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Local Anesthetics┼　(Department of Pharmacology Zhang Yan-mei ! &┐┌┌
Introduction┼　t┌Local anesthetics: Local anesthetics act by blocking both sensory and motor nerve conduction to produce a temporary loss of sensation without a loss of consciousness. Unlike general anesthetics, they normally do not cause central nervous system (CNS) depression. General anesthetics act on the CNS or autonomic nervous system to produce analgesia, amnesia, or hypnosis.
f¶┼Z　″ Zm　″ Z¶ └　€　€　€　'┘┐┐┌　Mechanism of action┼　Local anesthetics slow the propagation of nerve impulses by reducing the rate of rise of action potential and the rate of repolarization. The increased threshold for electrical excitability results in a complete block of conduction. Local anesthetics specifically block nerve conduction by interfering with cell membrane permeability to sodium, particularly voltage-dependent Na+ channnel. P ″　″ €　€　€　,
{♬┌└　7┘┐♬┌　Mechanism of action┼　c. Its action is use-dependence. Reasons: -----anaesthetic molecules gain access to the channel more readily when the channels is open. -----anaesthetic molecules have higher affinity for inactivated than for resting channels.　4┌1 ┌└T ┌└K　(┐└┌　Mechanism of action┼　(2) A differential sensitivity of nerve fibers to local anesthetics has been identified and characterized. The smallest unmyelinated fibers, which conduct impulses for pain, temperature, and autonomic activity, conduct slowly and are the first to be blocked by local anesthetics. Critical length is the exposure time required by an anesthetic in order for it to exert its action; smaller nerve fibers have a proportionally smaller critical length. 2k┌U┌ ″ k┐└U┌┘┐€　x

┌└<┌ 0┐ Pharmacokinetics┼ Absorption: Systemic absorption of injected local anesthetic from the site of administration is modified by several factors, including dosage, site of injection, drug-tissue binding, the presence of vasoconstricting substances, and the physiochemical properities of the drug. Distribution: be related with tissue perfusion, liposolubility, and pH. Excretion: first-order kinetics, t is constant. R └ └ ;┐└ └ (┐└ > $ ┌└>♬┌└< 1┐◘┌ Therapeutic uses┼ [┌Surface anaesthesia: nose, mouth, bronchial tree (usually in spray form), cornea, urinary tract. Not effective for skin.. (2) Infiltration: direct injection into tissues to reach nerve branches and terminals. Used in minor surgery. Adrenaline often added as vasoconstrictors (not with fingers or toes, for fear of causing ischaemic tissue damage) .{ ″ P ″ ₱₩┌└ ,◘ ┌└O┌ ┌└┼ 2┐ ┌ Therapeutic uses┼ (3) Conduction anaesthesia (nerve-block anaesthesia): Local anaesthetics is injected close to nerve trunks (e.g. branchial plexus, intercostal or dental nerves), to produce a loss of sensation peripherally. Used for surgery, dentistry.
r┌✲ ┌└♬ ┌└ ┌└) ┌└ ┌└^┌ 8┐✲┌ Therapeutic uses┼ (4) Subarachnoidal anaesthesia (spinal anaesthesia): LA injected into the subarachnoid space, to act on spinal roots and spinal cord. Used for surgery to abdomen, pelvis or leg. Main risks are respiratory depression and hypotension. `┌|♬┌└┌ ┌└ ┌└↑ ┌└ 9┐┼┌ Therapeutic uses┼ (5) Epidural anaesthesia: LA injected into epidural space, blocking spinal roots. Used for spinal anaesthesia, also for painless childbirth. 4 <┌♬ ┌└J ┌└!┌) ┘┐┘┌ Adverse effects┼ A┌(1) Central nervous system: ---- At low doses, they include sleepiness, light-headedness, visual and auditory disturbances, and restlessness. ----At higher concentration, nystagmus and muscular twitching may occur. Finally, overt tonic-clonic convulsions followed by central nervous system depression and death may occur. B┌┌B┌┐└ , 8 ┌└P ,┘┐|┌ Adverse effects┼ (2) Respiratory and cardiovascular system: ---- Respiratory failure secondary to CNS depression is a late stage of intoxication. ----Hypotension is a late effect that can occur as the result of myocardial depression, and perpheral arterial vasodilation and automic nerves. > .┘┐ ┌ Adverse effects┼ h(3) Allergic reactions: Include allergic dermatitis, urticaria, hypotension, tachycardia and arrhythmia. i┌i 5 ┌└+ 4┐ ┌ Procaine┼ Pharmacokinetics: ----It is well absorbed following parenteral administration and is rapidly metabolized by pseudocholinesterase. It has short duration of action (30-45 min). ----The metabolic product of procaine hydrolysis is PABA, which inhibits the action of sulfonamides. ,4 ┌└.¶┌└ :┐◀┌ Procaine┼ \Therapeutic uses: -----It can be used in all kinds of anesthesia except surface anaesthesia.]┌↕┘ 赳 P ┌└┐ ;┐↕┌ Procaine┼ Adverse effects: CNS---restlessness, shivering, anxiety, occasionally convulsions followed by respiratory depression. CVS--- bradycardia and decreased cardiac output, vasodilation. Allergic reactions. 4◘ ┌└▼ ┌└╢┌ 3┐ ┌ Lidocaine Pharmacokinetics: It is rapidly absorbed after parenteral administration and is metabolized in the liver by microsomal mixed-function oxidases. & P‼ $ $ F5 ┌└3 ┌└┼◘┌└┐┌ =┐‼┌ Lidocaine Pharmacologic effects: ----Rapid onset of anesthesia. ----Minimal local irritation. ----A greater potency and longer duration of action than procaine. ----Moderate topical activity. . P┤ $ $ >┐┴┌ Lidocaine Therapeutic uses: It be used widely for local anesthetic, and intravenously, as an antiarrhythmic agent. Its duration of action is 1.5 h. Adverse effects: as procaine, but less tendency to cause CNS effects. > P↕ $ $‼ $ 7┐$ ″X♬┌└x┌ 5┐ ┌ Tetracaine Pharmacokinetics: ----It is approximately 10 times more potent (more toxic) than procaine. ----Its onset of action is approximately 1-3 min, and its duration of action is between 2 and 3 h. $ Z‼ $?┐┬┌ Tetracaine >┌Therapeutic uses: -----A 2% solution is used topically on mucous membranes. ----- Tetracaine hydrochloride is a commonly used local anesthetic for spinal anesthesia and , in this context, usually is combined with 10% dextrose to increase the specific gravity so that the solution is heavier than cerebrospinal fluid. $?┌┌┼Z↕ $ -┌ S ┌└ 6┐ ┌ Bupivacaine Pharmacokinetics: ----It is more potent and has a longer duration of action than other LA, lasting for more than 24 h in some situations, possibly as a result of increased tissue binding. @┐┼┌ Bupivacaine Therapeutic uses: -----It can be used in infiltration anaesthesia, conduction anaesthesia, and epidural anaesthesia. Adverse

effects: -----As lidocaine, but greater cardiotoxicity. 4 2 j6 ┌└ ┌└✡ ┌└
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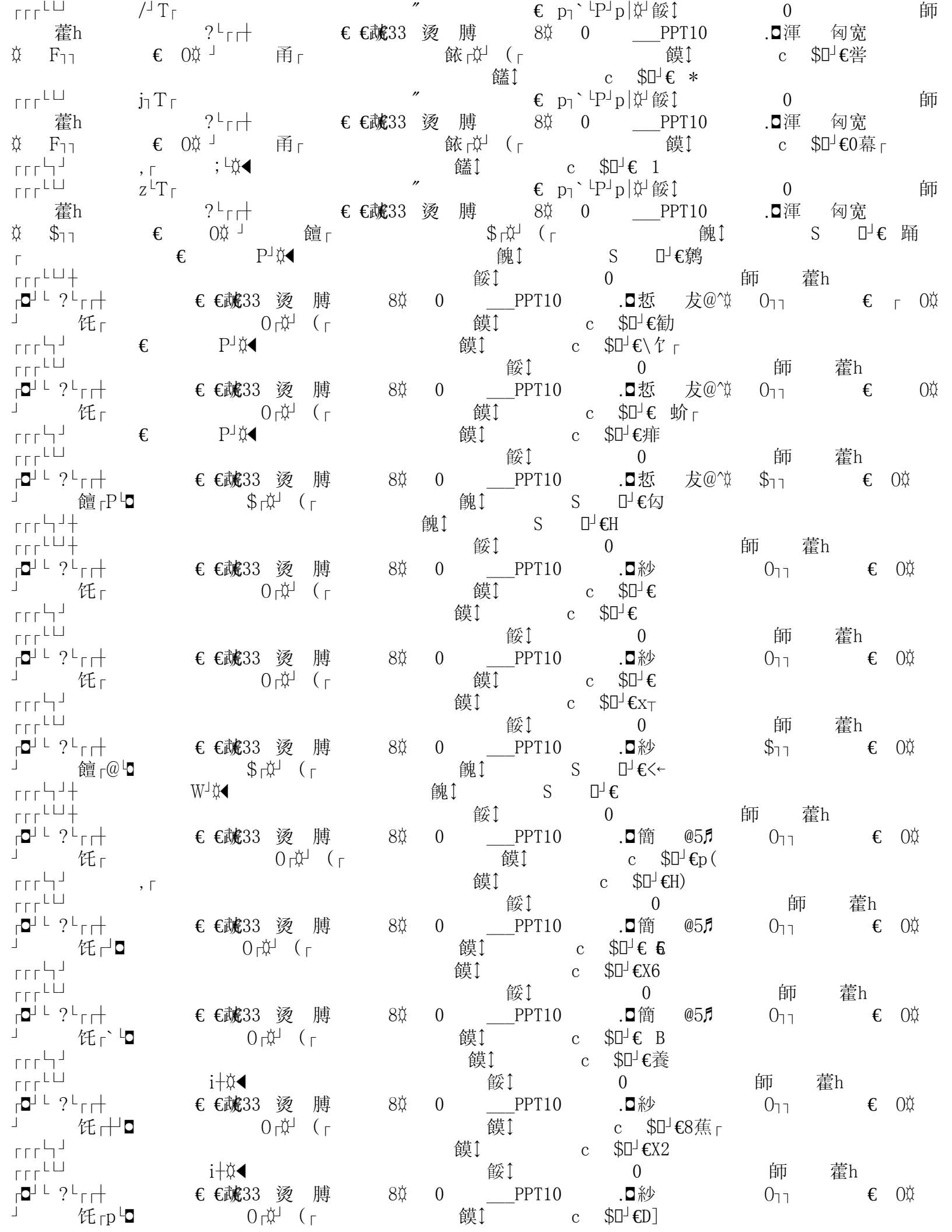

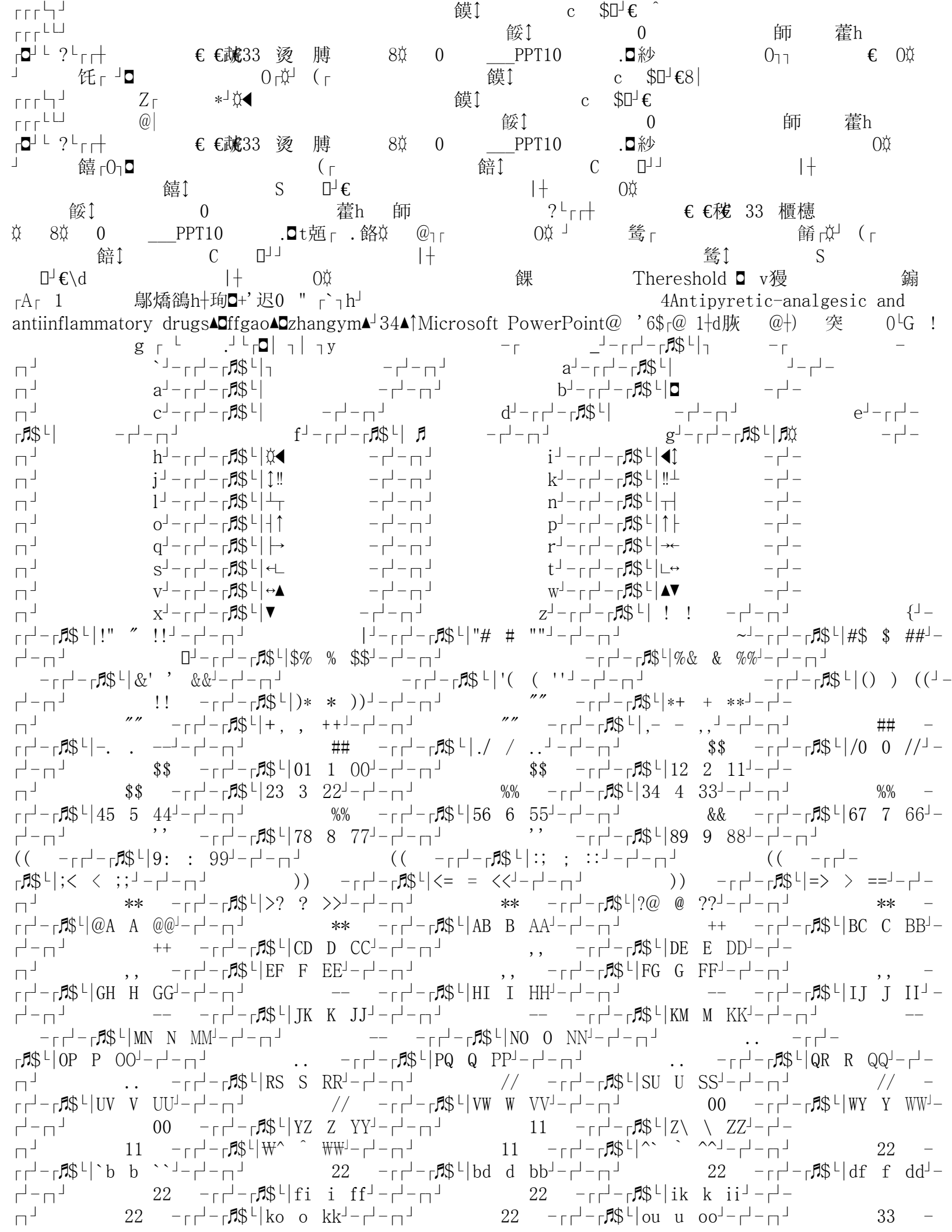

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