International Journal of Psychology and Health Science (IJPHS)
GREENATION Publisher
+62 813 8765 4578 http://greenpub.org editor@greenpub.org Jl. Kapt. A. Hasan, Telanaipura Jambi - Indonesia.
DOI: https://doi.org/10.38035/ijphs.v2i2
Received: May 30th, 2024, **Revised:** June 17th, 2024, **Publish:** June 30th, 2024
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Diagnosis and Management of Pneumocystis Carinii Pneumonia (PCP) in HIV Patients at Klungkung Regional Hospital

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Abstract: Pneumocystis carinii pneumonia (PCP) is an opportunistic infection caused by the fungus Pneumocystis jerovecii. This condition generally occurs in immunocompromised patients, especially in HIV patients, if not treated optimally, it can be life threatening. This infection is the most common opportunistic infection in HIV patients, especially in patients with CD4 cells less than 200 cells/ul. The following is a case of PCP in HIV infection at the Klungkung Regional Hospital. **Case Report:** Patient AMA, 52 years old came with the main complaints of shortness of breath, cough since 1 week, and fever. On examination the patient was conscious (E4V5M6) and appeared moderately ill. Blood pressure 130/80 mmHg, pulse rate 106x/minute. Respiratory rate 24x/minute, axillary temperature 37^0C with oxygen saturation 95% with oxygen 4 lpm nasal cannula. On physical examination, rhonchi were found in the right and left paracardia. Routine blood examination found Hb 9.2g/dL, WBC 12.62 thousand/, hematocrit 26.3%, platelets 272 thousand/µL. Liver function examination SGOT 80 U/L, SGPT 74 U/L, urea 23mg/dL, creatinine 0.3mg/dL, NT-Pro BNP 4102 pg/mL, HIV test results showed reactive, IGRA negative. Microbiological examination of the sputum showed positive results for yeast cells and gram-negative bacilli. Chest x-ray examination revealed cardiomegaly with a CTR of 60%, showing pulmonary congestion and a pneumonic infiltrate. Thorax CT scan with results showing bronchitis accompanied by pneumonia and specific process, there is a picture of minimal bilateral pleural effusion, cardiomegaly with pulmonary congestion. The patient was given IVFD infusion therapy of NaCl 0.9% 12 tpm, omeprazole 2x40mg, ondancetron 3x4mg nystatin drop 100.00 units 4x1mL, curcuma 2x1, cotrimoxazole 3x 2 forte tablets. N-acetylcystein 3x200mg fluconazole 1x200mg IV, levofloxacin 1x750mg IV, ceftriaxone 1x2gr, nebulizer with a combination of ipratropium bromide 0.5ng and salbutamol 2.5mg every 8 hour, hydrocortisone 2x100mg IV, furosemide 3x20mg IV, spironolactone 1x50mg PO ivabradine 2x 5mg PO. **Discussion:** Adhesion pneumonsitis in the alveoli is a host inflammatory response that can cause significant damage to the lungs and

impaired gas exchange, causing hypoxia and respiratory failure. The definitive diagnosis of PCP is finding the organism in sputum histopathology originating from induction or BAL (Bronchoalveolar Lavage). Even though the patient's symptoms and clinical symptoms were not carried out, it was highly suggestive of PCP, this patient was diagnosed with PCP and given oral or intravenous Trimetroprim-sulfamethoxazole (TMX-SMX) therapy for 21 days to manage PCP. **Conclusion:** A PCP in HIV case infection in a 52 year old woman at Klungkung Regional Hospital has been reported. The patient was given co-trimoxazole therapy for 21 days as well as treatment for CHF.

Keywords: HIV, Cotrimosazole, PCP

INTRODUCTION

Pneumocystis carinii pneumonia (PCP) or better known as Pneumocystis jirovecii pneumonia is an opportunistic infection caused by the fungus Pneumocystis jerovecii. This condition generally occurs in immunocompromised patients and in some cases can be life threatening. Patients at high risk of experiencing this condition are patients with immune disorders, cancer, HIV, transplant recipients and patients taking immunosuppressive drugs. This infection is the most common opportunistic infection in HIV patients, especially in patients with CD4 cells less than 200 cells/ul.[1,2]

Pneumocystis is generally found in the lungs of healthy people, but can be a source of opportunistic infections as a cause of lung infections in immunocompromised individuals, especially in people with HIV and AIDS. Currently, HIV management is at an advanced stage, so that the incidence of PCP can be reduced compared to when there were no ARVs. In addition, before the discovery of PCP prophylaxis, PCP was the main cause of patient morbidity and mortality. However, PCP is still a complication that causes high morbidity and mortality. Where the PCP mortality rate reaches 10-20% in the initial infection and will increase along with the need for mechanical ventilation.

Currently, HIV and AIDS cases in Indonesia are a major problem in the health sector. The incidence of AIDS sufferers continues to increase, especially in the productive age range 25-49 years (65.5%) along with an increase in the death rate. From January to March 2023, 13,279 new HIV positive cases were found from 1,230,023 patients who were examined, and 10,924 patients or 82% had received ARVs. Death of AIDS sufferers is generally caused by complications of opportunistic infections and one of them is PCP.

Before the use of PCP and ARV prophylaxis, PCP occurred in 70-80% of patients with AIDS. It is estimated that 90% of PCP cases occur in patients with CD4<200 cells/mm3. Other factors that increase the risk of developing PCP are a CD4 cell percentage <14%, a history of previous PCP, oral candidiasis, a history of bacterial pneumonia, and weight loss.

At the beginning of the AIDS epidemic, PCP was a comorbidity that occurred in 67% of HIV and AIDS sufferers in America. Even before appropriate treatment was developed, PCP was the main cause of death for HIV and AIDS patients. Most new cases occur in patients who do not know their HIV status and are not receiving ARV therapy.

The diagnosis of PCP is very difficult because the symptoms, laboratory tests, and chest radiography are not pathognomonic for PCP. Even though there are these obstacles, detection of PCP cases as early as possible must still be done so that they can be treated immediately and prevent mortality.

METHOD

Patient with the initials AMA, aged 52 years came to the ER at Klungkung Regional Hospital on June 7 2024 with the main complaint of shortness of breath. She had shortness of breath for a week and have been getting worse since the morning. Previously, she felt shortness of breath with every heavy activity, but since this morning the shortness of breath has gotten worse and appears without activity. The patient also complained of coughing since 1 week, the cough was getting worse since morning with a cough with phlegm and sometimes producing yellow phlegm. The patient also complained of fever since morning and measured 38.1^0C and the patient had taken paracetamol twice at 09.00 am and 18.00. The patient complained of pain in the epigastrial area like being stabbed accompanied by nausea, vomiting was denied but the patient's eating and drinking was reduced. Previous history of systemic disease was denied, history of taking routine medications and drug allergies were also denied.

At the examination the patient was conscious with the Glasgow Coma Scale (GCS) E4V5M6 and appeared moderately ill. Blood pressure is 130/80 mmHg, with a regular pulse rate of 106x/minute. The patient's respiratory rate was 24x/minute, with rapid breathing, axillary temperature of 37^0C with oxygen saturation of 95% with 4 liters of oxygen per minute nasal cannula. On physical examination, rhonchi were found in both lung fields, particulary in the right and left paracardia.

On a routine blood test, the results showed Hb 9.2g/dL (N: 10.8-16.5 g/dL), WBC 12.62 thousand/µL (N: 3.5-10 thousand/µL) hematocrit 26, 3% (N: 35-55%) platelets 272 thousand/µL (N: 145-450 thousand/µL). On liver function examination, SGOT was found to be 80 U/L (N: 8-37 U/L) SGPT 74 U/L (N: 13-42 U/L). On kidney function examination, urea was 23mg/dL (N: 10-50mg/dL) and creatinine was 0.3mg/dL (N: 0.6-1.2mg/dL). Random blood sugar examination (GDS) 156mg/dL (N: 80-200mg/dL). NT-Pro BNP results showed 4102 pg/mL (N: 0-100 pg/mL). The HIV test results were reactive and an IGRA examination was carried out and the results were negative. On electrolyte examination, the results showed Na 143 mmol/L (N: 135-145mmol/L) K 3.7 mmol/L (N: 3.5-4.5mmol/L) and Cl 105 mmol/L (N: 95- 105mmol/L). Blood gas analysis results showed pH 7.45 (N: 7.35-7.5) PCO2 35.9mmHg (N: 35-45mmHg) HCO3- 24.7 mmol/L (N: 22-26 mmol/L) BE (B) 0.2mmol/L (N: (-2)-(+2)mmol/L) is impressively normal.

Microbiological examination of sputum using gram staining showed positive results for yeast cells and gram negative bacilli. The results of a chest X-ray examination showed cardiomegaly with a CTR of 60%, showing a picture of pulmonary congestion and a pneumonic infiltrate. The patient also had a CT scan of the thorax with the results showing bronchitis accompanied by pneumonia and specific process, there was a picture of minimal bilateral pleural effusion, cardiomegaly with pulmonary congestion.

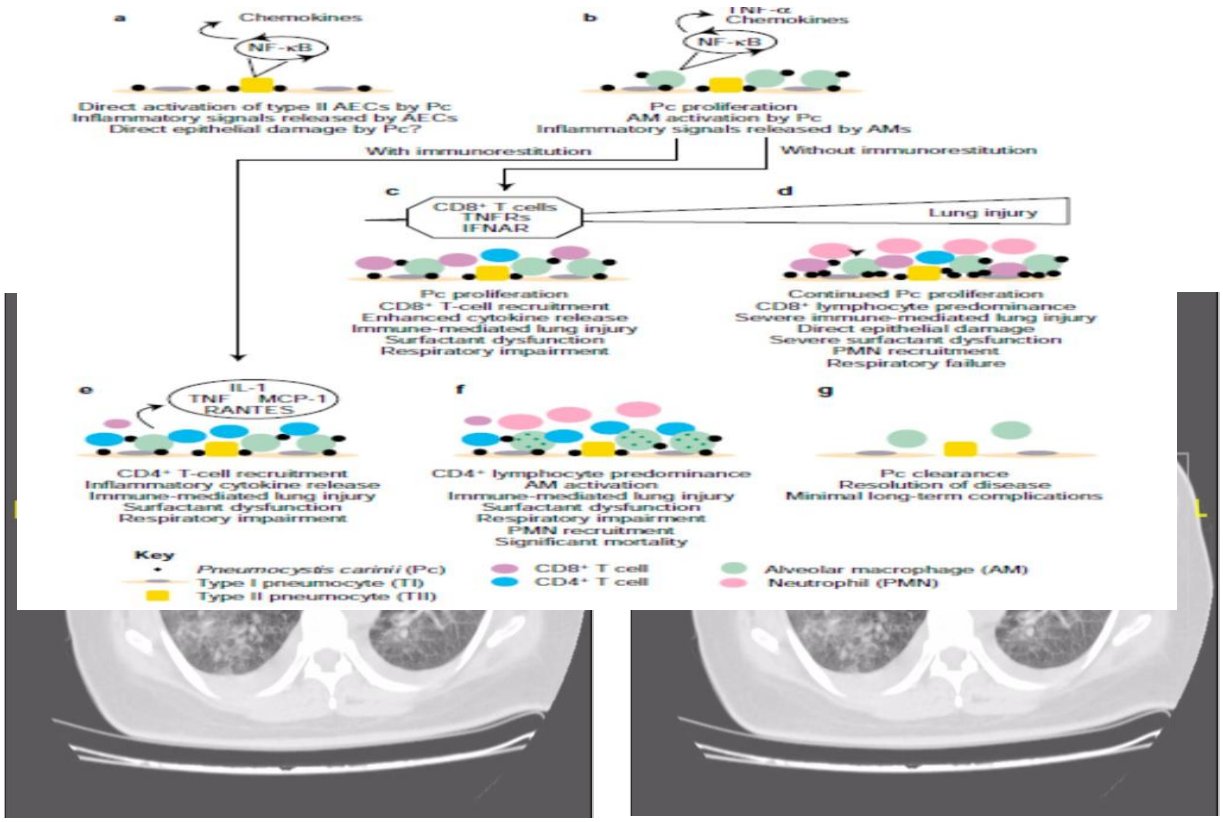
From the results of the history, physical examination and supported by supporting examinations, the patient was diagnosed with HIV positive PCP accompanied by congestive heart failure (CHF) with functional class III and mild anemia with normocytic hypochromic.

The patient was given IVFD infusion therapy of NaCl 0.9% 12 dpm, omeprazole 2x40mg, ondancetron 3x4mg nystatin drop 100.00 units 4x1mL, curcuma 2x1, cotrimoxazole 3x 2 forte tablets. N-acetylcystein 3x200mg fluconazole 1x200mg IV, levofloxacin 1x750mg IV, ceftriaxone 1x2gr, nebulizer with a combination of ipratropium bromide 0.5ng and salbutamol 2.5mg every hour, prednisone 2x40mg oral, furosemide 3x20mg IV, spironolactone 1x50mg oral ivabradine 2x5mg oral.

Picture 1. Radiology Result

RESULT AND DISCUSSION

PCP is a life-threatening fungal infection that generally occurs in immunocompromised patients. Transmission of PCP can occur via droplets from person to person or direct contact through cysts as an infective form in humans. Transmission can also occur in utero from mother to baby during birth, with trophozoites as the infective form. The incubation period ranges from



20-30 days with an attack time of 1-4 weeks.

This microorganism is an extracellular pathogen. The lungs are the primary site of infection. P. jiroveci is found in alveolar capillaries, interstitial intraveolar septum, and epithelial cells. Pneumonsitis adhesion to the alveoli is not the cause of alveolar damage, but this condition is a host inflammatory response that can cause significant damage to the lungs and impaired gas exchange, causing hypoxia and respiratory failure. In some conditions Pneumocystis is able to spread to extrapulmonary locations, such as liver, spleen, lymph nodes and bone marrow.

In the patient's vital signs, blood pressure was found to be within normal limits with an increased temperature since morning and an increased respiratory rate. The patient also complained of shortness of breath, so when she arrived she was given oxygenation and the measured saturation was 95% with a 4 lpm nasal cannula. The clinical symptoms of PCP including the classic triad, which are fever that is not too high, shortness of breath especially during activity and cough without phlegm. PCP symptoms can vary from being asymptomatic in 7% to causing severe symptoms. The progression of symptoms is usually slow, taking weeks or even months. T **Picture 2. Immunologycal Respon on PCP Infection** e, in immunodeficiency patients, the percentage of death can reach 100%.

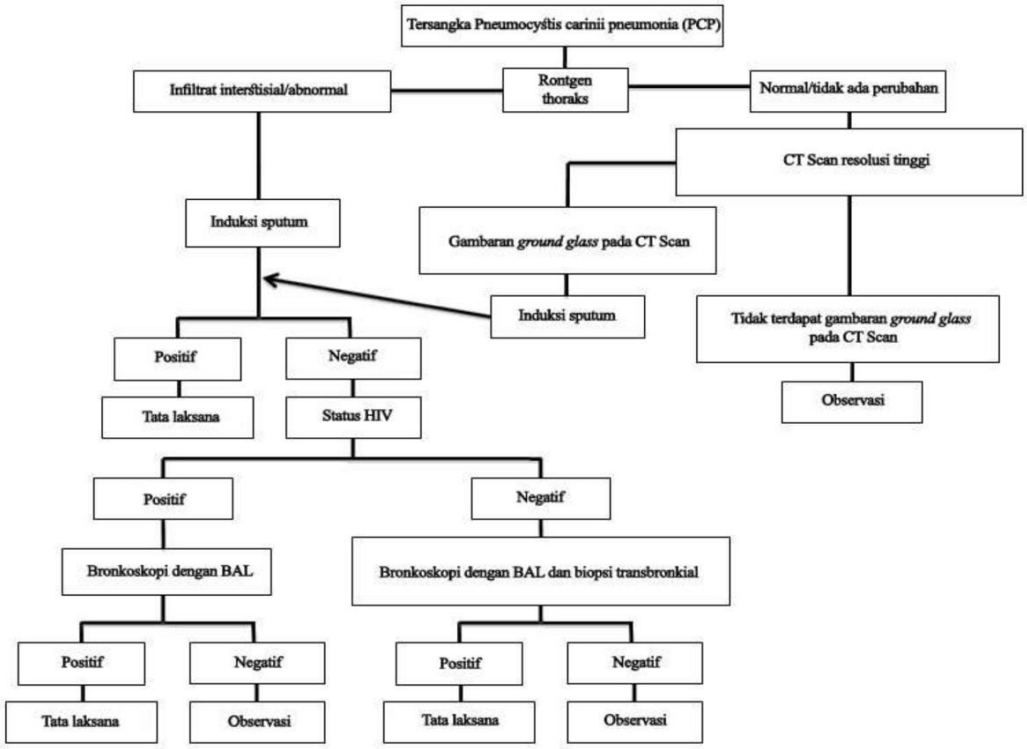
Physical examination for PCP is also non-specific, the patient found oral candidiasis which leads to an immunocompromised condition and is often referred to as a co-infection condition. Apart from that, in PCP you will find symptoms of lung disease such as rhonchi which in this patient are found in the cardial and paraphyllary right and left lungs on auscultation, but 50% of PCP patients will have normal lung sounds on auscultation.

Laboratory examination was carried out, Hb showed mild anemia (9.2 g/dL) with increased leukocytes. Anemia in HIV patients can occur due to two possibilities, the first one is activation of pro-apoptotic genes (due to a decrease in CD4 and an increase in the number of monocytes) and the second one caused by administration of zidovudine, as an antiretrovirus. For this patient, because the anemia was mild and had not received ARV therapy, it was suspected that decreased CD4 levels were the cause of the anemia. Leukocytosis (12.62 thousand/µL) in the patient is believed to be the result of bacterial pneumonia which also occurred in the patient, where this was proven by culture results which showed a slight development of gram-negative bacilli.

The transaminitis that occurred in the patient was suspected to be caused by nonalcoholic fatty liver disease (NAFLD). NAFLD is fat deposition in hepatocytes or steatosis in patients who have no history of alcohol consumption or little alcohol consumption. This condition can occur in patients due to imbalances in energy intake and use, disorders of lipid metabolism in the liver and adipocyte disorders. The prevalence of NAFLD in HIV is reported to continue to increase, especially in patients with HIV-HCV co-infection, reaching 40-69%. However, recent research also states that the condition of NAFLD without co-infection shows high prevalence (31%). In this patient, HBsAg and Anti-HCV examination was also carried out, the results were non-reactive, an abdominal ultrasound examination was also carried out and the results were hepatomegaly.

Because the patient also complained of shortness of breath during activity and the thorax x-ray and thorax CT scan showed cardiomegaly and pulmonary edema. The patient underwent an NT pro BNP examination and found an increase (4102 pg/mL). Heart failure is a

complex clinical syndrome that occurs due to abnormalities in the structure and/or function of the heart. The most common etiology of heart failure is dilated cardiomyopathy, both secondary and primary. In dilated cardiomyopathy there will be enlargement of one or both ventricles and decreased systolic function. The etiology of dilated cardiomyopathy in HIV patients remains uncertain. Some hypotheses of pathogenesis include myocarditis (direct HIV infection, opportunistic infection or viral infection), autoimmune response to viral infection, drug-induced



mitochondrial damage and nutritional deficiencies.

The patient also underwent an IGRA examination to exclude pulmonary TB and the results were negative. TB and HIV co-infection occurs when an HIV patient suffers from either active or latent TB infection. People who are HIV positive have a 30 times higher risk of TB compared to people who are HIV negative. Both TB and HIV infections will speed up the deterioration process. HIV infection will speed up the process from latent TB to active TB, while TB bacterial infection will worsen the condition of HIV patients.

Radiological examination can also help establish a diagnosis of PCP apart from being based on symptoms, physical examination and laboratories. CT scan of the thorax is a sensitive examination for PCP to support the results of chest x-ray although sometimes the radiological images in PCP patients are non-specific and pathognomonic. Where the patient found a picture of consolidation in the right and left lungs accompanied by an air bronchogram and a picture of bilateral pleural effusion. CT scan images generally show ground glass shadowing and consolidation. The ground-glass appearance is more dominant in the parahiler area. In more advanced conditions, septal lines will be found with or without intralobular lines superimposed

on the ground-glass appearance and consolidation. Other features that can be found are pulmonary nodules, pneumothorax and the presence of cavities.[1,14]

The definitive diagnosis of PCP is finding the organism in sputum histopathology originating from induction or BAL (Bronchoalveolar Lavage). However, BAL was not performed on this patient because the patient refused so no histopathological samples were obtained. However, because untreated PCP can be fatal and the patient's clinical and symptoms were highly suggestive of PCP, this patient was diagnosed with PCP and treated with PCP. [1]

Administration of Trimetroprim-sulfamethoxazole (TMX-SMX) both orally and intravenously for 21 days is a therapeutic option for PCP with or without HIV. In moderate-severe PCP (PaO2 <70 mmHg) intravenous administration of trimethoprim-sulfamethoxazole is recommended. Meanwhile, oral trimethoprim-sulfamethoxazole therapy is given for mild-moderate PCP (PaO2 ≥70 mmHg). The recommended dose for PCP therapy is 15-20 mg/kg trimethoprim per day and 75-100 mg/kg sulfamethoxazole per day divided into three or four doses. In PCP patients with HIV, the response to therapy generally occurs more slowly. In this patient, after the diagnosis of PCP was confirmed, cotrimoxazole was then given, equivalent to a dose of trimethoprim 15 mg/kgBW divided into 3 doses so that this patient received cotrimoxazole 3x2 tab forte (960mg).

The patient was also given bacterial pneumonia therapy. Levofloxacin 1x750 and ceftriaxone 1x2gr. This therapy is based on PNPK for treating pneumonia where beta lactams and floroquinolones are given. The patient was also given fluconazole and nystatin therapy for oral treatment of thrush. To treat CHF, the patient was given furosemide 3x20mg IV therapy, spironolactone 1x50mg oral, ivabradine 2x5mg oral. Ivabradin is a drug in the hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers class. The mechanism of ivabradine is to inhibit or block ion flow in the If channel. Thus reducing the slow depolarization phase of the action potential. This causes a decrease in heart rate. Furosemide therapy is given to treat congestive conditions in patients where furosemide will work as a diuretic by inhibiting sodium and chloride reabsorption in the ascending loop of Henle and in the proximal and distal renal tubules, thereby causing a natriuretic effect. Spironolactone is a class of MRA (Mineralocorticoid receptor antagonist) which functions to inhibit the secretion of aldosterone from its receptor in the renal tubules. This drug reduces sodium and water reabsorption, and inhibits potassium excretion in the distal tubule and collecting duct of the kidney.

The patient was also given hydrocortisone 2x100 mg IV therapy. The use of corticosteroids in PCP patients is as an anti-inflammatory therapy and to reduce lung injury. This therapy is based on research that found neutrophils and neutrophil products in the bronchoalveolar lavage (BAL) fluid of patients with severe PCP. Neutrophils are associated with poor outcome. Neutrophils are important mediators in Respiratory Distress Syndrome (RDS). Steroids will reduce neutrophil migration to sites of inflammation and reduce the activity of neutrophils and macrophages. Corticosteroids also interfere with the release and action of many inflammatory mediators such as neutrophil chemotactic factor, IL-8, arachidonic acid metabolism, platelet-activating factor and tumor necrosis factor.[18]

Steroid administration is especially used in patients with moderate and severe PCP. Steroids given simultaneously with PCP therapy will reduce mortality and the incidence of respiratory failure in patients. The recommended regimen on days one to five is oral prednisone 40mg twice daily. On days six to ten, oral prednisone is given 40 mg once a day and on days

eleven to twenty-one, it is given 20 mg once a day. If intravenous methyl is given, the dose is 75% of the prednisone dose.[18]

The severity of infection and high mortality of PCP patients make prevention very important in groups at risk. Trimetroprim-sulfamethoxazole is the main choice for primary and secondary prophylaxis besides dapsone, atovaquone and pentamidine. HIV patients are advised to receive PCP chemoprophylaxis if the CD4 count is less than 200 cells/µl or there is a history of oral candidiasis. Chemoprophylaxis is recommended to be given for life but can be stopped in patients who have undergone ARV therapy and CD4 becomes > 200 cells/ul for 3 months but can be given again if CD4 < 200 cells/ul.

CONCLUSION

A 52 year old female patient reported experiencing PCP due to HIV infection accompanied by CHF. The patient was given co-trimoxazole therapy for 21 days as well as treatment for CHF. Although the patient cannot make a definitive diagnosis, because the history, physical examination and supporting examinations are suggestive of PCP, the patient is given PCP therapy. This is done because if HIV infection is not treated with PCP, it will cause emergencies and significant complications.

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