case was it thought necessary to give bemegride (a reputed respiratory stimulant), but since its efficacy is doubtful, it will probably not be used in future cases.

Arsenical poisoning seems to be relatively more common in Cape Town than in the other 3 centres. We had 19 cases, mostly from the ingestion of ant-poison, but in a few instances 'sluggem' pellets, which contain metaldehyde as well as arsenic, had been taken. Full recovery followed in all but 2 of these patients, 1 dying shortly after admission. In the other case the child developed convulsions some months later, which may have been related to the previous arsenical ingestion.

TABLE II. FREQUENCY OF COMMONER POISONS

Poison	*Cape Town 1951-1958*	*Johannesburg 1948-1952*	*Johannesburg 1953-1955*	*Scottish hospitals 1931-1951*	*Durban 1949-1953*
Kerosene	43	152	119	31	42
Barbiturates ..	21	36	28	36	7
Arsenic	19	16	24	—	8
Salicylates	14	82	104	20	6
Caustic soda ..	3	57	17	4	9
Disinfectants ..	—	—	—	39	9
Camphor liniment ..	—	11	9	29	2
Turpentine	—	8	6	25	—
Ferrous sulphate ..	4	1	6	24	1
Total cases seen ..	166	594	527	296	126

Salicylate poisoning is seen quite often, and may carry a high mortality, especially when the drug is given in repeated doses to a febrile, dehydrated child. The high salicylate content of oil of wintergreen is well known,

about 45 gr. of salicylate per fluid drachm, but it is doubtful whether the public is aware of its lethal qualities.

A great many cases of *ferrous sulphate* poisoning, with a fairly high mortality rate, have been reported, especially from Great Britain. We had only 4 cases, all with minor symptoms and all recovering rapidly. The Johannesburg authors had only 1 case in their first report and 6 in their second.

TABLE III. TYPE OF POISONING AT GROOTE SCHUUR AND RED CROSS WAR MEMORIAL CHILDREN'S HOSPITALS (1951 - 1958)

	Eur.	*Col.*	*Afr.*	*Total*
A. Medicinal drugs:				
Barbiturates	14	7	0	21
Salicylates	10*	4	0	14
Sulphonamides	3	1	0	4
Ferrous sulphate	1	3	0	4
'Largactil'	0	3	0	3
Digitalis	3	0	0	3
Glyc. trinitrate	2	0	0	2
'Dexedrine'	2	0	0	2
Chloral	1	1	0	2
'Theominal', veg. lax., antihistamine, hyoscine—1 of each	4	0	0	4
INH	0	1	0	1
	40	20	0	60†
B. Household preparations:				
Kerosene	17	20*	6	43
Other hydrocarbons	4	2	0	6
Arsenic	12	7*	0	19
Insecticides	4	1	0	5
Caustic soda	2	0	1	3
Other corrosives	1	1	0	2
Alcohol	0	1	2	3
Antiseptics	3	0	0	3
Solder fluid (ZnCl)	2	0	0	2
Others, 1 each	6	1	0	7
	51	33	9	93†
C. Miscellaneous:				
Seeds	3	3	0	6
Belladonna (plant)	3	0	0	3
Scorpion bite	1	0	0	1
Snake bite, CO, and unknown poison—1 each	0	0	3	3
	7	3	3	13†

* One death in each of these groups.
† Grand total: 60 + 93 + 13 = 166.
Eur. = European, Col. = Coloured, and Afr. = African.

Table III gives the complete list of poisons for which the children were admitted to the 2 Cape Town hospitals.

KEROSENE POISONING

This was by far the commonest form of poisoning in the Cape Town hospitals, there being 43 cases in all. Seventeen were in European and 26 in non-European children.

Pulmonary Involvement

X-ray evidence of pulmonary involvement was very frequent, 27 of the 32 Groote Schuur Hospital cases showing infiltration of some part of the lung fields. The basal zones were always involved, commonly bilaterally. In a few of the more severe cases the hilar regions were also affected, but in none of the films did the upper lobes appear to be involved. That the changes occur early was shown by the fact that, in many of the patients who underwent X-ray examination in the casualty department soon after ingestion of the kerosene, infiltration was already apparent.

Clinical evidence of pulmonary involvement was present in the majority of cases, either at the time of admission or later, but some did not at any time have abnormal physical signs despite radiological changes. Although clinical recovery was rapid in most cases, the radiological signs tended to persist for some time. The average duration of stay in hospital was 9 days. Fever was present in more than 70% of patients, and a leucocytosis of over 10,000 per c.mm. was found in 17 out of 22 cases where a leucocyte count was recorded.

Nearly all patients underwent gastric lavage in the casualty department before admission to the wards. There is no proof that any became more ill because of this, but the procedure is unnecessary and, as is well known, lavage may be followed by regurgitation and further aspiration of kerosene.

How Does the Kerosene Reach the Lungs?

The usual story in our cases was the well-recognized one that on taking the kerosene the child immediately began to choke and cough — this direct aspiration of kerosene is the generally accepted route. It is, however, often stated that kerosene is also absorbed from the stomach and excreted into the alveoli through the pulmonary capillaries.

This view was advanced by Deichmann *et al.*[5] These workers introduced kerosene directly into the stomachs of several rabbits, and into the peritoneal cavities of others. They stated that on performing autopsies they found pulmonary changes, similar to those found after kerosene had been inhaled, in both groups of animals. Because of these findings they recommended stomach aspiration in cases of kerosene poisoning.

On the other hand, Lesser *et al.*[6] reported contrary results in similar experiments. Kerosene was run into the stomachs of 6 rabbits, but none of these showed any radiological or autopsy evidence of lung pathology. In 6 other rabbits, intratracheal instillation of kerosene resulted in both X-ray changes in the lungs and autopsy signs of oedema of the air passages with haemorrhages into the lung parenchyma. This work confirmed similar studies by Waring,[7] and by Reed *et al.*[8]

In 1954 Foley *et al.*[9] tied off the oesophagus in 10 rabbits and passed stomach tubes through openings below the ligatures. Kerosene was poured down the tubes and the animals were killed. Postmortem examination showed intense congestion of the brain but no lung changes either gross or microscopic. On the other hand, kerosene run down the trachea produced the same changes as found by others, namely haemorrhagic, necrotizing bronchopneumonia and 'asphyxial membranes' lining the alveoli.

Although there has been some experimental support for Deichmann and the matter cannot be said to be finally settled, it is evident that most workers favour aspiration as the sole cause of the lung pathology.

A point which probably supports aspiration is the finding, in our cases, and apparently in others also, that the upper zones of the lung fields always seem to be much less affected than the basal areas. This is contrary to what one would expect if there was a blood-borne carriage of kerosene to the lungs. Foley *et al.*[9] support this view.

In summary, kerosene is a very common form of poison-

ing in young children, although the mortality is low. X-ray changes in the lung fields occur in nearly every case even when there is no clinical evidence of pulmonary involvement. The respiratory pathology is probably solely the result of aspiration, and gastric lavage is to be deprecated.

SALICYLATE POISONING

This is one of the commonest forms of poisoning in the USA and elsewhere, and the many reports appearing on the subject indicate the magnitude of the problem.

Symptoms

Young children usually do not complain of the early symptoms of tinnitus, deafness and giddiness, and the most striking feature of salicylism in children is hyperventilation. There may also be fever, sweating, thirst and vomiting, all leading to dehydration. The child is often restless and drowsy and may become cyanosed. This may be followed by coma, convulsions and, finally, death from respiratory failure. There may be bleeding, particularly from the stomach or the nose, or into the skin, and intracranial bleeding has also been reported. This is usually due to hypoprothrombinaemia, but may rarely be the result of thrombocytopenia. Another complication which is mentioned by Hill[10] is a toxic encephalopathy.

The symptoms may suggest encephalitis, bronchopneumonia or diabetic ketosis, but the cerebrospinal fluid and lungs are found to be normal. Diagnostically, it is important to think of the possibility of salicylism in a child who is hyperventilating. The ferric chloride test will show the presence of salicylates in the urine and the serum-salicylate level may be high. This level, however, is variable, and Heymann *et al.*[11] reported cases from Johannesburg where symptoms were present with levels as low as 11 mg. per 100 ml. On the other hand, some of their patients had salicylate figures of 50 mg. per 100 ml. without symptoms.

Heymann's article on salicylate intoxication[11] discussed the problem fully and what follows is largely an amplification of that review, particularly with regard to the biochemical disturbance and treatment in the light of present-day opinion. Salicylate poisoning is so important that it seems worth while reiterating many of the points which Heymann made.

Mortality

This may be high, especially when a child receiving salicylates is already sick with fever, vomiting, poor fluid intake, and accompanying oliguria; the duration of the oliguria has an important bearing on the outcome of the case. If a healthy child swallows a quantity of salicylate the prognosis is usually better. This was well shown in Heymann's series.

Local Experience

In the 2 Cape Town hospitals there were 14 cases of salicylate poisoning, 10 of the children being Europeans. In nearly all of them the drug was self-administered and most recovered within a few days without trouble. Two cases, however, will be briefly described.

In the first, a child, aged 14 months, had been given intermittent doses of 'disprin' over a few days for a febrile illness. For 1 day before admission he had been restless and drowsy and had vomited all feeds. On admission he was hyperventilating and comatose. The serum salicylate level was 80 mg. per 100 ml., the CO_2 was 19 volumes %, and the blood urea 70 mg. per 100 ml. Under treatment he became hyperpyrexial and developed generalized convulsions. He improved physically but his final mental state was one of gross retardation, even allowing for the fact that he was said to have been somewhat backward in the past. There remained some uncertainty whether there was not in addition an encephalitis, as he had had measles a few weeks earlier. Alternatively, this may have been an example of the toxic encephalopathy mentioned by Hill.[10]

In the second case, a child aged 18 months was said to have swallowed about 1 oz. of oil of wintergreen. After stomach lavage the parents were allowed to take the baby home as there appeared to be no symptoms of poisoning but, on admission to the ward the next morning, she was cyanosed and very dyspnoeic, and rapidly became comatose. Convulsions followed, and the temperature rose to 106°F. Death occurred about 8 hours after admission despite treatment. At autopsy a very congested brain, with a subdural haematoma, was noted.

Pathology and the Biochemical Disturbance

It is thought that the first effect of salicylate is direct stimulation of the respiratory centre, resulting in hyperventilation and a respiratory alkalosis which may be severe enough to give rise to tetany. Corrective renal mechanisms come into play which bring about an increase in plasma chloride and decrease in bicarbonate and tend to reduce the alkalaemia. This may take some time, but there is probably some immediate buffering action by the haemoglobin and very likely by other mechanisms as well.

The result of all this is a change to a metabolic acidosis, which is enhanced by the acid salicylate still circulating and by the impaired renal function. Salicylates are slowly excreted even when renal function is normal and under the conditions mentioned above, excretion is even slower. The pre-existing state of dehydration and starvation in the sick child, together with the circulating salicylate, bring about a disturbance of carbohydrate metabolism with the development of ketosis, much as occurs in diabetic precoma. It would seem that salicylate interferes with several systems involved in carbohydrate metabolism.

A recent article by Winters and others[12] suggests that the position is even more complicated than outlined above, at any rate in infants and very young children. In 33 patients in this age group they found a simultaneous disturbance involving both a primary respiratory upset, shown by hyperventilation, and a primary metabolic disturbance, shown by ketosis. In other words, there appear to be several disturbances all operating simultaneously and the blood pH may be alkaline, acid or neutral. In older children and adults, however, the sequence seemed to be as outlined earlier.

Another toxic effect of salicylate is increase of the metabolic rate and heat production, presumably in skeletal muscle. If this effect exceeds the antipyretic effect of the drug, the heat loss from sweating and hyperventilation may be insufficient to control the patient's temperature, and hyperpyrexia may result.

Hyperventilation persists for some time and, in fact, prevents an extreme fall in blood pH. Stimulation of the respiratory centre by salicylate continues until the salicylate blood level has fallen considerably. Overbreathing, therefore, is not a good indication whether the disturbance is one of alkalosis or acidosis, and estimation of the blood pH is the only way to be sure of this since the CO_2 figures may well be low in either state.

The dehydration which occurs is said to be more the

result of water loss than of electrolyte depletion, and hypernatraemia may develop unless the relative excess of electrolytes can be removed. The volume of urine excreted may be insufficient to achieve this and the serum will then remain hyperosmolaric. Serum potassium is, however, sometimes decreased. The explanation for this is not clear, unless salicylate stimulates the pituitary gland to produce corticotrophic hormone with consequent potassium loss from adrenocortical activity.

Although laboratory findings may be somewhat variable, in the later stages, at any rate, they are likely to show a lowering of the following — CO_2-combining power, pH, prothrombin and possibly potassium; and an increase of sodium, urea and sugar.

TREATMENT OF SALICYLATE POISONING

Since there often is a delay in onset of symptoms, as in our second case, all patients attending hospital after ingesting salicylate should be admitted for observation.

The Rôle of Lavage

Washing out the stomach in cases of poisoning is a time-honoured form of treatment. Arnold *et al.*,[13] however, point out that since 1900 there has been only 1 report of an attempt to assess its value. This was done by Scandinavian workers who stated that in 80 cases treated in this way insignificant amounts of poison were recovered. It was felt that much of the poison had already passed beyond the stomach but that, in addition, a significant amount was washed into the intestines during the act of lavage.

To test this Arnold and his co-workers introduced salicylate into the stomachs of dogs and found that if lavage was delayed by 1 hour, little was recovered, but if done early, about 38% could be washed out. Using syrup of ipecacuanha as an emetic, they were able to recover 45% of the poison if the ipecacuanha was administered early, and 39% if late.

It would seem, therefore, that emesis, even if late, is as effective as early lavage. Not everyone would care to use this method, however, and the authors agreed that where there is severe depression of the central nervous system emesis is contra-indicated. Their recommendation was that if lavage is used, it should be preceded by aspiration to avoid driving the poison further along the gastro-intestinal tract. Bicarbonate solution should not be used as this may facilitate the absorption of salicylate. In any event, if hyperpnoea is already present, it is too late for lavage.

The Threat to Life

The immediate threat to life comes from hyperpyrexia and dehydration, and the initial treatment must be to correct these by efficient methods of cooling and by copious fluids, in most cases given intravenously.

An adequate fluid to use is ½-strength Darrow's solution in 2½% dextrose-water. Once laboratory reports are to hand, electrolytes may be further adjusted if necessary. The amount of fluid as suggested both by Segar and Holliday[14] and by Winters[15] is 20 - 50 ml. per kg. body weight for rehydration, in addition to the usual amounts for maintenance according to body weight. These will vary from 150 ml. per kg. body weight in infants under 1 year of age to 80 ml. per kg. body weight between 4 and 10 years. If dehydration is severe it may be necessary to give up to 100 ml. per kg. body weight for rehydration. It is difficult to give a hard and fast rule regarding the speed at which fluid should be given. To re-establish renal flow, intravenous fluids can be given quite rapidly for the first 6 - 8 hours. Some caution must, however, be exercised, since too rapid hydration has been followed in some instances by pulmonary oedema.

Alkalis or Not?

There is considerable controversy on this point. It was emphasized by Heymann[13] and also in a commentary in *Pediatrics*[16] that large amounts of alkali may easily throw the patient back into alkalosis. In *Pediatrics*, the writer stated that the hazard from alkalosis is often greater than the modest degree of acidosis being treated. A pH of less than 7·15 probably demands alkali therapy, but this must be strictly controlled by serial pH and CO_2 studies. It was stated that in most cases specific therapy against alkalosis is probably not necessary. Segar and Holliday[14] held the same views and stated that restoration of hydration and the addition of electrolytes will rapidly ameliorate the metabolic acidosis and restore renal function, with the resultant excretion of the various accumulated organic acids.

Winters[15] found that patients, properly hydrated and given the necessary electrolytes and carbohydrate but little or no alkali, usually began to recover. This recovery was, however, associated with a significant tendency towards the development of alkalosis, and this tendency was both aggravated and accelerated when large amounts of alkalinizing salts were given. He nevertheless recommended intravenous bicarbonate if the pH was 7·15 or less, but demanded pH and CO_2 estimations immediately after such infusion.

Alkalinization of the urine is known to increase the rate of excretion of salicylate, and 'diamox' has been tried by some workers with this in view. Some benefit seemed to result but convulsions occurred in certain patients and the wisdom of this form of treatment seems very doubtful.

Whitten *et al.*,[17] reporting to the American Pediatric Society recently, felt that the risk of accentuating the respiratory alkalotic phase by the use of alkalis, as many have claimed, was largely theoretical or based on only a few animal studies. They used intravenous alkalis in 21 children suffering from salicylate intoxication, whose ages ranged from 4 months to 4 years. There was full laboratory control throughout, and the authors claimed that the rate of excretion of salicylate and consequent decrease in its serum level was comparable with the cases treated by dialysis or exchange transfusion. It was in the paper by Heymann *et al.*[11] that exchange transfusion for salicylate poisoning was first reported. Since then Done and Otterness,[18] as well as others, have recommended this for severe cases.

Extracorporeal Dialysis

Another method of ridding the body of salicylate is by extracorporeal dialysis, but it has been said that this is impracticable in small children for technical reasons. It was interesting, therefore, to see a recent report by Spritz *et al.*[19] on the successful treatment of a 13 kg. boy using one coil of a Kolff twin-coil disposable artificial kidney. If the apparatus and a trained team are available, the

authors claim even better removal of salicylate than by exchange transfusion and feel that the method is indicated in all cases of salicylate poisoning showing hyperpyrexia, delirium, convulsions, coma or other signs of CNS involvement.

Other Factors

Vitamin K is needed to deal with the hypoprothrombinaemia, and vitamin C should also be given for possible capillary damage, since it has been shown experimentally that salicylates increase ascorbic acid excretion.

Care should be taken with drugs such as barbiturates, which may depress respiration, decrease CO_2 excretion and prevent the serum pH from returning to normal.

Suggested Plan of Treatment

1. Hospitalization of the patient.

2. If the patient is seen very early and is fully conscious, aspiration of stomach contents followed by lavage with water may be carried out, or alternatively an emetic may be given.

3. Half-strength Darrow's solution should be given either intravenously or by mouth, and on receipt of laboratory reports further adjustment of electrolytes may be made if necessary.

4. If the child is still acidotic after rehydration and the pH is found to be 7·15 or less, alkalis are indicated. If there are no facilities for pH studies and a considerable time has elapsed since the ingestion of the salicylate, it is probably safe to give alkalis if acidosis appears to be persisting after the child is fully hydrated. One-sixth molar lactate solution, 10 ml. per lb. body weight, given intravenously, is safer than bicarbonate, although the latter given in reasonable amounts by mouth would seem, after all, not to be harmful.

5. Vitamins K and C should be given intramuscularly.

6. In a severe case, and where facilities are available, exchange transfusion or extracorporeal dialysis may be very effective.

SUMMARY

An account is given of cases of poisoning in children admitted to 2 Cape Town hospitals over a period of several years.

Kerosene, the commonest form of poison in our series, is considered in some detail, particularly as regards the way in which it reaches the lungs.

The dangers of salicylates are stressed and current opinions are given concerning the rather complicated biochemical disturbances which occur in this type of poisoning. Controversial views on whether or not alkalis should be used in treatment are reviewed and a suggested plan of treatment is offered.

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REFERENCES

1. Drubin, R. and Cohen, H. (1955): S. Afr. Med. J., **29**, 101.
2. Friedlander, F., Drubin, R. and Veitch, M. (1956): Med. Proc., **2**, 575.
3. Craig, J. O. and Fraser, M. S. (1953): Arch. Dis. Childh., **28**, 259.
4. Simson, I. C. (1956): S. Afr. Med. J., **30**, 1030.
5. Deichmann, W. B., Kitzmiller, K. V., Witherup, S. and Johansmann, R. (1944): Ann. Intern. Med., **21**, 803.
6. Lesser, L. I., Weens, H. S. and McKey, J. D. (1943): J. Pediat., **23**, 352.
7. Waring, J. I. (1933): Amer. J. Med. Sci., **185**, 325.
8. Reed, E. S., Leiken, S. and Kerman, H. D. (1950): Amer. J. Dis. Child., **79**, 623.
9. Foley, J. C., Dreyer, N. B., Soule, A. B. and Woll, E. (1954): Radiology, **62**, 817.
10. Hill, F. S. (1954): *Practical Fluid Therapy in Pediatrics*, p. 193. Philadelphia and London: W. B. Saunders.
11. Heymann, S., Javett, S. N. and Rudolph, A. M. (1954): S. Afr. Med. J., **28**, 1092.
12. Winters, R. W., White, J. S., Hughes, M. C. and Ordway, N. K. (1959): Pediatrics, **23**, 260.
13. Arnold, F. J., Hodges, J. B., Barta, R. A., Spector, S., Sunshine, I. and Wedgwood, R. J. (1959): *Ibid.*, **23**, 286.
14. Segar, W. E. and Holliday, M. A. (1958): New Engl. J. Med., **259**, 1191.
15. Winters, R. W. (1959): Pediat. Clin. N. Amer., **6**, 281.
16. Commentary (1959): Pediatrics, **23**, 255.
17. Whitten, C. F., Kesaree, N. and Goodwin, J. F. (1959): Amer. J. Dis. Child., **98**, 492.
18. Done, A. K. and Otterness, L. J. (1956): Pediatrics, **18**, 80.
19. Spritz, N., Fahey, T. J., Thompson, D. D. and Rubin, A. L. (1959): *Ibid.*, **24**, 540.