ME-10 Insulin, thyroid, epinephrine and the drugs that cannot be made: the pre-pharmaceutical regimens

HEALING after the FALL, research library, ME-10

Researched 10 October 2026 by Claude Opus agent for THRIVING after the FALL, Book Four. Library document, unverified.

How to read this document

This report is about the people who will be alive on the day the supply ends and dead or disabled some time after: the insulin-dependent diabetic, the hypothyroid, the person without adrenal glands, the person who dies of a wasp sting in fifteen minutes. FO-01 has set the clock on which drug loss kills, ME-09 covers how long salvaged insulin, levothyroxine and adrenaline keep, and MA-02 covers bleeding after birth (THRIVING library, FO-01, ME-09 and MA-02). None of that is repeated. This report answers what those three leave open: when the vial is empty, what did people live on before the vial existed, for how long, and what can a district of 3,000 with a slaughterhouse honestly do.

On manufacture. The brief asks whether a district can make insulin or thyroid hormone from animals. The answer is given as the record shows it: who managed it, in what buildings, with what staff and what failure rate. No extraction method, no purification step and no reagent appears here, and none should enter the book. An unassayed hormone preparation is not a weak medicine. It is an unknown dose of a drug whose overdose kills in hours.

What the period practice claimed, what the clinical record showed and what I infer are kept apart throughout. My own arithmetic and judgement are marked [VERIFY].

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1. The clocks: how long without the drug

Type 1 diabetes. Days to weeks, fastest in the young and thin. Krzentowski and colleagues stopped the insulin pump in eight adults with no residual C-peptide: ketones rose from the first hour, and at six hours 3-hydroxybutyrate was 1,290 micromoles per litre and glucose 17.4 millimoles per litre (Krzentowski 1983, summary read). That is six hours in a rested, fed adult, and what follows depends on residual insulin. Where insulin is unaffordable today, Yudkin reports that life expectancy after diagnosis in parts of Africa may be as short as one year, and that 0.48 per cent of the world's insulin would treat every type 1 patient in the forty poorest countries (Yudkin 2000, abstract and secondary summary read).

Myxoedema. Weeks to years. Levothyroxine has a half-life of about one week, so someone who stops is biochemically hypothyroid within about four weeks (NHS Specialist Pharmacy Service 2026, read), with symptoms over months. Death comes as myxoedema coma, usually triggered by cold, infection, injury or a sedative, and reported mortality even in intensive care is 38.8 per cent pooled across 2004 to 2024 and 29.5 per cent in a Japanese database of 149

patients (StatPearls, summary read). Someone with no thyroid tissue at all is on this clock. Someone with partial failure may be on a much longer one.

Addison's disease. Two clocks. The slow one is wasting, weakness, darkening skin and salt loss over months. The fast one is adrenal crisis, which kills in a day and is set off by infection, vomiting, injury or the abrupt loss of the tablet. Before specific therapy, Thorn's yearly mortality as quoted by Evans, Flink and Hoilund was 43 per cent, falling to about 30 per cent on the salt-and-extract regimens of the 1930s and about 9 per cent on deoxycorticosterone (Evans, Flink and Hoilund 1943, read in full). Modern treated patients still have crises at about 6 to 8 per 100 patient-years and die of them at about 0.5 per 100 patient-years (Frontiers review 2022, read in part, and Bergthorsdottir 2009, abstract read). Losing hydrocortisone means roughly a two-in-five chance of death in the first year, concentrated at moments of stress.

Anaphylaxis. Minutes. Pumphrey's study of fatal United Kingdom reactions gives a median time from onset to arrest of 5 minutes for drugs, 15 for insect venom and 30 for food (Pumphrey 2000, abstract read). The district will not arrive in time.

FO-01 estimates about one type 1 diabetic per village of 300. Treated hypothyroidism is far commoner, so a village likely holds several people on thyroid replacement, while diagnosed Addison's disease runs near one per 10,000, so a district may have one or none [VERIFY].

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2. Type 1 diabetes before insulin: what the diet really bought

What the practice claimed. Frederick Allen at the Rockefeller Institute from 1914, and Elliott Joslin in Boston, held that the failing pancreas could be rested if the patient was fasted until the urine was sugar-free and then fed the smallest diet that held that state. It was never claimed as a cure, only as an extension of life.

What the record showed. Mazur's reading of Allen, Stillman and Fitz 1919 and of Joslin's tables is the best modern account (Mazur 2011, read in full). Of the Rockefeller series of 76 cases, 43 per cent were dead by late 1917, four of them from inanition, that is from starvation rather than from diabetes. Mortality by February 1918 fell steeply with age at onset: 75 per cent of the 8 patients aged 0 to 9, 71 per cent of 14 aged 10 to 19, 64 per cent of 14 aged 20 to 29, and 18 per cent of 11 aged 50 and over. Of the 11 patients under 20 among the first 44, 78 per cent were dead by October 1917. There were no untreated controls, which is why the diet's benefit cannot be quantified honestly. Joslin's figures agree from another hand: deaths among patients aged 10 or under ran at 824 per 1,000 in the Naunyn era of 1897 to 1914 and 386.2 per 1,000 in the Allen era of 1914 to 1922, 74 per cent of all pre-insulin deaths were ketoacidosis, and Joslin had lost 62 patients under 15 by 1916, every one to coma (Portuese and Orchard 1995, read).

What it cost. Allen's severe diets reached 400 kilocalories a day. Case 51, a child of 7, was held at about 700 kilocalories with a weekly fast day and died about two months later. Elizabeth Hughes, diagnosed in 1919 at 11, was fasted a week then held at about 500 kilocalories with one fast day a week, falling from 75 pounds to 55 and weighing 45 in the winter of 1921 to 1922 (Mazur 2011, and THRIVING library, SY-03). Phyllis Adams, aged 5, in Australia, lived eight months on a teaspoon of peanut butter, a lettuce leaf and junket a day, and weighed 10 kilograms when insulin reached her in 1922 (Auckland Medical History Society slides, read).

The honest conclusion. In children the diet roughly halved early mortality and bought months to a year or two, at that cost. In older, mild, probably type 2 cases it worked well, and those patients fill out the good survival figures. Reading a pre-1922 survival figure without its age and stage is the commonest error here.

Where I extend FO-01. Its bedside line for the dying diabetic child, salted fluids and comfort, stands. I add one thing for adults. A newly diagnosed adult who is not ketotic and not rapidly wasting probably has residual insulin, and for that person a low-carbohydrate diet with enough calories to hold weight is worth doing, because that is the group the record shows living for years. The distinction to teach is not the diagnosis but the ketones and the wasting.

3. Toronto 1922, and the honest answer on making insulin

On 11 January 1922 Leonard Thompson, aged 14 and diabetic for three years, was given 15 millilitres of the Banting and Best extract at Toronto General Hospital. It was impure. His blood sugar fell about a quarter, his glycosuria barely moved, and he developed a sterile abscess, so the injections stopped. On 23 January, after James Collip had produced a cleaner preparation, Walter Campbell gave it again, and this time glucose and urinary sugar fell and the ketones disappeared (Origins, Science Museum Group and Hektoen accounts, read as secondary summaries). Thompson died of pneumonia in April 1935, aged 26 or 27.

Three facts from the months that followed matter more here than the triumph.

1. **The potency vanished.** From about March to mid-May 1922 Collip's large batches had little or no potency and nobody could at first say why. In that insulin famine at least one patient died when the supply gave out.
2. **Purity was the problem, not discovery.** Extracts that lowered blood sugar had existed for twenty years and were toxic. Collip added purification, Eli Lilly added yield and standardisation (Rosenfeld 2002, abstract read, and American Chemical Society landmark account, read).
3. **Dosing needed a live-animal assay.** The Toronto committee defined one unit in 1922 as the quantity that lowers the blood glucose of a fasting rabbit to 2.5 millimoles per litre, which varies with the size and nutrition of the rabbit (Auckland Medical History Society, read, and Nature 1925, read). A United States Public Health Service document records Lilly using on the order of 100 to 500 rabbits per lot (CDC Stacks document, read).

The yield, which decides the question. By 29 November 1923 Connaught Laboratories were making about 250,000 units a week with 26 staff on day and night shifts, from pancreas fresh from abattoirs, in a plant costing over 35,000 dollars (Connaught news item, read). Against that, Rahmat-Ullah, Ahmed and Ahmad assayed pancreas from the Lahore slaughterhouses and found 892 to 1,002 units per kilogram in beef and 585 to 695 in mutton, far below Fisher and Scott's published figures, which ran from 29,000 to 38,800 units per kilogram in five-month foetal calves down to 1,700 to 2,000 in cows at 9 years (Rahmat-Ullah 1958, read in full). They blamed the animals, which walked to the city for a week or ten days and arrived frail, and the delay, because glands could not be handled within an hour of slaughter. Their conclusion was that the city's 30 to 40 kilograms of pancreas a day, about 30,000 units, was not worth a commercial plant unless the slaughterhouses were organised and freezing provided.

The arithmetic. An adult on roughly 40 units a day needs about 14,600 units a year, so at the Lahore content of about 900 units per kilogram, with recovery always below content, that is at least 16 kilograms of pancreas a year per patient and probably far more [VERIFY, my arithmetic]. The dose range itself, 0.5 to 1.0 units per kilogram per day for children with a registry mean near 0.86, is from secondary summaries of American Diabetes Association and ISPAD guidance [VERIFY].

The answer. A district of 3,000 cannot make insulin, and this is not a matter of effort or secrecy. Four things set the ceiling and none can be improvised: a cold chain from the killing floor, because the hormone is destroyed by the gland's own enzymes within the hour Lahore could not beat, a purification that removes the toxic fraction, because the impure extract gave Thompson an abscess and no useful fall in sugar, a bioassay, because without one the product has no dose and the first killer is hypoglycaemia rather than hyperglycaemia, and a chemist. The record shows the attempt without them: inert batches and a dead patient in the spring of 1922. The modern Open Insulin Project, with recombinant yeast in a funded laboratory, reports a lab-scale product and names yield as the unsolved bottleneck (Open Insulin Project pages, read). That is the floor of the modern attempt and it is far above a district.

What a district can do is keep the salvaged stock alive and ration it, by ME-09's storage methods and by a decision on priority made in advance (THRIVING library, ME-09).

4. Type 2 diabetes by diet, and the plant behind metformin

The diet. This is the one place in the report where the news is very good. DiRECT randomised primary-care patients with type 2 diabetes of up to six years' duration to a programme beginning with total diet replacement at about 825 to 853 kilocalories a day for three to five months, with stepped food reintroduction and withdrawal of diabetes drugs. At twelve months, remission off all drugs was 46 per cent, 68 of 149, against 4 per cent of controls (Lean 2018, published summary read). The effect tracked weight almost exactly: 86 per cent remission in those losing 15 kilograms or more, 57 per cent at 10 to 15, 34 per cent at 5 to 10 and 7 per cent at 0 to 5. Grade A, and a village can do it without a drug. The cautions are that the patient must come off any sulfonylurea or insulin as the diet starts, and that this is type 2 only.

Galega officinalis L., Fabaceae, goat's rue, aerial parts. A perennial shrub to about 1.5 metres with pinnate leaves of 4 to 8 pairs of elliptic sharp-tipped leaflets up to 2.5 centimetres, purple to light blue or white pea flowers and pods up to 5 centimetres. The dangerous confusions are with the vetches (Massey University poisonous plants database, read).

The tradition is European and mediaeval, the plant given for excessive urination. The record is that it is rich in guanidine, that guanidine was shown to lower blood glucose in 1918, that galegine and synthalin were used clinically in the 1920s and abandoned for toxicity and weak effect by the early 1940s, that Sterne reported metformin in 1957, and that phenformin and buformin were withdrawn in the late 1970s for lactic acidosis (Bailey 2017, abstract and secondary summary read).

The harm is documented in sheep. The toxins are canavanine, galegine and peganine, they remain active in dried hay, and the plant is worst in flower and fruit. Poisoned sheep show a latent period of 18 to 24 hours and then die within hours of pulmonary oedema, with no treatment (Massey University, read). A veterinary secondary source puts the dangerous intake at about 0.2 per cent of body weight [VERIFY].

Verdict. Grade D as a medicine and X as a dose. The plant is metformin's ancestor as willow is aspirin's, but with a far worse margin, and a village cannot know how much galegine is in a given plant on a given day. Carry Galega as history and as a poisonous plant to recognise. Eat less and walk more is the evidence-based treatment, and it is the better one.

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5. Hypothyroidism: Murray 1891, the grain, and why guessing kills slowly

The first record. On 13 April 1891 George Redmayne Murray treated a 46-year-old woman with myxoedema with a glycerin extract of sheep thyroid, injected under the skin, 1.5 millilitres twice a week. She was dramatically better within three months and lived to 74, about 28 years of treatment (Hektoen International account of Murray, read, citing Murray 1891 BMJ 2:796, original not read). Within eighteen months others found the gland worked by mouth, Hector Mackenzie reporting a case fed fresh sheep thyroid in October 1892. This is one of the clearest therapeutic successes in medicine, achieved with a sheep, a knife and a careful physician.

The harm arrived immediately. Fox reported a patient who took a double dose by mistake and had profuse sweating and weakness. Watson Williams fed a patient two raw glands a day in a sandwich, and after four the temperature was 101 degrees Fahrenheit with a fast pulse, followed by vomiting. An 1893 review recommended no more than one lobe two or three times a week and remarked on the difficulty of fixing a dose at all (contemporary review of the 1890s cases, read). Murray warned against pushing it in anyone with cardiac signs.

The dose, from two sources, with the difference stated. The unit is the grain, about 60 to 65 milligrams. One grain of United States Pharmacopeia thyroid contains about 38 micrograms of thyroxine and 9 micrograms of triiodothyronine, and the stated conversion is 1 milligram of extract to about 1.667 micrograms of levothyroxine, making 60 milligrams about 100 micrograms (NHS Specialist Pharmacy Service, read). A second published conversion

gives about 1.47 micrograms per milligram, making 60 milligrams about 88 micrograms (encyclopaedic summary of desiccated thyroid, read) [VERIFY]. The two differ by about an eighth, which shows how soft the conversion is. Triiodothyronine is roughly four times as potent by weight and peaks 2 to 5 hours after a dose, which is why extract produces palpitations and tremor that levothyroxine does not.

What the twentieth century learned about dosing it. McAninch and Bianco traced the recommendations (McAninch and Bianco 2016, read in full). In 1929 the advice was to start at 3 grains and titrate to the basal metabolic rate, in 1955 1.5 to 2 grains, by 1986 1 to 1.5 grains, and after the thyroid-stimulating hormone assay arrived the equivalent maintenance settled at about 100 to 150 micrograms of levothyroxine, down from a former 200 to 500. Once there was a blood test it turned out that doses normalising symptoms or metabolic rate had been supratherapeutic for decades.

And about standardising it. Potency between tablets ranged historically from double the stated metabolic activity to none detectable, and shelf life in humidity was poor. The pharmacopeia standard rested on iodine content, 0.17 to 0.23 per cent of the defatted gland, until 1985, when it was changed to measured hormone content because a study of ten compliant samples found four markedly off potency although all met the iodine specification (McAninch and Bianco 2016, read in full). That is decisive: iodine content is the only property of the gland a simple chemical test can reach, and it does not predict hormone content. Nor is poisoning by thyroid in meat theoretical. Hedberg and colleagues traced an outbreak of thyrotoxicosis in the American midwest between April 1984 and August 1985 to ground beef made from neck trimmings containing bovine thyroid, with 121 cases identified and gullet trimming subsequently banned (Colorado State University account of Hedberg 1987, read).

Verdict at the district rung. The record genuinely differs from insulin's and the book should not flatten the two. Thyroid hormone survives drying and works by mouth, so the thing is physically possible in a way insulin is not, and the 1890s proves it. But the 1890s proves the rest as well. The dose cannot be fixed by eye, the gland varies by species, season and animal, overdose accumulates over weeks rather than announcing itself, and the only assay a district could run is the one shown not to work. No preparation method is given in this book. The outcome is what can be said: a hypothyroid person given gland of unknown potency will be either still hypothyroid or slowly thyrotoxic, and the second is not obviously better, because chronic over-replacement causes atrial fibrillation and osteoporosis, and after the Fall a fractured hip in an old person is a death sentence.

The ranking to use. Ration salvaged levothyroxine, which ME-09 records as moisture-sensitive, so keep it dry and expect it to fade (THRIVING library, ME-09). Give it first to those with no gland at all, the pregnant and children, and let the mildly hypothyroid old go without. Grade A for levothyroxine, B for desiccated thyroid of known potency with a blood test, D and a warning for gland of unknown potency.

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6. Graves' disease: iodine, the knife, and the storm

I could not find a reliable untreated mortality figure for Graves' disease from before 1900 and the book should not invent one. What the record shows is that before iodine, surgery for the toxic goitre was lethal: Mayo's operative mortality was of the order of 4 to 5 per cent and Jonnesco in 1898 reported nearly 20 per cent mortality with fewer than 40 per cent cured (Kopp 2023, read, with thyroid-history summaries, read).

Plummer's iodine. Henry Plummer gave Lugol's iodine before thyroidectomy from 1922 and published in JAMA in 1923. Symptoms abated within days and Mayo's surgical mortality fell below 1 per cent (Kopp 2023, read in full). This is among the highest-value facts here, because iodine is salvageable, storable, cheap and fast.

The catch is real. Iodine escapes. Suppression of the gland by a large iodine load, the Wolff-Chaikoff effect described in 1948, is temporary, and the gland escapes over weeks, after which the extra iodine can worsen the thyrotoxicosis. Iodine-induced thyrotoxicosis was named Jod-Basedow by Kocher in 1910, and deaths from hyperthyroidism rose in

the late 1920s as iodine came into wide use (Kohn 1976, cited in Kopp 2023). Japanese series do show iodine working longer term in selected patients, with response around 60 to 80 per cent and remission around 40 per cent in a 2024 review (Okamura 2014, American Thyroid Association summary read). Escape is why it is not standard therapy, and giving it without a plan for the sixth week is a way of killing someone slowly.

Thyroid storm. Mortality was 10.7 per cent in the Japanese nationwide surveys of 2004 to 2008 and 5.5 per cent at 30 days in a 2024 prospective registry, with older reports from 10 to 75 per cent (Furukawa 2024, abstract and institutional summary read). Those are intensive-care numbers and they do not transfer. Without a thionamide, iodine alone in a storm can worsen it, which is why protocols give iodine at least an hour after the antithyroid drug. The stated adult doses, from secondary clinical sources, are saturated potassium iodide 5 drops every 6 hours or Lugol's solution 4 to 8 drops every 6 to 8 hours.

Verdict. Grade B for iodine as short-term control, with the explicit limit that it buys days to weeks, and grade C as the only thing available, with the plan stated in advance. Thyroidectomy at a district is grade X: without iodine, transfusion or a safe airway it would reproduce the 20 per cent, not the 1.

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7. Addison's disease: salt first, and the truth about liquorice

The first century. Osler's patient in 1896 had a glycerol extract of sheep adrenals and died in crisis when it stopped. Adams collected 97 cases of adrenal organotherapy in 1903: 7 made worse, 43 with no real benefit, 31 markedly improved and 16 permanently relieved, while adrenal grafting from dogs killed all three patients within three days (The Hospital, 10 October 1903, read in full). Evans, Flink and Hoilund are blunt about why in 1943: the crude cortical extracts were toxic, and preparations from whole adrenals contained adrenaline as well. Injecting crude adrenal extract is condemned by the contemporary record.

What changed the disease was salt. Loeb's demonstration in 1933 was the turning point, with Wilder in 1936 adding potassium restriction. The regimen Evans and colleagues describe is a diet cooked and seasoned with salt, supplying about 4 grams a day, plus 9 to 12 grams added, for a total of about 16 to 18 grams, with individual cases running from 8 to 20 grams. Their deoxycorticosterone figures quantify what salt is worth: a patient taking 12 grams of salt a day needed about 3 milligrams of the hormone, at 4 grams about 12 milligrams, and under 2 grams 23 to 30 milligrams. Salt is not a placebo. Their patient instructions transfer unchanged to a district: report a sudden weight gain of 5 pounds or a total gain of 10 pounds, which signals oedema, and increase salt at the first sign of infection. Hypothyroidism commonly accompanies Addison's disease, so two of this report's problems often sit in one patient.

Glycyrrhiza glabra L., Fabaceae, liquorice, root and stolons. A perennial of 50 centimetres to 2 metres with sticky imparipinnate leaves of 9 to 17 leaflets, pale blue to violet pea flowers in racemes, and stolons 1 to 2 centimetres thick whose cut surface shows yellow radial wood and tastes strongly sweet (Cretan flora and VicFlora, read, VicFlora giving 5 to 17 leaflets). The dangerous lookalike is Abrus precatorius, called Indian liquorice, whose root was used as a liquorice substitute in India and whose seeds contain abrin, fatal dose quoted at 0.1 to 1 microgram per kilogram, with deaths from one or two chewed seeds (INCHEM poisons monograph, read). Astragalus glycyphyllos is also called wild liquorice and I could not source its safety [VERIFY].

The pharmacology is real and specific. Glycyrrhetinic acid, the active metabolite of glycyrrhizin, inhibits renal 11-beta-hydroxysteroid dehydrogenase type 2, the enzyme that keeps cortisol off the mineralocorticoid receptor. Inhibited, the patient's own cortisol acts on that receptor, holding sodium and losing potassium. The resulting pseudohyperaldosteronism is hypertension, hypokalaemia and, at the extreme, weakness and paralysis (van Uum 2005, read in full). Borst and colleagues showed in the Lancet in 1953 that liquorice and cortisone act synergistically in Addison's disease.

The finding that decides its use. Liquorice needs cortisol to work, because its whole mechanism is to let the

patient's own cortisol reach the receptor. In complete adrenal failure there is none to potentiate, and a review of the related compound carbenoxolone notes benefit appearing in patients with residual adrenal tissue. My conclusion is that liquorice is a useful adjunct in partial adrenal insufficiency and close to useless as sole treatment in someone with none [VERIFY, my inference from the mechanism and from Borst's synergy result].

The dose, with the disagreements. The regular safe intake is put at 100 milligrams of glycyrrhizin a day by the Scientific Committee on Food in 2003 and by JECFA in 2004, both noting that sensitive people react at or below it (SKLM 2005, read, and BfR 2023, read). The root contains up to 14 per cent glycyrrhizin, and glycyrrhetinic acid in confectionery averages about 2 milligrams per gram but ranges from 0.026 to 98, a spread of nearly four thousandfold (van Uum 2005). Van Gelderen's trial gave 0, 1, 2 or 4 milligrams per kilogram per day for eight weeks and found pseudohyperaldosteronism in 9 of 11 subjects at 4 and none at 2 (SKLM 2005). Sigurjonsdottir gave 50 to 200 grams a day, that is 75 to 540 milligrams of glycyrrhetinic acid, for two to four weeks and found a linear systolic rise of 3.1 to 14.4 millimetres of mercury (Sigurjonsdottir 2001, secondary summary read). The European Medicines Agency monograph gives 1.5 grams of root in 150 millilitres as an infusion twice daily, for no more than four weeks and not under 18 (EMA assessment report, read).

Who must never have it. Hypertensives, people with heart disease or low potassium, people on diuretics or digoxin, and pregnant women. The BfR reviews Raikkonen's work on more than 250 grams a week in pregnancy, concludes that the data cannot support a causal claim, and still advises pregnant women to avoid large regular amounts (BfR Communication 10/2023, read in full). The book should keep that shape: the evidence is weak, the advice is still to avoid.

Verdict. Salt is grade B and the backbone. Liquorice is grade C as an adjunct in partial insufficiency and grade D otherwise, with a named harm.

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8. Epinephrine, and anaphylaxis without an ampoule

The history. Oliver and Schafer showed in 1894 that adrenal extracts raised blood pressure, Abel named his product epinephrin in the late 1890s but had isolated a derivative, and Jokichi Takamine obtained the crystalline substance in 1901 (secondary accounts, read). The natural medullary secretion is a mixture of adrenaline and noradrenaline, one reason crude extract behaves differently from the pure drug.

Why crude extract cannot be dosed. The therapeutic adult dose is 0.5 milligrams into muscle, and the margin to hypertensive crisis, pulmonary oedema or ventricular arrhythmia is not large even at a known concentration. An extract of unknown strength offers no way to land inside it, and the 1943 review names adrenaline in whole-adrenal preparations as a source of toxicity rather than benefit (Evans, Flink and Hoilund 1943). Adrenal medulla extract is not a substitute for an ampoule.

The reference doses, so a district knows what it has lost. Resuscitation Council UK 2021 gives intramuscular adrenaline at 1 milligram per millilitre: 0.5 milligrams for adults and children over 12, 0.3 for 6 to 12 years, 0.15 for 6 months to 6 years and 100 to 150 micrograms under 6 months, repeated after 5 minutes if needed (Resuscitation Council UK 2021, read in full). The World Allergy Organization agrees that intramuscular adrenaline is first line and notes that autoinjectors are scarce in much of the world (Cardona 2020, abstract read). ME-09 has the stability: about two years past expiry near full strength, four years about four-fifths, ten years half to three-quarters (THRIVING library, ME-09).

What helps when there is no ampoule, and how thin the evidence is.

- **Posture.** Pumphrey's series of 88 fatal reactions found 4 patients dying within seconds of being moved more upright and 5 held upright while unconscious who died (Pumphrey 2003, via BestBets, read). Lying flat with

the legs raised is the one free intervention with a body of evidence behind it, and that evidence comes from deaths rather than a trial.

- **Fluid.** The Resuscitation Council tables note that a 500 to 1,000 millilitre crystalloid bolus restored venous return more effectively than a single intramuscular dose of adrenaline. A district with fluid and a needle has something real.
- **Antihistamines and steroids.** No randomised trial exists for either. Sheikh's Cochrane review found none, Choo, Simons and Sheikh screened 2,496 reports and found no trial of glucocorticoids, and the Resuscitation Council recommends strongly against relying on antihistamines for respiratory or cardiovascular symptoms. They are for the itch and the rash.
- **Ephedra and Datura.** ME-07 grades ephedra C as a low-dose adult decoction for asthma and X as a stimulant, with stroke risk above about 32 milligrams a day of alkaloid, and Datura stramonium C with no dose given (THRIVING library, ME-07). I searched for evidence of ephedrine in anaphylaxis and found none. The claim that ephedra substitutes for adrenaline is unsupported and implausible, because ephedrine is a weak indirect sympathomimetic with a slow oral onset while anaphylaxis kills in minutes. The book should say so, because this claim will circulate after the Fall.

The hardest fact. Adrenaline was given in 62 per cent of Pumphrey's fatal cases but before arrest in only 14 per cent, and some reactions are fatal whatever is done (Pumphrey 2000). The district's real work is prevention.

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9. Two more that cannot be dosed: pituitary extract and dicoumarol

Posterior pituitary extract, pituitrin. Henry Dale described the oxytocic action of the posterior pituitary in 1906, and Blair Bell and Hicks took it to patients in Liverpool in 1909, where it proved effective in the atonic bleeding uterus while raising blood pressure at the same time (contemporary accounts, read as summaries, and Anderson 1914, metadata only). Hofbauer used it in labour from 1911, and later reports described intracranial haemorrhage in the infant and ruptured uterus in the mother. Kamm separated the oxytocic from the pressor fraction only in 1928. The point is the same as for insulin and adrenaline: a crude extract contains both, cannot be separated at a district, and the pressor fraction is not an inert passenger in a woman who is bleeding. Uterine massage, salvaged ergometrine or misoprostol and tranexamic acid are the answer, as MA-02 sets out (THRIVING library, MA-02).

Melilotus officinalis (L.) Lam. and Melilotus albus Medik., Fabaceae, sweet clover. M. officinalis is a biennial to about 1.5 metres with trifoliate serrate leaflets 10 to 25 millimetres, yellow petals 4 to 6 millimetres, slender racemes to 20 centimetres and a wrinkled pod of about 3 millimetres. M. albus is the white-flowered equivalent (Flora of New Zealand, read, and United States Forest Service species review, read). The plant is harmless as properly cured hay. When it moulds, fungal action converts its coumarin to dicoumarol, which blocks vitamin K.

Veterinarians in Ontario and North Dakota described the bleeding disease in cattle in the 1920s, 30 to 50 days after the spoiled hay was first fed, and found that removing the hay or transfusing corrected it. In 1933 a Wisconsin farmer brought a dead heifer and a can of unclotted blood to Karl Link's laboratory, Harold Campbell isolated the agent in June 1939, and warfarin followed in 1948 (Hektoen International history of anticoagulants, read). The Merck Veterinary Manual gives the cattle exposure as roughly 20 to 30 milligrams of dicoumarol per kilogram of hay over several weeks, with a delay stretching to months at low dose, and lists lameness from bleeding into joints, haematomas and nosebleeds, with deaths at injury, surgery or calving (Merck Veterinary Manual, reviewed June 2025, read).

The plant belongs in the book twice. As a hazard it is the reason to inspect hay and never feed mouldy sweet clover, especially before castration, dehorning or calving. As a would-be medicine it is grade X: the content depends on which mould grew on which bale, and the margin between useful anticoagulation and fatal haemorrhage is measured by a laboratory test that will not exist.

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10. The rundown plans, disease by disease

Type 1 diabetes. Count the units on day one, divide by the daily dose, write the date. Move to fewer carbohydrates and regular small meals so that less insulin is needed, and keep the stock cool. In the last weeks tell the patient and the family what is coming and when. A child should not be put on a starvation diet, because it does not work and adds hunger to dying. The comfort is warmth, company, fluid and the truth that the coma itself is not painful.

Type 2 diabetes. This patient usually does better after the Fall than before, provided sulfonylureas and insulin are withdrawn as the food reduces. Watch for hypoglycaemia in the first fortnight. The target is weight, and 15 kilograms is the number.

Hypothyroidism. Count tablets, halve the dose in the mild and the old before anyone is cut off, give the full dose to the pregnant, the child and the person with no gland. Expect symptoms four to six weeks after the last one. The hypothyroid person dies in winter, so warmth, food, no sedatives and early hard treatment of infection are genuine treatment.

Graves' disease. When the thionamide runs out, thyrotoxicosis returns over weeks. Salvaged iodine buys days to weeks and the patient should be told it will stop working. Rest, cooling, fluids and any salvaged beta-blocker are the rest of the plan.

Addison's disease. Stretch the steroid to the smallest dose that keeps the patient upright and eating, never stopping it. Add salt at once towards 16 to 18 grams a day and increase it with any infection. With residual gland function, liquorice may be added within section 7's limits under blood-pressure watch. In crisis, without hydrocortisone, the district can offer salted fluid, warmth and company.

Anaphylaxis. Write down everyone with a history and keep any salvaged ampoule with them rather than in a central store. Avoidance is the treatment.

Evidence grades

Remedy or practice	For	Grade	Basis
Salvaged insulin, rationed	Type 1 diabetes	A	Standard of care, ME-09 for stability
Allen diet, adults with residual insulin	Type 1	B	Mazur 2011, Joslin, no controls
Allen diet, children	Severe type 1	X	75 to 78 per cent mortality, inanition deaths
Low-carbohydrate adequate-calorie diet	Non-ketotic new adult case	C	Inference from the age gradient [VERIFY]
District manufacture of insulin	Type 1	X	Toronto 1922, Lahore 1958, no assay
Low-energy diet to 15 kg loss	Type 2	A	Lean 2018, 46 against 4 per cent remission
Galega officinalis, aerial parts	Type 2	D, X as a dose	Bailey 2017, Massey toxicology
Salvaged levothyroxine, rationed	Hypothyroidism	A	Standard of care
Desiccated thyroid of known potency	Hypothyroidism	B	1890s record, McAninch and Bianco 2016

Remedy or practice	For	Grade	Basis
Gland of unknown potency	Hypothyroidism	D, named harm	1890s overdoses, Hedberg 1987
Lugol's iodine, short term	Thyrotoxicosis	B	Plummer 1923, Kopp 2023
Iodine as long-term sole therapy	Graves'	C, escape	Okamura 2014, Kohn 1976
Thyroidectomy at a district	Graves'	X	Pre-iodine mortality 4 to 20 per cent
Salt, 16 to 18 g a day	Addison's	B	Loeb 1933, Evans 1943, DOCA sparing
Liquorice root as adjunct	Partial adrenal insufficiency	C	Borst 1953, van Uum 2005
Liquorice alone	Complete adrenal failure	D	Needs cortisol to act [VERIFY]
Crude adrenal extract, injected	Addison's, anaphylaxis	X	Adams 1903, Evans 1943
Supine with legs raised	Anaphylaxis	B	Pumphrey 2003
Intravenous fluid bolus	Anaphylaxis	B	Resuscitation Council UK 2021
Antihistamines, steroids	Anaphylaxis	D	No randomised trial, Cochrane
Ephedra as adrenaline substitute	Anaphylaxis	X by absence	No evidence found
Posterior pituitary extract	Bleeding after birth	X at a district	Unseparable pressor fraction
Dicoumarol from spoiled Melilotus	Anticoagulation	X	Uncontrollable, delayed

Means ledger

Rung	Diabetes	Thyroid	Adrenal	Anaphylaxis
Hands and knowledge	Recognise ketoacidosis, name the prognosis	Recognise myxoedema, keep warm, no sedatives	Recognise crisis, lie flat, legs up	Lie flat, never upright
Hearth	Salted and sweetened fluids, low-carbohydrate meals	Warmth, food, early care of infection	Salt in every meal, more when ill	Keep the reactor from the trigger
Garden and still	Nothing for type 1, diet for type 2	Nothing reliable	Liquorice as adjunct, pressure watched	Nothing that works in 5 minutes
Village dispensary	Ration insulin, test urine, sick-day rules	Ration levothyroxine, halve mild doses	Ration steroid, stock salt, crisis plan	Ampoules with the named patients

Rung	Diabetes	Thyroid	Adrenal	Anaphylaxis
District infirmary	Cool store, register, triage. Cannot make insulin	Could prepare gland, cannot assay it, so should not	Intravenous saline. Cannot make steroid	Intravenous fluid, airway care
Pre-Fall hospital	Insulin, blood gases, intensive care	Levothyroxine, TSH assay, intensive care	Hydrocortisone, fludrocortisone	Adrenaline, airway, intensive care

What each rung changes. Hands to hearth buys comfort and a little time. Hearth to garden changes the outcome only for the adrenal patient. Garden to dispensary brings rationing, the biggest lever in this report, because a stock divided by evidence of need rather than by chance saves more lives than any preparation a district could attempt. Dispensary to infirmary brings intravenous fluid, which saves adrenal crises and some anaphylaxis and does nothing for type 1 diabetes. The ceiling of the district rung is that it can stretch, allocate, rehydrate and keep warm, and cannot manufacture any of these four hormones to a dose.

Harm test

Salvaged insulin. The error that kills is a dose without food, or a fresh strong lot after a weak one, which ME-09 names the fresh-stock overdose (THRIVING library, ME-09). Hypoglycaemia is sweating, trembling, hunger, confusion, aggression, then fit and coma, and it kills faster than hyperglycaemia. Treat with 15 to 20 grams of fast sugar, rechecked at 15 minutes and repeated (American Diabetes Association 2025, read, and Cochrane CD013283, abstract read, which found oral glucose better than buccal at 20 minutes on very low certainty evidence). Never put sugar in the mouth of an unconscious person, who will aspirate it.

Thyroid of uncertain potency. The error kills slowly. Weeks of over-replacement give palpitations, weight loss, tremor and insomnia, then atrial fibrillation, bone loss and at the extreme storm, and it kills the old and the cardiac. There is no safe titration without a blood test, and even slow stepping by pulse and weight produced the decades of over-replacement McAninch and Bianco document.

Iodine in thyrotoxicosis. Without a plan it buys weeks and then worsens things through escape, and before a thionamide in storm it can worsen the storm. Jod-Basedow is a real risk of any mass iodine programme where goitre is common.

Salt loading. Diarrhoea at high doses, and oedema or heart failure in anyone with a heart or kidney problem. Evans's weight rule, a sudden 5 pound or total 10 pound gain, is the monitor and needs only a scale.

Liquorice. Harm at or below 100 milligrams of glycyrrhizin a day in sensitive people and reliably at 4 milligrams per kilogram per day over eight weeks. Never for the hypertensive, the person on a diuretic or digoxin, anyone with heart or kidney disease, or the pregnant. No household measure by volume is safe.

Galega. Pulmonary oedema and death in sheep after 18 to 24 hours, with no treatment. **Adrenaline.** Overdose or intravenous use gives hypertensive crisis, pulmonary oedema and arrhythmia. **Mouldy sweet clover.** Delayed fatal haemorrhage in stock at injury, surgery or calving.

Red flags

1. A thin, thirsty child or young adult passing large volumes of urine, vomiting, breathing deeply, with sweet breath and falling consciousness. Ketoacidosis, fatal without insulin.
2. A diabetic sweating, confused or fitting. Hypoglycaemia, reversible in minutes with sugar. Act before you think.

3. A hypothyroid person cold to the touch, slow, swollen and drowsy, especially in winter or after infection or a sedative. Myxoedema coma kills a third even in hospital. Warm slowly, treat the infection, give nothing sedating.
4. A thyrotoxic person with fever, racing or irregular pulse, agitation or confusion. Thyroid storm. Cool, hydrate, use any beta-blocker.
5. Anyone known to have Addison's disease, or on long-term steroid, who is vomiting, collapsed, confused or shocked. Adrenal crisis. Salted fluid by mouth or vein, flat, warm. Most die without hydrocortisone.
6. Anyone sat or stood up during a severe allergic reaction. People have died in seconds from that movement. Lie them flat with the legs raised.
7. A swollen tongue, a hoarse voice or a whistling intake of breath after a sting, bite or food. The airway is closing and there are minutes.
8. New darkening of the skin with weakness, weight loss and faintness on standing in someone off their steroid. The crisis is coming. Start salt now.
9. A hypothyroid or Addisonian woman who is pregnant. Both untreated harm the pregnancy, and both go to the front of the rationing queue.
10. Any bleeding animal after exposure to mouldy sweet clover hay. Remove the hay from the whole herd at once.

The case against

Against the pre-insulin diet. Mazur is the clearest critic of the received story: no controls, benefit confounded by age and severity, four deaths from starvation in one series. Any account presenting the Allen diet as a survivable alternative to insulin is contradicted by the primary numbers.

Against home manufacture of insulin. Banting and Best, with a university laboratory, could not reliably produce a potent extract, Collip could not reproduce his own result for two months in 1922, and a patient died in the gap, while Rahmat-Ullah and colleagues, with a slaughterhouse city, an animal house and a bioassay, concluded the enterprise was not worth starting. If those two could not do it, a district cannot.

Against desiccated thyroid. McAninch and Bianco's history is the case against, and the NHS Specialist Pharmacy Service puts the modern version plainly: unlicensed, a higher risk of thyrotoxicosis than levothyroxine, and long-term risks of osteoporosis and arrhythmia. The deeper objection is the assay, because four of ten pharmacopeia-compliant samples were markedly off potency while meeting the iodine specification.

Against liquorice. The SKLM and BfR assessments agree that the margin is narrow and that content varies wildly. Beside that, my mechanistic objection stands: without cortisol there is nothing to potentiate.

Against the adjuncts in anaphylaxis. The Cochrane reviewers found no randomised evidence at all, and Pumphrey shows that many patients die even with adrenaline, which is the argument for prevention rather than a cupboard of substitutes.

Against the romance of the hospital. Insulin, levothyroxine and hydrocortisone are irreplaceable and this report says so repeatedly. But salt is not a poor relation of deoxycorticosterone, it does most of the same work, and diet is not a poor relation of metformin, it outperforms it for remission. The district's leverage is real. It is simply not where the romance puts it.

10-line summary

1. Insulin cannot be made at a district, and the men who discovered it could not reliably make it for four months.
2. Without insulin, type 1 diabetes kills in days to weeks in a child and months to a couple of years in a mild adult case.
3. Allen's diet roughly halved early mortality in children at the cost of starvation and did not avert death.

4. Type 2 diabetes remits in 46 per cent of patients on a low-energy diet with 15 kilograms of weight loss, with no drug at all.
5. Thyroid hormone works by mouth and survives drying, but unassayed gland cannot be dosed and the iodine test does not predict potency.
6. Thyroid over-replacement was routine for most of the twentieth century until a blood test existed, and it causes fibrillation and fractures.
7. Iodine controls thyrotoxicosis within days and escapes within weeks, so it buys time and is not a cure.
8. In Addison's disease, salt at 16 to 18 grams a day does much of the hormone's work and is the cheapest high-value intervention here.
9. Liquorice works by letting the body's own cortisol reach the mineralocorticoid receptor, so it helps partial failure and barely touches complete failure.
10. In anaphylaxis without an ampoule, lie the patient flat and give fluid. Antihistamines, steroids and ephedra are not substitutes.

Open questions

- The true untreated survival of myxoedema and of Graves' disease before 1891 and before 1922. No quantified figure found, and the book should not invent one.
- The time from stopping hydrocortisone to adrenal crisis. Every protocol warns against abrupt withdrawal and none gives a distribution of times.
- Whether a dried gland preparation could be titrated safely by pulse, weight and symptoms over months. The historical answer appears to be no, but it was never tested against a modern standard.
- The hypoglycaemia death rate in the first year of insulin. Banting, Campbell and Fletcher reported 50 patients treated by December 1922 and I could not reach the text on hypoglycaemic incidents.
- Whether liquorice has any measurable benefit in complete adrenal failure. The mechanism says no and the direct evidence is in 1951 to 1953 papers I could not read in full.
- The current state of the Open Insulin Project beyond a lab-scale claim with yield unresolved.

Sources to read in full

1. Mazur 2011, Nutrition Journal, on the Allen diet and its primary series.
2. Evans, Flink and Hoilund 1943, on Addison's disease. Pre-cortisone practice with doses, mortality and patient instructions.
3. Rahmat-Ullah, Ahmed and Ahmad 1958, on the insulin content of slaughterhouse pancreas.
4. McAninch and Bianco 2016, Annals of Internal Medicine, on the history of treating hypothyroidism.
5. Kopp 2023, Thyroid, on a century of iodine in Graves' disease.
6. van Uum 2005, Netherlands Journal of Medicine, on liquorice and hypertension.
7. Portuese and Orchard 1995, Diabetes in America chapter 10, for mortality across the Naunyn, Allen and insulin eras.
8. Resuscitation Council UK 2021 anaphylaxis guideline with its evidence-to-decision tables.
9. Bliss 1982, The Discovery of Insulin. Named in the brief, not obtained.

At the bedside after the Fall

A household needs salt, sugar or honey, clean water, a blanket, a way to keep a vial cool, and a written list of who takes what and how much is left. The skill is recognising four things: the thirsty vomiting diabetic breathing deeply, the sweating confused diabetic who needs sugar now, the cold swollen slow hypothyroid person in winter, and the collapsed vomiting person who takes steroids. The first failure to expect is that someone stops a drug abruptly, to save it or because it ran out uncounted, and is in crisis within days.

A village of 300 needs a register of every person on insulin, thyroid hormone, steroid or an adrenaline pen, with dose and stock, kept by one named person. It needs salt in quantity, a scale, and urine testing for sugar and ketones if strips survive. It needs the sick-day rules taught to every family: more fluid and more salt in any illness for the Addisonian, more fluid and never stop the insulin for the diabetic. The first failure to expect is that stock will be shared by sympathy rather than by clock.

A district of 3,000 needs the registers combined, a cool store, a written allocation policy agreed before it is needed, and intravenous fluid with needles and the skill to use them, which turns adrenal crisis and some anaphylaxis from fatal into survivable. What it should not build is an attempt to manufacture insulin, thyroid or adrenal extract, which the record says will consume the district's effort and produce something that cannot be dosed. The first failure to expect at this rung is exactly that attempt, launched with good intentions after the first child dies.

Protocols

A. Counting down a hormone stock. 1. On day one count every unit or tablet in the village, including partial vials. 2. Divide by the daily dose in use, write the end date on the register and tell the patient. 3. Reduce only where evidence allows: never insulin in type 1, never steroid in Addison's, levothyroxine only in mild cases and the old. 4. Review monthly and add anyone newly found. 5. Store insulin cool by ME-09's methods and levothyroxine airtight and dry.

B. Hypoglycaemia in a conscious person. 1. Give 15 to 20 grams of fast sugar, about one level tablespoon of sugar or honey. 2. Wait 15 minutes. If still sweating, shaking or confused, repeat once. 3. When recovered, give a meal with starch and protein. 4. If no recovery after two doses, keep them warm, on their side, and treat as serious illness. 5. Never put sugar into the mouth of an unconscious person. Smear it inside the cheek with them on their side and pour nothing in.

C. The diabetic sick day, while insulin lasts. 1. Never stop insulin because the patient is not eating. 2. About a cupful of fluid every hour, alternating salted and sweet. 3. Test urine for ketones four times a day if strips exist. 4. Vomiting with deep breathing and drowsiness means ketoacidosis. Tell the district at once.

D. Adrenal insufficiency, daily and sick day. 1. Daily, cook with salt and add 9 to 12 grams more across the day, towards about 16 to 18 grams total, by measured spoon and not by pinch. 2. Weigh weekly. A sudden 5 pound or total 10 pound gain means too much, so reduce. 3. At any fever, vomiting, diarrhoea or injury, increase fluid and salt at once. 4. If steroid remains, never stop it abruptly and never miss a dose during illness. 5. In crisis, lie flat with legs raised, give salted fluid by mouth or by vein, keep warm.

E. Liquorice root as an adjunct, partial adrenal insufficiency only. 1. Exclude everyone who must not have it: hypertension, heart or kidney disease, low potassium, diuretics, digoxin, pregnancy, under 18. 2. Use the European monograph strength as a ceiling, 1.5 grams of root in 150 millilitres of water as an infusion twice a day, for no more than four weeks. 3. Measure blood pressure before starting and weekly. Stop at a systolic rise above about 10 millimetres of mercury, any swelling, weight gain or muscle weakness. 4. Give potassium-rich food throughout and stop at once for cramps or weakness. 5. Remember it does little or nothing if there is no adrenal function at all.

F. Anaphylaxis without adrenaline. 1. Lie the patient flat at once and raise the legs. Do not sit them up, stand them up or walk them anywhere, even if they ask. 2. If breathing makes lying flat impossible, keep them as low as they can tolerate. 3. Remove the trigger if it is still present, such as a sting. 4. Give fluid into a vein if the district can, 500 to 1,000 millilitres in an adult, as fast as it runs. 5. Protect the airway by position, on the side if unconscious, and be ready to breathe for them. 6. Use salvaged adrenaline if there is any, 0.5 milligrams into the outer thigh muscle for an adult, 0.3 for 6 to 12 years, 0.15 for 6 months to 6 years, repeated after 5 minutes without improvement. 7. Do not rely on antihistamines or steroids to save a life. 8. Watch at least 6 hours, because a quarter of those resuscitated die later.

G. Iodine for thyrotoxicosis, if it is all there is. 1. Decide in advance what happens when it stops working, because it will within weeks. 2. Give it only to someone genuinely thyrotoxic, not to a goitre alone. 3. In storm, give any thionamide first and iodine at least an hour later, never the reverse. 4. Cool, hydrate, and rest the patient in a dark quiet room. 5. Stop and reconsider if they worsen after the first week, which may be escape or Jod-Basedow.

Numbers to carry

1. **Six hours.** From stopping insulin to ketosis and a glucose of 17 millimoles per litre in a resting adult.
2. **Three quarters.** The proportion of children under 10 dead within a few years even on the best pre-insulin diet.
3. **Fifteen grams of sugar, fifteen minutes.** The dose and the recheck for hypoglycaemia.
4. **Fifteen kilograms.** The weight loss that puts 86 per cent of type 2 diabetics in remission.
5. **Four weeks.** From the last levothyroxine tablet to biochemical hypothyroidism.
6. **Sixty milligrams to one hundred micrograms.** One grain of desiccated thyroid against its levothyroxine equivalent, with published conversions differing by about an eighth.
7. **Sixteen to eighteen grams of salt a day.** The Addisonian regimen before cortisone, and the difference between needing 3 milligrams of deoxycorticosterone and needing 30.
8. **Forty-three, thirty, nine.** Yearly per cent mortality in Addison's disease before therapy, on salt and extracts, and on deoxycorticosterone.
9. **One hundred milligrams of glycyrrhizin a day.** The regular upper limit for liquorice, below which sensitive people still react.
10. **Five, fifteen, thirty minutes.** Median time to arrest in fatal anaphylaxis from drugs, venom and food. Lie them flat.

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